

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

**FORM 10-K**

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2022

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 001-36544

**Sage Therapeutics, Inc.**

(Exact Name of Registrant as Specified in its Charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

215 First Street  
Cambridge, Massachusetts  
(Address of Principal Executive Offices)

27-4486580  
(I.R.S. Employer  
Identification No.)

02142  
(Zip Code)

(617) 299-8380

(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	SAGE	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes  No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	<input checked="" type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging Growth Company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the Registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant as of June 30, 2022 was approximately \$1,685,744,591, computed by reference to the closing price of the registrant's common stock on the Nasdaq Global Market reported for such date.

As of February 8, 2023, there were 59,717,608 shares of common stock, \$0.0001 par value per share, outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Part III of this Annual Report on Form 10-K incorporates by reference certain information from the registrant's definitive Proxy Statement for its 2023 annual meeting of shareholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year end of December 31, 2022. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as part of this Form 10-K.

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## Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve risks and uncertainties. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may”, “will”, “should”, “expects”, “intends”, “plans”, “anticipates”, “believes”, “estimates”, “predicts”, “potential”, “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our views as to the potential for approval by the U.S. Food and Drug Administration, or FDA of our new drug application, or NDA, for zuranolone (SAGE-217) as a treatment for major depressive disorder, or MDD, and postpartum depression, or PPD; our belief in the adequacy of the data we submitted in support of our NDA for zuranolone; the expected review timelines of such NDA; and the potential for future launch and commercialization of zuranolone in MDD and/or PPD, and the potential timing of such activities, if our NDA is approved;
  - our views as to the potential for zuranolone for the treatment of MDD and PPD, if approved, including the potential product profile and treatment benefit, our commercialization strategy, plans, and expectations and the potential for zuranolone to be developed in additional indications;
  - our plans for the development of our other product candidates for the treatment of brain health diseases and disorders, and potentially for other indications; our plans with respect to other research and development activities; and expected timelines for our planned activities;
  - our ability, within the expected time frames, to initiate clinical trials and non-clinical studies of existing or future product candidates, including pivotal clinical trials, and to successfully complete and announce the results of ongoing or future clinical trials;
  - our belief as to potential outcomes of our clinical development and commercialization activities;
  - our views as to potential future results of our ongoing commercialization efforts in the U.S. with respect to ZULRESSO® (brexanolone) CIV injection, which is approved in the U.S. for the treatment of postpartum depression, or PPD, in adults;
  - our plans and potential outcomes with respect to interactions with regulatory authorities;
  - our plans for and the potential costs, benefits and outcomes of our existing collaborations with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, and Shionogi & Co., Ltd., or Shionogi, and our plans for and potential outcomes of any additional business development efforts;
  - our plans and expectations with respect to the potential development of any product or product candidate for markets outside the U.S.;
  - our expectations and estimates regarding: the level of expenses we may incur in connection with our activities; use of cash and projected cash on hand at any given timepoint; timing of future cash needs; capital requirements; sources of future financings; timing of receipt of potential milestone payments; and our ability to obtain additional financing when needed to fund future operations;
  - our expectations with respect to the availability of supplies of ZULRESSO or of zuranolone and our other product candidates, and the expected performance of our third-party manufacturers, including conformity with applicable regulatory requirements;
  - our ability to obtain and maintain intellectual property protection for our proprietary assets and other forms of exclusivity relevant to our business;
  - the estimated number of patients with diseases or disorders of interest to us and the potential size of the market for ZULRESSO in PPD, for zuranolone in MDD and PPD, if approved, and for our other product candidates in the indications we are pursuing or plan to study;
  - the potential for our current product and current or future product candidates, if successfully developed and approved, for the indications and in the markets for which they are approved and our ability to serve those markets;
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- the potential for success of competing products that are or become available for PPD or MDD or any of the other indications that we are pursuing or may pursue in the future with our products and our product candidates;
- the impact of changes to the macroeconomic environment on our activities, business and results of operations, and the potential success of our efforts to address or mitigate such impact; and
- other risks and uncertainties, including those listed under Part I, Item 1A, Risk Factors.

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our business and future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part I, Item 1A, Risk Factors and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

We may from time to time provide estimates, projections and other information concerning, among other things, our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information we provide in this Annual Report. Unless otherwise expressly stated, we obtained this industry and business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties; industry, medical and general publications; government data; and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

### **Summary of Risks Related to our Business**

Our business, prospects, financial condition, and operating results are subject to numerous risks and uncertainties that you should be aware of before making an investment decision, as more fully described under Part I, Item 1A, Risk Factors and elsewhere in this Annual Report. These risks may include, but are not limited to, the following:

- Our future business prospects depend heavily on our ability, with our collaborator Biogen, to gain regulatory approval of zuranolone (SAGE-217) for the treatment of adults with MDD and PPD, and to successfully commercialize zuranolone in those indications, if approved. While our NDA for zuranolone is currently under review by the FDA, we cannot be certain that the FDA will grant approval of zuranolone in the indications we are seeking. The FDA may find that the design and results of our development program are not sufficient for regulatory approval of zuranolone for the treatment of MDD and PPD or may decline to approve our NDA for other reasons. Although we have been granted priority review, the FDA may not meet expected review timelines. Even if zuranolone is approved as a treatment for MDD and PPD, we may not be successful in our commercialization efforts. Any setback or delay in obtaining regulatory approval for zuranolone or in our ability to commence marketing of zuranolone, if approved, may have a material adverse effect on our business and prospects.
  - Our future business prospects also depend heavily on our ability to successfully develop and gain regulatory approval of other product candidates beyond zuranolone. We cannot be certain that we or our collaborators, where applicable, will be able to initiate new clinical trials, complete ongoing clinical trials, or announce results of ongoing or future clinical trials of our other product candidates on the timelines we expect or at all, or that the results of our development programs will be positive or sufficient to file for regulatory approval. Decisions or actions of the FDA or other regulatory agencies may adversely affect our plans, progress or results at any stage of development. We cannot be certain that we or our collaborators will be able to successfully file or obtain regulatory approval for, or successfully commercialize, if approved, any such product candidates on the timelines we expect or at all. Any setback or delay in obtaining regulatory approval for any of our product candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.
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- We may never be able to generate meaningful revenues from sales of ZULRESSO® (brexanolone) CIV injection, or revenues at levels or on timing necessary to support our investment and goals.
  - If the affected populations for indications our products and product candidates are targeting, including the addressable markets within such populations, or the number of patients within such markets who are actually treated with our products, including zuranolone, if successfully developed and approved, are smaller than we anticipate, or our other assumptions with respect to the potential markets for our products and product candidates are incorrect, our ability to achieve profits from the commercialization of such products, if approved, at the levels or on the timing we expect could be materially adversely impacted.
  - Positive results from non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates in the same indications or other indications. Interim results from non-clinical studies and clinical trials may not be predictive of results of such non-clinical studies or clinical trials once completed. The results of non-clinical studies or clinical trials of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval.
  - If serious adverse events or other undesirable side effects are identified during the use of any of our marketed products or product candidates, including during commercial use, in clinical trials or under an expanded access program, if initiated for any of our products or product candidates, such events may adversely affect market acceptance or result in other significant negative consequences for an approved product; delay or prevent further development or regulatory approval with respect to product candidates; or cause regulatory authorities to require labeling statements, such as boxed warnings, or a Risk Evaluation and Mitigation Strategy, on approved products.
  - We rely completely on third-party suppliers to manufacture commercial supplies of ZULRESSO and clinical drug supplies for our product candidates and intend to rely on third-party manufacturers for commercial supplies of zuranolone, if approved, and of any of our other product candidates that are successfully developed and approved for marketing. Any impairment of the ability of our third-party suppliers to supply product or to meet applicable regulatory standards may significantly negatively impact our ability to achieve our goals and plans and to meet the expectations for our business.
  - Zuranolone, if approved, and any of our other current product candidates, if successfully developed and approved, and other future products, if any, may not have the profile we expect in clinical practice after launch or may not achieve broad market acceptance for the approved indications, or reimbursement at sufficient levels, and the results of our commercialization efforts may not meet our expectations, which may limit the revenue that we generate from sales of such products.
  - Competing therapies may exist or could emerge that adversely affect the amount of revenue we are able to generate from the sale of ZULRESSO, zuranolone, if approved, or any of our other current or future product candidates, if successfully developed and approved.
  - Our existing collaborations with Biogen and Shionogi, and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, including appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected if any of our collaborators fails to perform its obligations or terminates our collaboration in whole or in part.
  - We may not be successful in our efforts to identify new targets, generate new compounds, and successfully bring such new compounds through investigational new drug application-enabling non-clinical studies. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.
  - If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our products or product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.
  - For certain of our products and product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, or if we are not able to obtain licenses to intellectual property we may determine we need in the future, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved.
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- Existing or future laws, regulations, executive orders or policies aimed at reducing healthcare costs may have a material adverse effect on our business or results of operations.
  - We are subject to healthcare laws and regulations, which could expose us to the risk of criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings if we or our employees are alleged or determined not to have complied with such laws and regulations.
  - We have not generated significant revenue to date. We have incurred significant operating losses since our inception, and anticipate that we will incur losses for the foreseeable future.
  - We may need to raise additional funding in the future, which may not be available on acceptable terms, or at all. Raising additional capital, even opportunistically, may cause dilution to our existing stockholders, restrict our operations or require us to relinquish valuable rights.
  - The changes to the macroeconomic environment, including the healthcare and vendor staffing shortages and disruption to the U.S. healthcare system that began as a result of the COVID-19 pandemic, may continue to adversely impact our business, including our sales of ZULRESSO and our initiation, conduct and completion of clinical trials.
  - The Inflation Reduction Act of 2022 and other existing, pending or future federal and state reforms aimed at reducing healthcare costs, including pricing and reimbursement of pharmaceutical products, may in the future result in reduced reimbursement and access for our approved products or cause us to curtail certain development plans because of concerns about commercial viability, any of which could adversely affect our ability to commercialize our products and generate revenue and negatively impact our business, results of operations and financial condition.
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*All brand names or trademarks appearing in this report are the property of their respective owners. Unless the context requires otherwise, references in this report to "Sage," the "Company," "we," "us," and "our" refer to Sage Therapeutics, Inc. and its subsidiaries.*

## Item 1. Business

### Overview

We are a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. We are currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry. Our focus as a company is on brain health, and we are currently targeting two critical central nervous system, or CNS, receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of GABA<sub>A</sub> receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders.

Our first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. for the treatment of postpartum depression, or PPD, in adults. We launched ZULRESSO commercially in the U.S. for the treatment of PPD in June 2019. ZULRESSO may only be administered in qualified medically-supervised healthcare settings. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of GABA<sub>A</sub> receptors.

We also are developing a portfolio of other novel compounds that target GABA<sub>A</sub> receptors including our most advanced product candidate, zuranolone (SAGE-217). Zuranolone is a novel oral compound being developed for the treatment of major depressive disorder, or MDD, and PPD. In December 2022, we, and our collaboration partner, Biogen, completed submission of a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, seeking approval of zuranolone for the treatment of both MDD and PPD. The NDA was accepted for filing and granted priority review by the FDA in February 2023, with a Prescription Drug User Fee Act, as amended, or PDUFA, target action date of August 5, 2023. The FDA granted Fast Track designation to zuranolone for the treatment of PPD in early 2022 and previously granted zuranolone Breakthrough Therapy designation and Fast Track designation for the treatment of MDD. Zuranolone is a neuroactive steroid that, like brexanolone, is a positive allosteric modulator of GABA<sub>A</sub> receptors, targeting both synaptic and extrasynaptic GABA<sub>A</sub> receptors. We may in the future develop zuranolone for other affective disorders.

To date, we have completed six pivotal clinical trials of zuranolone, four in MDD and two in PPD. The completed pivotal trials evaluating zuranolone for the treatment of PPD and three of the four completed pivotal trials evaluating zuranolone for the treatment of MDD met their primary endpoints.

We are jointly developing zuranolone and another of our late-stage compounds, SAGE-324, in the U.S. with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, under a collaboration and license agreement, or the Biogen Collaboration Agreement, that became effective in December 2020.

Under the Biogen Collaboration Agreement, we will also jointly commercialize products containing zuranolone, which we refer to as Licensed 217 Products, and products containing SAGE-324, which we refer to as Licensed 324 Products, with Biogen in the U.S. if our development efforts are successful. We refer to the Licensed 217 Products and Licensed 324 Products individually as a Product Class and collectively as the Licensed Products. In addition, we have granted Biogen sole rights to develop and commercialize the Licensed Products outside the U.S., other than in Japan, Taiwan and South Korea, or the Shionogi Territory, with respect to zuranolone, where we have granted rights to Shionogi & Co., Ltd., or Shionogi. We refer to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the Biogen Territory.

We also have a collaboration agreement with Shionogi for the development of zuranolone in the Shionogi Territory. In September 2021, Shionogi reported completion of a Phase 2 clinical trial of zuranolone for the treatment of patients

with moderate to severe MDD in Japan, which Shionogi reported achieved its primary endpoints. Shionogi has also reported that it is conducting two Phase 3 trials of zuranolone for the treatment of patients with moderate to severe MDD as a monotherapy and as an add-on to other antidepressants, and announced that, pending results from these trials, it is aiming to submit an NDA to the Pharmaceuticals and Medical Devices Agency in Japan in the first quarter of 2024 seeking approval of zuranolone for the treatment of MDD.

SAGE-324 is a novel GABA<sub>A</sub> receptor positive allosteric modulator intended for chronic oral dosing. We are currently enrolling patients with essential tremor in a Phase 2b placebo-controlled dose-ranging clinical trial of SAGE-324, known as the KINETIC 2 Study. In May 2022, we also initiated an open-label Phase 2 clinical trial designed to evaluate the long-term safety and tolerability of SAGE-324 in patients with essential tremor, with incidence of treatment-emergent adverse events as the primary endpoint. This is intended to be a multi-year clinical trial, and will initially be open to rollover patients from other SAGE-324 clinical trials in patients with essential tremor, including the KINETIC 2 Study. We believe SAGE-324 also has potential for the treatment of a number of other neurological conditions, including epilepsy and Parkinson's disease. Additional development plans for SAGE-324 will be determined as part of our strategic collaboration with Biogen.

Our second area of focus for development is novel compounds that target the NMDA receptor. Our lead product candidate selected in this area is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition-related disorders associated with NMDA receptor dysfunction, including cognition dysfunction associated with diseases such as Huntington's disease, Parkinson's disease and Alzheimer's disease. The FDA has granted SAGE-718 Fast Track designation as a potential treatment for patients with Huntington's disease. SAGE-718 is currently being studied in several ongoing clinical trials, including the placebo-controlled Phase 2 DIMENSION Study, the placebo-controlled Phase 2 SURVEYOR Study, and the Phase 3 open-label PURVIEW Study evaluating patients with Huntington's disease cognitive impairment; the double-blind placebo-controlled Phase 2 PRECEDENT Study evaluating SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease; and the randomized placebo-controlled Phase 2 LIGHTWAVE Study evaluating SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease.

We have other programs at earlier stages of development with a focus on both acute and chronic brain health disorders. We expect to continue our work on allosteric modulation of the GABA<sub>A</sub> and NMDA receptor systems in the brain. The GABA<sub>A</sub> and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future. We also believe that we may have the opportunity to use our scientific approach to explore targets beyond the GABA<sub>A</sub> and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health.

## **Our Strategy**

Our goal is to build a top-tier biopharmaceutical company that is the leader in developing and commercializing life-changing brain health medicines. Our current focus is on building on our opportunities in depression, neurology, and neuropsychiatry. Key elements of our strategy are to:

- gain regulatory approval of zuranolone for the treatment of PPD and MDD in the U.S., continue permitted pre-launch and launch-readiness activities for zuranolone, launch and commercialize zuranolone, if approved, and potentially advance development of zuranolone in additional indications, all as part of our strategic collaboration with Biogen;
- continue our commercialization efforts with respect to ZULRESSO for the treatment of PPD in the U.S., with a primary focus in geographies that have existing, active ZULRESSO treating sites;
- complete the ongoing and planned clinical trials of SAGE-324 as part of our strategic collaboration with Biogen;
- complete ongoing and planned clinical trials of SAGE-718;



- support our collaboration with Biogen with respect to zuranolone and SAGE-324 in the U.S., and support Biogen's development of zuranolone and SAGE-324 in the Biogen Territory and Shionogi's development of zuranolone in the Shionogi Territory;
- advance our earlier-stage compounds;
- continue our research and development efforts to evaluate the potential for our existing product candidates for the treatment of additional indications or in new formulations;
- identify new targets, and generate and test new compounds and product candidates, with a focus on indications where we believe we can make well-informed, rapid go/no-go decisions, with the goal of developing a diversified portfolio of assets with differentiated features;
- prepare and file NDAs with the FDA, and conduct permitted pre-launch activities with respect to any of our other product candidates that we believe have been successfully developed;
- commercialize any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- continue to add personnel at the appropriate time, as our efforts and activities progress, including personnel to support ongoing zuranolone commercialization efforts, such as launch planning, permitted payor engagements, scientific exchange, disease awareness education, and ongoing product development, and to support launch of zuranolone in MDD and PPD, if approved;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone and SAGE-324 in the European Union, or EU, and other jurisdictions outside the U.S., and determine how best to move forward where and when it may make business and strategic sense;
- continue to build, maintain, defend, leverage, and expand our intellectual property portfolio, including by utilizing the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities to lessen our long-term reliance on the success of any one program and to facilitate long-term growth; and
- continue to explore opportunities to establish licenses, collaborations, or other agreements or alliances with other biotechnology and pharmaceutical companies, at the appropriate time, where we believe a collaboration will add significant value to our efforts, including through capabilities, infrastructure, speed or financial contributions, or to acquire new compounds, product candidates or products if we believe such opportunities will help us achieve our goals or meet other strategic objectives.

## Understanding the Foundations of Our Approach

The CNS is composed of a vast and complex network of different structures and cell types, most of which serve, directly or indirectly, to provide a means for the nervous system to signal or communicate with other nerve cells to regulate brain function. The cell type responsible for this signaling is called a neuron. One way chemical or electrical signals exert their effects on neurons is by traveling across a physical gap located between two neurons, called a synapse. Presynaptic neurons transmit signals whereas postsynaptic neurons react to the signals. The human brain contains approximately 86 billion neurons, each having hundreds to tens of thousands of synapses to allow for this communication. This process is essential to all things, from organ function to movement, memory and all behavioral processes. Neurotransmission is the process by which signaling molecules, called neurotransmitters, are released by a presynaptic neuron, travel over the synaptic space and bind to and interact with receptors on a postsynaptic neuron. Depending on the nature of the neurotransmitter and receptor, this interaction results in excitation, inhibition or modulation of the receiving neuron's behavior.

We are currently focused on developing drugs based on selective allosteric modulation of neurotransmitter receptors in the CNS. Allosteric modulators are a class of small molecules that interact at a site different from the site where neurotransmitters bind, and allow the potential for fine-tuning of neuronal signals. We believe that nowhere in the body is it more important to maintain normal rhythms than in the brain, and accordingly we believe that allosteric modulation approaches are well-suited for the treatment of diseases and disorders of the brain.

We utilize our proprietary chemistry capabilities to design and identify drug candidates that target critical CNS proteins and have properties aligned to the indications of interest. Our goal is to select for development compounds that we believe are capable of varying degrees of desired activity rather than complete activation or inhibition.

Our focus as a company is on brain health, and we are currently targeting two critical CNS receptor systems: GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function in part via activation of GABA<sub>A</sub> receptors. GABA<sub>A</sub> receptors play a key role in regulating neuron excitability. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. NMDA receptors serve a critical role in CNS-related activities. Dysfunction in these systems is implicated in a broad range of brain disorders.

Our proprietary chemistry platform is currently centered on our knowledge of the chemical scaffolds of endogenous neuroactive steroids. We have leveraged this platform to assemble a chemistry portfolio of greater than 10,000 compounds. We believe our proprietary chemistry platform allows us to:

- control important properties such as half-life, brain penetration and the types of receptors our drugs act upon, thereby modulating either inhibition or excitation either acutely or chronically; and
- create drugs that are designed to exert control over the intensity of receptor activation or deactivation, with the potential to hit targets in the brain with more precision, with the goal of increased tolerability and fewer off-target side effects than current CNS therapies or previous therapies that have failed in development.

We target diseases and disorders of the brain where we believe patient populations are easily identified, clinical endpoints are well-defined, and development pathways are feasible.

## Our Product Pipeline

The following table summarizes the status of our product and product candidate portfolio as of the filing date of this Annual Report.

COMPOUND	PARTNER	INDICATIONS	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGISTRATION	MARKETED
<b>DEPRESSION</b>								
ZULRESSO® (brexanolone) CIV injection		Postpartum Depression						
Zuranolone (SAGE-217)	Biogen SHIONOGI	Major Depressive Disorder						
		Postpartum Depression						
		Treatment Resistant Depression						
		Generalized Anxiety Disorder						
		Bipolar Depression						
<b>NEUROLOGY</b>								
SAGE-324	Biogen	Essential Tremor						
		Epileptiform Disorders						
		Parkinson's Disease						
SAGE-689		Acute GABA Hypofunction						
<b>NEUROPSYCHIATRY</b>								
SAGE-718		Huntington's Disease Cognitive Dysfunction						
		Parkinson's Disease Cognitive Dysfunction						
		Alzheimer's Disease Mild Cognitive Impairment and Mild Dementia						
<b>EARLY DEVELOPMENT</b>								
SAGE-319		GABA Hypofunction						
SAGE-421		NMDA Hypofunction						

*Light shades indicate trials in the planning or evaluation stage*

### ZULRESSO® (Brexanolone) CIV Injection

Our first product, ZULRESSO, is a proprietary IV formulation of brexanolone. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of GABA<sub>A</sub> receptors. We launched ZULRESSO commercially in the U.S. in June 2019 for the treatment of PPD in adults, after approval by the FDA and completion of controlled substance scheduling of brexanolone by the U.S. Drug Enforcement Administration, or DEA, and incorporation of the scheduling into the FDA-approved label and other product information. The DEA placed ZULRESSO into Schedule IV of the Controlled Substances Act, or CSA. ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO must be administered in a medically-supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategy, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. Patients who are prescribed ZULRESSO are required to enroll in a registry which may allow us to compile additional information to further our understanding of the risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO and management of the risk. Given the mode and setting of administration of ZULRESSO and the requirements of the REMS program, ZULRESSO has been administered to date primarily to treat women with severe PPD, and we expect that to continue to be the case.

PPD is one of the most common medical complications during and after pregnancy, and is characterized by depressive symptoms that may occur during pregnancy or following childbirth up to 12 months. PPD symptoms may include sadness and depressed mood; anxiety or agitation; loss of interest in daily activities; changes in eating and sleeping habits; feeling overwhelmed; fatigue and decreased energy; inability to concentrate; hypervigilance about the baby or lack of interest in the baby; and feelings of worthlessness, shame or guilt. In the U.S., estimates of mothers experiencing symptoms of PPD each year vary state-to-state from 9.7% to 23.5%, with an overall average of 13.2%. Based on these data, we estimate that approximately 500,000 women in the U.S. each year may experience symptoms of PPD, and approximately 28% are formally diagnosed. We estimate that 20% to 30% of women diagnosed with PPD will experience severe symptoms. PPD can lead to devastating consequences for a woman and for her family. Suicide is one of the leading causes of maternal death following childbirth.

ZULRESSO is the only pharmacological therapy specifically approved for PPD. The current standard of care for PPD is comprised of psychotherapy and, in women with moderate or severe PPD, the cautious use of pharmacological therapies such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

Naturally occurring allopregnanolone is found at its highest levels in women during the third trimester of pregnancy, returning to normal levels generally within 24 hours after giving birth. Levels of allopregnanolone have been found to be lower in women with PPD than in healthy women. It may be that women with PPD are particularly sensitive to the rapid decline in allopregnanolone after birth, potentially causing GABA<sub>A</sub>-system mediated mood disruption. These data led to our interest in evaluating allosteric modulators of the GABA<sub>A</sub> receptor—such as brexanolone and zuranolone—for the treatment of PPD.

The approval of ZULRESSO in the U.S. was based on positive results from our HUMMINGBIRD Phase 3 clinical program, which was comprised of two multicenter, randomized, double-blind, parallel-group, placebo-controlled, Phase 3 clinical trials designed to evaluate the safety and effectiveness of brexanolone in women with PPD, with supportive evidence from a Phase 2 clinical trial of brexanolone in PPD. Results from the HUMMINGBIRD Phase 3 clinical program were published in the September 22, 2018 issue of *The Lancet*.

### **Zuranolone (SAGE-217)**

Our most advanced product candidate is zuranolone (SAGE-217), a novel oral compound being developed for the treatment of MDD and PPD. In December 2022, we and our collaboration partner, Biogen, completed submission of an NDA to the FDA seeking approval of zuranolone for the treatment of MDD and PPD. The NDA was accepted for filing and granted priority review by the FDA in February 2023, with a PDUFA target action date of August 5, 2023. Zuranolone is a neuroactive steroid that, like brexanolone, is a positive allosteric modulator of GABA<sub>A</sub> receptors, targeting both synaptic and extrasynaptic GABA<sub>A</sub> receptors. We also believe zuranolone has potential in other indications such as treatment resistant depression, bipolar depression and generalized anxiety disorder. We are jointly developing zuranolone in the U.S. with Biogen under the Biogen Collaboration Agreement that became effective in December 2020, and will jointly commercialize zuranolone in the U.S. if our development efforts are successful and zuranolone is approved in the U.S. The Biogen Collaboration Agreement covers any products incorporating zuranolone. We have granted Biogen sole rights to develop and commercialize the Licensed 217 Products outside the U.S., other than in the Shionogi Territory, where we have granted rights to Shionogi. The FDA granted Fast Track designation to zuranolone for the treatment of PPD in early 2022, and previously granted zuranolone Breakthrough Therapy designation and Fast Track designation to zuranolone for the treatment of MDD.

MDD is a serious mental health disorder commonly characterized by symptoms of depressed mood and/or loss of interest in pleasurable activities causing impairment in daily life. MDD is characterized by a period of depressive symptoms lasting at least two weeks and is associated with changes in affect, cognition, and function. In typical depressive episodes, the person experiences depressed mood, loss of interest and enjoyment, and reduced energy leading to diminished activity for at least two weeks. Many people with MDD also suffer from anxiety symptoms as a symptom of their depression and medically unexplained somatic symptoms. A person with moderate or severe MDD will typically have difficulties carrying out his or her usual work, school, domestic or social activities due to symptoms of depression. Antidepressants are widely used for the treatment of MDD, but many patients do not adequately respond to existing treatments. According to estimates, approximately 21 million adults in the U.S. reported at least one major depressive episode in 2021. Among U.S. adults reporting at least one major depressive episode in 2021, approximately 12.6 million (61%) received treatment within the prior year; and 10.5 million received pharmacologic treatment. Research conducted between April 2020 and December 2022 reported a three- to four-fold increase in symptoms of depression among adults in the U.S. compared to prior to the COVID-19 pandemic. Preclinical and clinical evidence suggest the role of GABA<sub>A</sub> receptor dysfunction in depression. Low GABA and allopregnanolone levels have been found in the brain, cerebrospinal fluid and plasma of depressed patients. In 2018, the incremental economic burden of MDD was an estimated \$326 billion in the U.S.

To date, we have completed six pivotal clinical trials evaluating zuranolone, four in MDD and two in PPD, the results of which have been previously disclosed. The completed pivotal trials evaluating zuranolone for the treatment of PPD and three of the four completed pivotal trials evaluating zuranolone for the treatment of MDD met their primary endpoints. We announced results from the following clinical trials of zuranolone in either 2021 or 2022:

- **SKYLARK Study (completed)**

In June 2022, we announced that the SKYLARK Study, a Phase 3 placebo-controlled clinical trial evaluating a two-week course of zuranolone 50 mg in women with PPD, met its primary and all key secondary endpoints. Women treated with zuranolone 50 mg (n=98) demonstrated a statistically significant and clinically meaningful improvement in depressive symptoms at Day 15, the primary endpoint, and at Days 3, 28, and 45, key secondary endpoints, in each case compared to women treated with placebo (n=97) as measured by a change from baseline in the 17-item Hamilton Rating Scale for Depression, or HAMD-17, total score. The least-squares mean change from baseline (standard error) in HAMD-17 total score at Day 15 for women who received zuranolone 50 mg was -15.6 (0.82) compared with -11.6 (0.82) for women who received placebo (LS mean difference -4.0 points; p=0.0007). Zuranolone 50 mg was generally well-tolerated and demonstrated a safety profile consistent with that observed in prior clinical studies. In women who experienced treatment emergent adverse events, or TEAEs, the majority were mild to moderate in severity. The most common treatment emergent adverse events (>5% in the zuranolone 50 mg arm) were somnolence, dizziness, sedation, headache, diarrhea, nausea, urinary tract infection and COVID-19.

- **CORAL Study (completed)**

In February 2022, we announced results from the CORAL Study, a placebo-controlled Phase 3 clinical trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with a newly administered open-label ADT, compared with open-label standard of care ADT co-initiated with placebo, as an acute rapid response treatment in patients with MDD. Patients in the clinical trial received zuranolone 50 mg co-initiated with an open-label standard of care ADT or open-label standard of care ADT co-initiated with placebo once nightly for 14 days followed by continuation of the ADT for an additional short-term follow-up period. The study results showed a mean change from baseline in the HAMD-17 total score of  $-8.9 \pm 0.39$  (n=210) at Day 3 for patients in the zuranolone co-initiated with ADT arm compared with  $-7.0 \pm 0.38$  (n=215) mean change from baseline for patients in the ADT co-initiated with placebo arm. The key secondary endpoint measured the treatment effect over the two-week treatment period at all scheduled visits (measured using equal weighted means for Days 3, 8, 12 and 15 of the study). The mean change over the treatment period for patients who received zuranolone co-initiated with an ADT was  $-11.7 \pm 0.40$  (n=210) compared with  $-10.1 \pm 0.39$  (n=215) for patients who received ADT co-initiated with placebo. Other secondary endpoints demonstrated a statistically significant reduction in HAMD-17 score in the zuranolone co-initiated with ADT arm compared to the ADT arm at Days 8 and 12, while Day 15 demonstrated numerical superiority and Day 42 showed equivalence. The results also indicate that zuranolone 50 mg co-initiated with a standard of care ADT was generally well-tolerated with no new safety signals identified. The majority of patients in the study experienced TEAEs that were mild or moderate in severity, consistent with previous data. The adverse events occurring 10% or higher in either treatment arm (zuranolone with ADT vs. ADT with placebo) were somnolence (18.4% vs. 8.3%), dizziness (13.2% vs. 7.3%), headache (11.8% vs. 14.7%), and nausea (9.0% vs 23.4%). The percentage of patients reporting TEAEs leading to drug discontinuation was 6.6% in the zuranolone co-initiated with an ADT arm, and 3.7% in the ADT co-initiated with placebo arm, respectively. The percentage of patients reporting TEAEs leading to discontinuation of ADT were 7.5% in the zuranolone co-initiated with an ADT arm, and 5.5% in the ADT co-initiated with placebo arm, respectively.

- **WATERFALL Study (completed)**

In June 2021, we announced that the WATERFALL Study, a pivotal, Phase 3, double-blind, randomized, placebo-controlled clinical trial evaluating the efficacy and safety of zuranolone 50 mg in adults aged 18 to 64 years with MDD, met its primary endpoint. In the WATERFALL Study, zuranolone 50 mg showed a statistically significant and clinically meaningful reduction in depressive symptoms as measured by HAMD-17 total score at Day 15 (p-value=0.0141) compared to placebo. Patients in the zuranolone arm with a

decrease in HAMD-17 baseline score of  $\geq 50\%$  at Day 15 retained on average 86% of their HAMD-17 improvement at Day 42 (four weeks after dosing ended). A rapid onset of treatment effect was seen in the HAMD-17 results at Days 3, 8 and 12. Zuranolone was generally well-tolerated in the WATERFALL Study and demonstrated a safety profile consistent with previous clinical studies. The rate of TEAEs reported in the zuranolone group was 60.1% (161/268) compared to the placebo group at 44.6% (120/269). The majority of the TEAEs reported were mild to moderate. The most common TEAEs that were reported by  $\geq 5\%$  of patients treated with zuranolone (rates compared to placebo) included somnolence 15.3% (3.0%), dizziness 13.8% (2.2%), headache 10.8% (7.8%), and sedation 7.5% (0.4%). These events predominantly occurred during the 14-day treatment period. Throughout the study, a total of four patients reported serious adverse events, two (0.7%) each in the zuranolone and placebo groups; no deaths occurred in the study. The percent of patients reporting TEAEs leading to drug discontinuation was 3.4% (9/268) and 1.5% (4/269), in the zuranolone and placebo groups, respectively.

- **SHORELINE Study (ongoing)**

We are also conducting an open-label Phase 3 clinical trial, known as the SHORELINE Study, evaluating the safety, tolerability, and need for repeat dosing with zuranolone in adults with MDD, in which patients receive an initial two-week course of zuranolone and those who have a clinical response (decrease in HAMD-17 baseline score of  $\geq 50\%$ ) from the first cycle have the opportunity to be followed for up to one year and are eligible to receive as-needed retreatment during the follow-up period. The need for repeated dosing is assessed every 14 days based on the results of a patient-reported Patient Health Questionnaire-9 score ( $\geq 10$ ) and HAMD-17 assessment ( $\geq 20$ ). The protocol of the clinical trial requires a minimum of 56 days between zuranolone 14-day courses, to allow for a maximum of five treatments during the follow-up period.

In December 2021, we reported 12-month data from the 50 mg cohort of the SHORELINE Study. Data reported for this cohort of patients (n=199), showed that a majority of the patients who had a clinical response to the initial 14-day course received only one two-week course of treatment in total during their time in the study and nearly 80% received only one or two treatment courses in total. Specifically, of the 146 patients who had a clinical response to the initial 2-week treatment, 80 (54.8%) patients received only the single initial zuranolone course during their time in the study, while 36 (24.7%) received a total of two course, 15 (10.3%) received a total of three courses, 10 (6.8%) received a total of four courses and 5 (3.4%) received a total of five courses in total. Zuranolone 50 mg was generally well-tolerated with no new safety finding or trend identified in the long-term safety data available to date on patients followed up to one year who received a single or repeat dosing courses. Safety was assessed during treatment and in between treatment courses and over multiple treatment courses to help inform tolerability over time. Over the entire study, 137 of 199 (68.8%) patients who initiated treatment with zuranolone 50 mg reported at least one TEAE, similar to the previously reported 30 mg cohort. The most common TEAEs that were reported by  $\geq 5\%$  of patients treated with zuranolone were somnolence (32; 16.1%), dizziness (30; 15.1%), headache (25; 12.7%), sedation (20; 10.1%), insomnia (14; 7.0%), nausea (13; 6.5%), and tremor (11; 5.5%). The majority of patients reported TEAEs with a maximum severity of mild to moderate.

The data from the 50 mg cohort is consistent with 12-month data we reported in March 2021, from the completed 30 mg cohort of the SHORELINE Study. In the 30 mg zuranolone cohort, approximately 70% of participants with a clinical response to an initial 2-week treatment required at most one additional zuranolone treatment during their time in the 12-month study. Of the 489 patients who responded to the initial 14-day treatment course and continued in the study, 210 (42.9%) patients received only the single initial zuranolone course during their time in the study, while 125 (25.6%) received a total of two courses, 58 (11.9%) received a total of three courses, 53 (10.8%) received a total of four courses, and 43 (8.8%) received a total of five courses. In the 30 mg cohort, 368 (51%) patients reported at least one TEAE. The most common TEAEs that were reported by  $\geq 5\%$  of patients treated with zuranolone were somnolence (86; 11.9%), headache (103; 14.2%), and dizziness (54; 7.4%). Most of the reported TEAEs were mild or moderate.

Enrollment in the 50 mg cohort of the SHORELINE Study has been completed and the study is ongoing.

Shionogi has reported that it is conducting two Phase 3 trials of zuranolone for the treatment of patients with moderate to severe MDD as a monotherapy and as an add-on to other antidepressants, and announced that, pending results from these trials, it is aiming to submit an NDA to the Pharmaceuticals and Medical Devices Agency in Japan in the first quarter of 2024 seeking approval of zuranolone for the treatment of MDD. In September 2021, Shionogi announced that it achieved the primary endpoints from a Phase 2 clinical trial of zuranolone for the treatment of patients with moderate to severe MDD in Japan. The data reported by Shionogi for this Phase 2 study showed significant improvement over placebo from day three (first observation) to day 15 (end of administration) of change in HAMD-17 total score from baseline in a group of 85 patients who received zuranolone 20 mg once daily for two weeks and a group of 82 patients who received 30 mg once daily for two weeks, as compared to 82 patients who received the placebo. Shionogi reported that all adverse events were mild or moderate. Shionogi previously completed a Phase 1 clinical trial in Japan to evaluate the safety and tolerability of zuranolone in Japanese and Caucasian subjects.

We may consider additional development opportunities for zuranolone as part of the Biogen collaboration.

## **SAGE-324**

In addition to zuranolone, we have a portfolio of other novel compounds that target GABA<sub>A</sub> receptors, including SAGE-324, which we are jointly developing with Biogen under the Biogen Collaboration Agreement. SAGE-324 is a novel GABA<sub>A</sub> receptor positive allosteric modulator intended for chronic oral dosing. In April 2021, we and Biogen reported topline results from our placebo-controlled Phase 2 clinical trial evaluating the safety and efficacy of SAGE-324 for the treatment of essential tremor, known as the KINETIC Study. Essential tremor is a neurodegenerative condition characterized by rhythmic trembling most commonly of the upper limbs, including the hands. The head, voice, legs or trunk may also be affected. Symptoms generally evolve over time, are persistent, and affect patients' ability to function independently. Essential tremor is among the most common movement disorders, estimated to affect more than 6 million adults in the U.S. Adults of all ages can be impacted by essential tremor, though risk increases with age. First-line treatments for essential tremor include  $\beta$ -adrenergic blocker propranolol and anticonvulsant primidone.

The Phase 2 KINETIC Study evaluating SAGE-324 for the treatment of adults with essential tremor (n=67 full analysis set) achieved its primary endpoint of a statistically significant reduction from baseline compared to placebo in The Essential Tremor Rating Assessment Scale, or TETRAS, Performance Subscale Item 4 upper limb tremor score on Day 29 (p-value=0.049), which corresponded to a 36% reduction from baseline in upper limb tremor amplitude in patients receiving SAGE-324 compared to a 21% reduction in patients receiving placebo. Patients were randomized 1:1 to receive SAGE-324 (60 mg) or matched placebo once daily in the morning. The trial evaluated treatment of SAGE-324 at the higher end of the dose range and the daily dose could be down-titrated to 45 mg or 30 mg. Activities of daily living, or ADL, scores showed a statistically significant correlation with upper limb tremor score at all timepoints. Although the clinical trial was not powered to fully examine TETRAS ADL, SAGE-324 was numerically superior to placebo at all time points during treatment. Reported TEAEs were generally consistent with the safety profile of SAGE-324 previously reported. The most common TEAEs that were reported by 10% or more of patients in the SAGE-324 treatment group and at a rate at least twice as high as that of patients in the placebo group were: somnolence 68%; dizziness 38%; balance disorder 15%; diplopia 12%; dysarthria 12%; and gait disturbance 12%. In the KINETIC Study, patients with a more severe tremor at baseline (at or above the median TETRAS Performance Subscale upper limb tremor Item 4 score of 12) (n=47) who received SAGE-324 demonstrated a statistically significant reduction (p-value=0.007) from baseline in TETRAS Performance Subscale Item 4 upper limb tremor score compared to placebo at Day 29, corresponding to a 41% reduction from baseline in upper limb tremor amplitude in patients receiving SAGE-324 compared to an 18% reduction for placebo.

A Phase 2b double-blind, randomized, placebo-controlled, dose-response study of SAGE-324 in patients with moderate to severe essential tremor, known as the KINETIC 2 Study, is currently enrolling patients and we expect to complete enrollment in late 2023. The primary aim of the KINETIC 2 Study is to evaluate different doses of SAGE-324 in reducing upper limb tremors. The primary endpoint of the study is change from baseline in TETRAS Performance Subscale Item 4 total score at Day 91. In May 2022, we initiated an open-label Phase 2 clinical trial designed to evaluate the long-term safety and tolerability of SAGE-324 in patients with essential tremor, with incidence of treatment-emergent adverse events as the primary endpoint. This is intended to be a multi-year clinical trial, and will initially be open to rollover patients from other SAGE-324 clinical trials in patients with essential tremor, including the KINETIC 2 Study.

We believe SAGE-324 also has potential for the treatment of a number of other neurological conditions, including epilepsy and Parkinson's disease.

We are jointly developing SAGE-324 in the U.S. with Biogen, and will jointly commercialize Licensed 324 Products with Biogen in the U.S. if our development efforts are successful and SAGE-324 is approved in the U.S. We have granted Biogen sole rights to develop and commercialize SAGE-324 outside the U.S. We may consider additional development plans and opportunities for SAGE-324 as part of our collaboration with Biogen.

## **SAGE-718**

Our second area of focus is the development of novel compounds that target the NMDA receptor. Examples of indications involving NMDA receptor dysfunction include certain types, aspects or subpopulations of a number of diseases such as Huntington's disease, Parkinson's disease, Alzheimer's disease, depression, attention deficit hyperactivity disorder, schizophrenia, and neuropathic pain.

Our lead product candidate selected in this area is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition-related disorders associated with NMDA receptor dysfunction, including cognition dysfunction associated with diseases such as Huntington's disease, Parkinson's disease and Alzheimer's disease.

### ***Huntington's disease***

The FDA has granted SAGE-718 Fast Track designation as a potential treatment for Huntington's disease. SAGE-718 is currently being studied in three ongoing clinical trials in patients with Huntington's disease cognitive impairment:

- **DIMENSION Study**

In February 2022, dosing commenced in the DIMENSION Study, a double-blind placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment. The DIMENSION Study is designed to evaluate the efficacy of once-daily dosed SAGE-718 over three months.

- **SURVEYOR Study**

In March 2022, we initiated the SURVEYOR Study, a placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment, with a healthy volunteer component, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.

- **PURVIEW Study**

In December 2022, we initiated the PURVIEW Study, a Phase 3 open-label study to evaluate the long-term safety and tolerability of SAGE-718 in patients with Huntington's disease cognitive impairment.

### ***Parkinson's disease***

In May 2021, we announced results from the 14-day dosing cohort, or Cohort A, of a Phase 2a open-label clinical trial of SAGE-718 evaluating patients with mild cognitive impairment due to Parkinson's disease, known as the PARADIGM Study. In Cohort A of the clinical trial, eight patients aged 50 to 75 years with mild cognitive impairment due to Parkinson's disease received 3 mg of SAGE-718 daily for 14 days. Patients showed performance improvements from baseline on multiple tests in the cognitive domain of executive function during the 14 days of treatment. Emerging signals on several measures also suggested improved performance from baseline on cognitive tests in the domains of learning and memory over a similar timeframe.

In October 2022, we presented additional results from the 28-day cohort, or Cohort B, of the open-label PARADIGM Study. In Cohort B of the clinical trial, seven patients aged 50 to 75 years with mild cognitive impairment due to Parkinson's disease received 3 mg of SAGE-718 daily for 28 days. Patients showed performance improvements



from baseline on multiple tests in the cognitive domain of executive function during the 28 days of treatment, as well as during the 14 day follow-up period. SAGE-718 was generally well-tolerated in both cohorts of the study; there were no serious adverse events reported, and no TEAEs were determined to be related to SAGE-718 or resulted in study drug discontinuation or withdrawal from the study. As expected, given its profile, SAGE-718 demonstrated neutral results in certain tests of attention and psychomotor speed.

In March 2022, we initiated a double-blind, placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease, known as the PRECEDENT Study. The PRECEDENT Study is designed to evaluate the safety and efficacy of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease over 42 days, followed by a controlled follow-up period.

### *Alzheimer's disease*

In December 2021, we reported topline data from the LUMINARY Study, a Phase 2a open-label clinical trial of SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease (n=26 full analysis set), who received 3 mg of SAGE-718 daily for 14 days. The results showed performance improvements from baseline on five out of five unique tests in the cognitive domain of executive function and two out of four unique tests in the cognitive domains of learning and memory during the 14 days of treatment, consistent with positive signals seen in open-label clinical trials evaluating SAGE-718 as a treatment for cognitive impairment due to Parkinson's disease and Huntington's disease. Patients also showed performance improvement as measured by the Montreal Cognitive Assessment (MoCA) Test, a global measure of cognition, that reached statistical significance at Day 28 when compared to baseline in patients treated with SAGE-718. In certain tests of attention and psychomotor speed, SAGE-718 demonstrated neutral results. SAGE-718 was generally well tolerated in the LUMINARY Study. Seven subjects reported a total of 11 TEAEs, seven of which were considered related to the study treatment and all of which were rated as mild or moderate in severity. The most commonly reported TEAEs were headache (n=2) and constipation (n=2). In December 2022, we initiated the LIGHTWAVE Study, a randomized placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease.

### **Further Exploration of GABA<sub>A</sub> and NMDA Receptors and New Areas of Interest**

We expect to continue to focus our research and development efforts on allosteric modulation of the GABA<sub>A</sub> and NMDA receptor systems in the brain. Our portfolio of novel GABA<sub>A</sub> receptor positive allosteric modulators includes SAGE-689, a product candidate in Phase 1 clinical development intended for intramuscular administration. We also have other compounds at earlier stages of development with a focus on both acute and chronic brain health disorders, including SAGE-319, an extrasynaptic GABA<sub>A</sub> receptor-preferring positive allosteric modulator, which we plan to move into Phase 1 clinical development. SAGE-319 is being evaluated for its potential use as an oral therapy in treating disorders of social interaction. We also have earlier stage compounds focused on NMDA receptor modulation, including SAGE-421, an NMDA receptor positive allosteric modulator that we plan to study for potential use in neurodevelopmental disorders and cognitive recovery and rehabilitation. The GABA<sub>A</sub> and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement among others. We believe that we may have opportunities to develop molecules from our internal portfolio to address a number of these disorders in the future. Our ability to identify and develop such novel brain health therapies is enabled by our proprietary chemistry platform that is centered, as a starting point, on knowledge of the chemical scaffolds of certain endogenous neuroactive steroid compounds. We believe our knowledge of the chemistry and activity of allosteric modulators allows us to efficiently design molecules with different characteristics. This diversity enables us to regulate important properties such as half-life, brain penetration and receptor pharmacology to develop product candidates that have the potential for better selectivity, increased tolerability, and fewer off-target side effects than either current therapies or previous therapies which have failed in development. We believe that we may also have the opportunity to use our scientific approach to explore targets beyond the GABA<sub>A</sub> and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health disorders.

We believe our broad potential pipeline lessens our reliance on the success of any one program. We believe our ability to design and develop novel molecules with distinct profiles and receptor subtype selectivity may also provide us with the option, if we choose, to potentially partner certain assets with third parties who possess the development and commercialization capabilities to pursue these programs, like our strategic collaboration with Biogen. We may also

evaluate opportunities to acquire new compounds, product candidates or products from other companies or from academic institutions if we believe such opportunities will help us achieve our goals or meet other strategic objectives.

## **Manufacturing and Supply**

We neither own nor operate, and currently have no plans to own or operate, any manufacturing facilities. We currently source all of our clinical and non-clinical material supply through third-party contract manufacturing organizations, or CMOs. We have also sourced our existing inventory of our proprietary formulation of ZULRESSO for commercial sale from CMOs, and intend to source all of our future commercial supplies of ZULRESSO and zuranolone and other product candidates, if approved by the FDA, from CMOs.

We have long-term supply agreements with our CMOs with respect to ZULRESSO drug substance and drug product. We have an inventory of ZULRESSO drug substance and drug product in place to help mitigate any potential supply risks. All commercial supplies are intended to be manufactured applying current Good Manufacturing Practices, or cGMP.

We are working closely with our CMOs to prepare for the potential commercialization of zuranolone in the U.S., if approved, and are in the process of completing validation batches for zuranolone. We have a long-term supply agreement with our contract manufacturer for zuranolone drug product. We have established relationships with two CMOs under which the CMOs have agreed to manufacture clinical and commercial supplies of drug substance for zuranolone under master service and quality agreements. We intend to enter into long-term commercial supply agreements with our CMOs for zuranolone drug substance. We believe that, if zuranolone were approved, we will have sufficient zuranolone drug substance and drug product for potential commercial launch later this year.

We have established relationships with CMOs under which the CMOs manufacture clinical and non-clinical supplies of drug substance and drug product for SAGE-324, SAGE-718 and other product candidates on a purchase order basis under master service and quality agreements. All clinical supplies of drug substance and drug product are intended to be manufactured under cGMP. Starting materials and key intermediates to support the production of these product candidates are manufactured by other CMOs. We do not currently have arrangements in place for either long-term supply or redundant supply of drug substance or drug product for SAGE-324 or SAGE-718. We intend to put a long-term supply agreement in place at the appropriate time for drug substance and drug product for our product candidates, if development continues. We plan to mitigate potential commercial supply risks for any products that are approved in the future through inventory management and through exploring additional manufacturers to provide drug substance or drug product. We also intend to improve the manufacturing process for our product candidates and manufacture clinical supplies as development progresses.

ZULRESSO, zuranolone, SAGE-324 and SAGE-718 are small molecules isolated as stable crystalline solids. We believe the syntheses of ZULRESSO, zuranolone, SAGE-324 and SAGE-718 are reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale manufacturing and do not require unusual equipment in the manufacturing process. We expect to continue to identify and develop drug candidates that are amenable to cost-effective manufacturing at contract manufacturing facilities.

## **Sales and Marketing**

Our first product, ZULRESSO, was made commercially available in the U.S. as a treatment for PPD in adults in June 2019. Our revenue from sales of ZULRESSO has been negatively impacted by significant barriers arising from the complex requirements for treatment and by the lasting effects of the COVID-19 pandemic. ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO is approved for administration only in a medically-supervised healthcare setting that has been certified under a REMS program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat women with PPD are complex and time-consuming. These actions include becoming REMS-certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor-by-payor basis under commercial coverage. The availability, terms and timing of coverage for ZULRESSO vary from payor to payor, both for commercially insured patients and from state Medicaid systems, and we have encountered

some states that impose significant coverage restrictions or lengthy delays on reimbursement of ZULRESSO. As a result, certain healthcare settings will not treat Medicaid patients with ZULRESSO even if they are active sites of care for ZULRESSO. These requirements have created significant barriers to treatment for women with PPD. We expect these barriers will continue to negatively impact ZULRESSO revenue growth.

These barriers were compounded by the COVID-19 pandemic and continue to be impacted by related disruptive effects on the U.S. healthcare system and other changes to the macroeconomic environment. The spread of COVID-19 in the U.S. resulted in a significant number of sites of care pausing, limiting or delaying treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe that, at certain points during the pandemic, concerns about exposure to the virus or its variants caused a significant reduction in the number of women with PPD seeking treatment with ZULRESSO and in the number of physicians willing to prescribe it, and that difficulties in accessing treatment with ZULRESSO have since been compounded by healthcare staffing shortages and other changes to the macroeconomic environment. Given the ongoing disruption to the healthcare system in the U.S., including as a result of staffing shortages, we cannot predict for how long and to what extent ZULRESSO sales will be adversely impacted by these factors.

Our ZULRESSO commercial operations, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach to our commercial efforts will continue to substantially limit the revenue opportunity for ZULRESSO. Given the limited focus of our commercial efforts, the number of new healthcare settings that become treating sites for ZULRESSO may be very limited. We may also find that certain healthcare settings that have in the past been active treating sites may not be willing to remain infusion-ready as a result of the complex requirements related to administration of ZULRESSO and compliance with the REMS, related limitations and restrictions, or because of actual or perceived difficulties obtaining satisfactory reimbursement or limitations on reimbursement or for other reasons, including staffing shortages. Healthcare settings that are active sites may also limit capacity used for ZULRESSO infusions or continue to wait to gain more experience with the clinical profile of ZULRESSO and to secure direct experience with reimbursement prior to increasing patient intake. Sage Central, our patient support center located in Raleigh, North Carolina, continues to provide a range of patient support resources to assist women with PPD and their families in the ZULRESSO treatment journey. In addition, our commercialization infrastructure includes capabilities in medical affairs, market access, manufacturing, quality control, drug safety and pharmacovigilance, health economics and outcomes research (HEOR), and compliance.

In December 2022, we completed our submission of an NDA to the FDA seeking approval of zuranolone for the treatment of MDD and PPD. In February 2023, our NDA was accepted for filing and granted priority review by the FDA with a PDUFA target action date of August 5, 2023. Permitted pre-launch activities, including efforts focused on disease state education in MDD and PPD, scientific exchange and permitted interactions with payers, as well as pre-launch planning and launch-readiness activities for zuranolone are underway, and we are actively working on our commercialization strategy and launch-readiness activities with Biogen in the event we are successful in our efforts to gain regulatory approval of zuranolone in the U.S. for MDD and/or PPD. In anticipation of our potential commercial launch of zuranolone in the U.S., if approved, we have begun to build additional sales and marketing capabilities in the U.S. If zuranolone receives regulatory approval for the treatment of MDD and/or PPD in adults, we expect that it may be prescribed by both specialty physicians (such as psychiatrists and obstetricians/gynecologists) and primary care physicians. We also plan to leverage additional promotional strategies to provide product education to healthcare providers and patients with MDD and PPD if zuranolone is approved, and these efforts will be supplemented with disease education efforts geared towards MDD and PPD patients and providers disseminated through similar channels. These strategies include, but are not limited to, direct-to-patient and direct-to-consumer advertising delivered through a range of media, as well as online physician education.

As described above, we and Biogen have agreed as part of our collaboration that, if zuranolone and SAGE-324 are successfully developed and approved, we will jointly commercialize the products in the U.S., including sharing equally in sales and marketing activities and profits and losses in the U.S. If we obtain regulatory approval of such products, Biogen will record sales of Licensed 217 Products and we will record sales of Licensed 324 Products. We have granted Biogen sole rights to commercialize the Licensed Products outside the U.S., other than in the Shionogi Territory with respect to zuranolone, where we have granted such rights to Shionogi.

## Licenses

We have entered into several material license agreements with respect to our product and clinical-stage product candidates, which are described below.

### *CyDex Pharmaceuticals*

In September 2015, we amended and restated our existing commercial license agreement with CyDex Pharmaceuticals, Inc., a wholly owned subsidiary of Ligand Pharmaceuticals Incorporated, or CyDex. Under the terms of the commercial license agreement, as amended and restated, CyDex has granted us an exclusive license to CyDex's Captisol drug formulation technology and related intellectual property for the manufacture of pharmaceutical products incorporating brexanolone and the Company's compound known as SAGE-689, and the development and commercialization of the resulting products for the treatment, prevention or diagnosis of any disease or symptom in humans or animals other than (i) the ocular treatment of any disease or condition with a formulation, including a hormone; (ii) topical ocular treatment of inflammatory conditions; (iii) treatment and prophylaxis of fungal infections in humans; and (iv) any ocular treatment for retinal degeneration.

Pursuant to and during the term of the CyDex license, we are required to use commercially reasonable efforts to continue active, diligent development of the licensed product, to seek regulatory approval of the licensed product and to commercialize the licensed product following regulatory approval. We must deliver periodic progress reports to CyDex.

We are obligated to make milestone payments under the amended and restated license agreement with CyDex based on the achievement of clinical development and regulatory milestones in the amount of up to \$0.8 million in clinical milestones and up to \$3.8 million in regulatory milestones for each of the first two fields with respect to brexanolone; up to \$1.3 million in clinical milestones and up to \$8.5 million in regulatory milestones for each of the third and fourth fields with respect to brexanolone; and up to \$0.8 million in clinical milestones and up to \$1.8 million in regulatory milestones for one field with respect to SAGE-689. The CyDex license is perpetual until terminated. We may terminate the CyDex agreement for convenience upon providing 180 days' prior written notice to CyDex. Either party has the right to terminate the agreement for failure to cure a material breach in the applicable cure period. We pay royalties to CyDex on sales of ZULRESSO, and will also be required to pay royalties on sales of SAGE-689, if successfully developed, in the low single digits based on levels of net sales.

We are also party to a supply agreement with CyDex. Under the supply agreement, we are required to purchase all of our requirements for Captisol with respect to brexanolone and SAGE-689 from CyDex, and CyDex is required to supply us with Captisol for such purposes, subject to certain limitations.

### *University of California*

In October 2013, we entered into a license agreement with The Regents of the University of California, or the Regents, which was amended in May 2014. Pursuant to this agreement, and subject to certain rights of the U.S. government and rights retained by the Regents, the Regents granted us a non-exclusive, non-transferable license under all personal property rights of the Regents covering the tangible personal property in an investigational new drug, or IND, application package owned by the Regents, or the Data, and a specified quantity of cGMP grade allopregnanolone, or the Material, to (i) use the Data for reference or incorporation in an IND for the use of the Material as a treatment of status epilepticus, or SE, essential tremor and/or PPD and (ii) use the Material or modifications of the Material to develop a pharmaceutical formulation for clinical trials for SE, essential tremor and/or PPD. The rights licensed to us are not sublicensable.

This agreement required us to make up to \$0.1 million in milestone payments in connection with the first derived product that met the relevant milestones, all of which we have already paid. We must also pay royalties of less than 1% to the Regents on ZULRESSO and for each other derived product, if any, for a period of 15 years following the first commercial sale of such derived product. This agreement will terminate on the earlier to occur of (i) 27 years after the effective date or (ii) 15 years after the last-derived product is first commercially sold. We may terminate this agreement early for convenience upon providing 60 days' prior written notice to the Regents. The Regents may terminate this agreement early in the event of material default, including failure to provide timely progress reports, after the applicable cure period, or in the event of our bankruptcy. In the event of early termination of this agreement, we have the right to sell any partially made derived products for a period of 120 days from the date of termination, but would not otherwise have rights after termination under the licensed rights to make, have made, use, sell, have sold, offer for sale or import products containing allopregnanolone.

In June 2015, we entered into an exclusive license agreement with the Regents whereby we were granted an exclusive license to certain patent rights related to the use of allopregnanolone to treat various diseases. In exchange for such license, we paid an upfront payment of \$50,000, and made annual maintenance fees of \$15,000 until the calendar year following the first sale of ZULRESSO. We are obligated to make milestone payments following the achievement of specified regulatory and sales milestones of up to \$0.7 million and \$2.0 million in the aggregate, respectively. We pay royalties to the Regents at a low single digit percentage of net sales of ZULRESSO, subject to specified minimum annual royalty amounts. Unless terminated by operation of law or by acts of the parties under the terms of the agreement, the license agreement will terminate when the last-to-expire patents or last-to-be abandoned patent applications expire, whichever is later.

#### ***Collaboration and License Agreement with Biogen***

In November 2020, we entered into the Biogen Collaboration Agreement with Biogen for the development, manufacture and commercialization of Licensed 217 Products and Licensed 324 Products, which became effective in December 2020.

We and Biogen have agreed that we will jointly develop and commercialize the Licensed Products in the U.S., and that Biogen solely will develop and commercialize the Licensed Products outside the U.S., except, with respect to the Licensed 217 Products, in the Shionogi Territory. Each of us and Biogen is obligated to use commercially reasonable efforts to develop at least one product in each Product Class in the U.S., and Biogen is also obligated to use commercially reasonable efforts to develop at least one product in each Product Class in the Biogen Territory. We and Biogen have agreed to share jointly in the performance of the activities under the Biogen Collaboration Agreement in the U.S. and to share all costs for activities under the Biogen Collaboration Agreement solely for the U.S. equally. The Biogen Collaboration Agreement provides that Biogen has sole responsibility and decision-making authority with respect to such activities in the Biogen Territory. Biogen is solely responsible for all costs for activities under the Biogen Collaboration Agreement in the Biogen Territory. We have an Opt-Out Right (as defined below) in the U.S. with respect to a Product Class.

We have granted to Biogen a non-transferable, sublicensable, except for certain specified exceptions, license to certain of our intellectual property as needed to perform the activities under the Biogen Collaboration Agreement. Such license is co-exclusive with us in the U.S. and exclusive, even as to us, in the Biogen Territory, subject to certain retained rights to allow us to exercise our rights and perform our obligations under the Agreement and with respect to the Shionogi Territory.

Our activities for the U.S. are conducted pursuant to joint development plans agreed to by us and Biogen, on a Licensed Product-by-Licensed Product basis, and overseen by a joint steering committee, or the JSC. The JSC is composed of an equal number of representatives from each of us and Biogen.

Under the terms of the Biogen Collaboration Agreement, Biogen paid us an upfront payment of \$875.0 million on December 31, 2020. For so long as a Licensed Product is being sold in the U.S., we and Biogen will share in all operating profits and losses arising from such Licensed Product in the U.S. (50 percent us and 50 percent Biogen). The Biogen Collaboration Agreement provides that Biogen will record sales of Licensed 217 Products globally. We will record sales of Licensed 324 Products in the U.S. and Biogen will record sales of Licensed 324 Products outside of the U.S., in each case if Licensed Products are successfully developed and approved. We have the right to opt out of such profit- and loss-sharing on a Product Class-by-Product Class basis in the U.S., or in each case, an Opt-Out Right. If we elect to exercise our Opt-Out Right with respect to a Product Class, we have agreed to transition to Biogen applicable development and commercial activities for such Product Class for the U.S., and Biogen has agreed to assume sole operational and financial responsibility for such activities.

The Biogen Collaboration Agreement provides for aggregate regulatory/commercial milestone payments from Biogen to us for (i) Licensed 217 Products of up to \$475.0 million, including milestones totaling \$225.0 million related to the first commercial sale of zuranolone in MDD and PPD in the U.S., if approved, and (ii) Licensed 324 Products of up to \$520.0 million. It also provides for aggregate one-time sales milestone payments from Biogen to us of (i) up to \$300.0 million for each Product Class if we have not exercised our Opt-Out Right with respect to such Product Class and (ii) up to \$525.0 million for each Product Class if we have exercised our Opt-Out Right with respect to such Product Class.

Biogen has also agreed to pay us tiered royalties based on net sales of the Licensed Products in the Biogen Territory of high-teens to low-twenties percentages. If we have exercised our Opt-Out Right in the U.S. with respect to a Product Class, Biogen has agreed to pay us specified royalties based on net sales of the Licensed Products of such Product Class. Royalty payments may be reduced in certain specified customary circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may never receive any milestone payments or any royalty payments from Biogen.

During the term of the Biogen Collaboration Agreement, neither us nor Biogen nor any of our respective affiliates is permitted outside of the Biogen Collaboration Agreement to directly or indirectly develop, manufacture, conduct medical affairs activities or commercialize certain products in specified indications, or enter into agreements or arrangements with third parties to perform any of the above activities.

Unless earlier terminated, the Biogen Collaboration Agreement expires on a Licensed Product-by-Licensed Product and country-by-country basis on the later of (i) in the Biogen Territory, the expiration of the royalty term for such Licensed Product in such country or (ii) in the U.S., until the parties agree to permanently stop commercializing such Licensed Product. Biogen may terminate the Biogen Collaboration Agreement for convenience in its entirety or on a Product Class-by-Product Class basis or as to a region by providing advance written notice. Either us or Biogen may terminate the Biogen Collaboration Agreement (i) in the event of a material breach in whole or in part, by the other party subject to a cure period and (ii) in the event of the insolvency of the other party, in each case subject to specified conditions.

In connection with the execution of the Biogen Collaboration Agreement, we and BIMA also entered into a stock purchase agreement, or the Biogen Stock Purchase Agreement, for the sale and issuance of 6,241,473 shares of our common stock, or the Biogen Shares, to BIMA at a price of approximately \$104.14 per share, a premium of 40% over the volume-weighted average share price for the 30 days ending on the day prior to entry into the Biogen Stock Purchase Agreement, for an aggregate purchase price of \$650.0 million. The sale of the Biogen Shares was consummated on December 31, 2020.

We have granted BIMA specified demand and piggyback registration rights with respect to the Biogen Shares. The Biogen Stock Purchase Agreement also includes standstill provisions, lock-up restrictions and a voting agreement with respect to the Biogen Shares. Pursuant to the terms of the Biogen Stock Purchase Agreement, BIMA has agreed not to, and to cause its affiliates not to, directly or indirectly acquire our securities, seek or propose a tender or exchange offer or merger between us and BIMA, solicit proxies or consents with respect to any matter, or undertake other specified actions, in each case subject to specified conditions. The standstill restrictions terminate on the earliest of (i) a specified regulatory milestone under the Biogen Collaboration Agreement, (ii) the date one year following the termination of the Biogen Collaboration Agreement and (iii) December 28, 2027.

BIMA also agreed not to, and to cause its affiliates not to, sell or transfer any of the Biogen Shares for a period of eighteen months from the closing of the sale of the Biogen Shares, which period expired on June 30, 2022, and to limit sales and transfers of the Shares for an additional eighteen-month period, in each case subject to specified conditions and exceptions.

#### ***Collaboration Agreement with Shionogi & Co., Ltd.***

In June 2018, we entered into a collaboration agreement with Shionogi. Pursuant to this agreement, Shionogi is responsible for all clinical development, regulatory filings and commercialization of products containing zuranolone for the treatment of MDD and potentially other indications in the Shionogi Territory. Shionogi made an upfront payment of \$90.0 million in 2018, and we will be eligible to receive additional payments of up to \$485.0 million if certain regulatory and commercial milestones are achieved by Shionogi.

Under the terms of the agreement, the potential future milestone payments include up to \$70.0 million for the achievement of specified regulatory milestones, up to \$30.0 million for the achievement of specified commercialization milestones, and up to \$385.0 million for the achievement of specified net sales milestones. We will receive tiered royalties on sales of zuranolone in the Shionogi Territory, if development efforts are successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or any royalty payments from Shionogi.

Shionogi has also granted us certain rights to co-promote zuranolone in Japan. As between us and Shionogi, we maintain exclusive rights to develop and commercialize zuranolone outside of the Shionogi Territory. The upfront cash payment and any payments for milestones and royalties are non-refundable and non-creditable.

The agreement with Shionogi will terminate on a licensed product-by-licensed product basis on the date on which the royalty term has expired in each country in the Shionogi Territory for such licensed product and will ultimately expire upon the expiration of the last-to-expire royalty term. Shionogi may remove South Korea or Taiwan from the covered territories, for any reason or no reason upon 180 days' prior written notice. Shionogi may terminate the agreement in its entirety for any reason or no reason upon 180 days' prior written notice. Shionogi may also terminate the agreement in the event of a serious adverse event or a clinical failure upon 60 days' written notice to us. Either party may terminate this agreement early in the event of an uncured material breach within 180 days' after notice is delivered to the other party.

#### **Intellectual Property**

We strive to protect the proprietary know-how and technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture, and any other aspects of inventions that are commercially important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. To protect our rights to our proprietary know-how and technology, we require all employees, as well as our consultants and contract research organization, or CROs, when feasible, to enter into agreements that generally require disclosure and assignment to us of ideas, developments, discoveries and inventions made by these employees, consultants, and CROs in the course of their service to us.

We plan to continue to expand our intellectual property estate by filing patent applications directed to compositions, methods of use, treatment and patient selection, formulations and manufacturing processes created or identified from our ongoing development of our product candidates. Our success will depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation and may pursue in-licensing opportunities to develop and maintain our proprietary position. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and patent scope can be reinterpreted by the courts after issuance. Moreover, many jurisdictions, including the U.S., permit third parties to challenge issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing, or may in the future pursue, will issue as patents in any particular jurisdiction or whether the claims of any issued patents will be enforceable or provide sufficient protection from competitors.

Because patent applications in the U.S. and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by our issued patents, our pending patent applications or of patent applications we may file in the future. Moreover, we may have to participate in interference proceedings or derivation proceedings declared by the U.S. Patent and Trademark Office, or U.S. PTO, or similar proceedings outside the U.S., to determine priority of invention.

## **Patents**

We hold issued patents and pending patent applications in the U.S., and in certain foreign countries. Our intellectual property holdings include, but are not limited to:

- One issued U.S. patent, exclusively licensed to us, covering a method of using our proprietary brexanolone formulation to treat PPD, which will expire in 2033; one U.S. issued patent and one granted patent in Europe covering our proprietary formulation of brexanolone, which will expire in 2033; and one U.S. issued patent covering the dosage regimen of brexanolone to treat PPD, which will expire in 2037;
- Pending U.S. and foreign patent applications covering certain aspects of brexanolone, including courses of treatment, dosage regimens, methods for manufacturing, and additional uses of the formulation of brexanolone to treat various brain health diseases and disorders, including PPD;
- One issued U.S. patent covering the composition of matter of zuranolone, three issued U.S. patents covering methods of using zuranolone, one granted European patent covering the composition of matter of zuranolone, and one granted European patent covering methods of using zuranolone, each of which expires in April 2034, subject to any potential extensions; one issued U.S. patent covering solid forms of zuranolone, which expires in August 2037, subject to any potential extensions; and pending U.S. and foreign patent applications covering zuranolone, uses of zuranolone to treat various brain health diseases and disorders, and solid forms of zuranolone;
- Issued patents covering the composition of matter for SAGE-324 in Europe and Japan, expiring in May 2035, and U.S. and foreign patent applications covering SAGE-324, SAGE-319, and many other modulators of the GABA<sub>A</sub> receptor and uses of these compounds to treat various brain health diseases and disorders;
- Two issued U.S. patents covering composition of matter and method of use of SAGE-689 which expire in December 2033, and U.S. and foreign patent applications covering SAGE-689 and uses of SAGE-689 to treat various brain health diseases and disorders. These patents and patent applications are co-owned with Washington University, and Sage has an exclusive license to Washington University's rights in these patents and patent applications; and
- U.S. and foreign patents and patent applications covering SAGE-718 and many other modulators of the NMDA receptor, and uses of these compounds to treat various brain health diseases and disorders.

## ***Patent Term***

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the U.S. PTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may also be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA



approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug, and/or a method of manufacturing the FDA-approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. Some foreign jurisdictions, including Europe and Japan, also have patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extension on patents covering those products, their methods of use, and/or methods of manufacture.

## Trade Secrets

In addition to patents, we may rely on trade secrets and know-how to develop and maintain our competitive position. Companies typically rely on trade secrets to protect aspects of their business that are not amenable to, or that they do not consider appropriate for, patent protection. We protect trade secrets, if any, and know-how by establishing confidentiality agreements and invention assignment agreements with our employees, and, where feasible, with consultants, scientific advisors, contractors and certain other entities with whom we do business. These agreements generally provide that all confidential information developed or made known during the course of an individual or entity's relationship with us must be kept confidential during and after the relationship. These agreements also generally provide that all relevant inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, designed to guard against misappropriation of our proprietary information by third parties.

## Competition

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our product or product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products or targeting similar indications will increase.

Currently, there are no pharmacological therapies specifically approved for the treatment of PPD other than ZULRESSO. Current standard of care for PPD commonly consists of psychotherapy; however, patients with moderate or severe PPD are often prescribed antidepressant medications such as SSRIs and SNRIs.

Our most advanced product candidate is zuranolone, for which we filed an NDA with the FDA seeking approval for the treatment of MDD and PPD. Patients with MDD are typically treated with a variety of antidepressant medications, including SSRIs, SNRIs and atypical antipsychotics. If approved, zuranolone may also face competition for the treatment of MDD from AXS-05, a combination formulation of an NMDA receptor antagonist, dextromethorphan, with bupropion, an FDA-approved antidepressant affecting norepinephrine and dopamine, which such combination formulation was approved in August 2022 by the FDA for the treatment of MDD in adults. Zuranolone, if approved, may also face competition from esketamine, which is approved for the treatment of treatment-resistant depression and depressive symptoms in adults with MDD with acute suicidal ideation or behavior, and from cariprazine, which was recently approved for the adjunctive treatment of MDD in patients who are receiving ongoing antidepressant therapy. A number of other companies are developing product candidates intended for the treatment of MDD. Furthermore, if zuranolone is successfully approved for PPD and commercialized, it could further limit our commercial opportunity for ZULRESSO.

In the field of neuroactive steroids focused specifically on modulation of GABA<sub>A</sub> receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc., or Marinus. In March 2022, Marinus announced that the FDA had approved ganaxolone, a known GABA<sub>A</sub> positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other GABA<sub>A</sub> competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. for the treatment of epilepsy and panic disorder.

SAGE-324, a novel GABA<sub>A</sub> receptor positive allosteric modulator, is in Phase 2 development for essential tremor. If successfully developed and approved as a treatment for essential tremor, SAGE-324 will face competition from current first-line treatments which include  $\beta$ -adrenergic blocker propranolol and anticonvulsant primidone. Other companies are also developing potential treatments for essential tremor, including a T-type calcium channel modulator that Jazz

Pharmaceuticals, Inc. is currently evaluating in Phase 2b development and a Phase 2 T-type calcium channel modulator being developed by Praxis.

A number of companies are working to develop products designed to modulate the NMDA receptor. Aptinyx Inc. has two Phase 2 NMDA receptor modulators in development for multiple indications, targeting two indications each, including NYX-458 being developed for the treatment of cognitive impairment in Parkinson's disease. Novartis AG, following its acquisition of Cadent Therapeutics, Inc., is also developing its own NMDA receptor positive allosteric modulator, CAD-9303, which is currently being investigated in cognitive impairment associated with schizophrenia. In addition, Vaccinex, Inc. is evaluating VX15/2503, a monoclonal antibody against the protein semaphorin 4D (SEMA4D), as a treatment for cognitive impairment in Huntington's disease. Several companies have developed or are developing products for the treatment of Alzheimer's disease.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. We expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are perceived to be safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

### **Government Regulation**

Government authorities in the U.S. at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring/pharmacovigilance, safety and periodic reporting, marketing and export and import of drug products. Generally, before a new drug can be marketed in a given jurisdiction, considerable data demonstrating its quality, safety and efficacy must be obtained and/or generated, organized into a format specific to each regulatory authority, submitted for review and the drug must be approved by the relevant regulatory authority or authorities.

### **U.S. Drug Development**

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject a company to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's delay or refusal to approve pending applications, withdrawal of an approval, a clinical hold on a clinical investigation, warning or untitled letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the U.S. The process required by the FDA before a drug may be marketed in the U.S. requires substantial time, effort and financial resources and generally involves the following:

- Completion of extensive non-clinical studies and testing, sometimes referred to as non-clinical laboratory tests, non-clinical animal studies and formulation studies, in accordance with applicable regulations, including the FDA's current Good Laboratory Practice, or GLP, regulations;
- Submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, or ethics committee representing each clinical trial site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes collectively referred to as good clinical practice, or GCP, to establish the safety and efficacy of the proposed drug for each proposed indication;
- Submission to the FDA of an NDA for marketing approval of a new drug;
- Determination by the FDA within 60 days of its receipt of an NDA to accept and file the NDA for review;
- Satisfactory completion of a potential FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Potential FDA audit of the non-clinical and/or clinical trial sites that generated the data in support of the NDA; and
- Payment of applicable user fees and FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee and scheduling by the DEA, if applicable, prior to any commercial marketing or sale of the drug in the U.S.

The data required to support an NDA are generated in two distinct development stages: non-clinical and clinical. For new chemical entities, the non-clinical development stage generally involves synthesizing the active component, developing the formulation and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which support subsequent clinical testing. Non-clinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of the non-clinical tests must comply with federal laws and regulations, including, for animal studies, the Animal Welfare Act and GLP. The sponsor must submit the results of the non-clinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. These studies are typically referred to as IND-enabling studies.

An IND is a request for authorization from the FDA to administer an investigational drug product to humans. Some non-clinical testing may continue even after the IND is submitted, but an IND must become effective before human clinical trials may begin. The central focus of an IND submission is on the general investigational plan and the protocols for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials, including whether subjects will be exposed to unreasonable health risks, and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development generally involves the administration of the drug candidate to healthy volunteers and then to patients with the disease or condition being studied under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials must be conducted in accordance with GCPs, which establish standards for conducting, recording data from, and reporting the results of, clinical trials, and are

intended to assure that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected. GCPs include the requirement that all research subjects provide their informed consent for their participation in any given clinical trial. Clinical trials are conducted under protocols describing, among other details, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants, and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Companies sponsoring the clinical trials, investigators, and IRBs also must comply with, as applicable, regulations and guidelines for obtaining informed consent from the study patients, following the protocol and investigational plan, adequately monitoring the clinical trial, and timely reporting of adverse events. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. Foreign studies conducted under an IND must meet the same requirements that apply to studies being conducted in the U.S. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with GCP, including review and approval by an independent ethics committee and compliance with informed consent principles, and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary.

## Clinical Trials

Clinical trials are generally conducted in three phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacologic action, side effect tolerability and safety of the drug.
- Phase 2 clinical trials typically involve studies in patients afflicted with the target disease to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, as well as identification of possible adverse effects and safety risks and preliminary evaluation of efficacy.
- Phase 3 clinical trials generally involve large numbers of patients afflicted with the target disease at multiple sites (typically from several hundred to several thousand subjects), and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval and labeling. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended for drugs intended for chronic dosing to mimic the actual use of a product during marketing.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, increased rates of serious suspected adverse events, or findings from other studies or from animal or in vitro testing that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. Success in one phase does not mean that the results will be observed in subsequent phases. Each phase may involve multiple studies. If concerns arise about the safety of the product candidate, the FDA or other regulatory authorities can stop clinical trials by placing them on a “clinical hold” pending receipt of additional data, which can result in a delay or termination of a clinical development program. The sponsoring

company, the FDA, or the IRB may suspend or terminate a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk.

Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial, and may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry ([clinicaltrials.gov](https://clinicaltrials.gov)) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The failure to submit clinical trial information to [clinicaltrials.gov](https://clinicaltrials.gov), as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to \$10,000 for each day the violation continues. Although the FDA has historically not enforced these reporting requirements due to HHS's long delay in issuing final implementing regulations, those regulations have now been issued and the FDA has issued several Notices of Noncompliance to manufacturers since April 2021.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, we must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

## **NDA and FDA Review Process**

The results of non-clinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be offered for sale in the U.S.

In addition, under the Pediatric Research Equity Act certain NDAs or supplements to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. Under the Best Pharmaceuticals for Children Act, the FDA may also issue a Written Request asking a sponsor to conduct pediatric studies related to a particular active moiety; if the sponsor agrees and meets certain requirements, the sponsor may be eligible to receive additional marketing exclusivity for its drug product containing such active moiety.

Under PDUFA, each NDA must be accompanied by a user fee, unless subject to a waiver. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2023, the user fee for an application requiring clinical data, such as an NDA, is approximately \$3.24 million. PDUFA also imposes an annual prescription drug program fee for human drugs of approximately \$0.4 million. Fee waivers or reductions are

available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan-designated indication.

The FDA reviews all NDAs submitted before it accepts them for filing, and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA aims to complete its initial review of an NDA and respond to the applicant within 10 months from the filing date for a standard NDA and, and within six months from the filing date for a priority NDA. The FDA does not always meet its PDUFA target action dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA, the FDA will generally conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether the facilities comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications.

Before approving an NDA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements and integrity of the data submitted in the NDA. With passage of FDORA, Congress clarified the FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to the FDA as well as other persons holding study records or involved in the study process.

The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation process for an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. For example, the advisory committee may recommend or the FDA may determine that a REMS program is necessary to ensure safe use of the product. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

After the FDA evaluates an NDA, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or one or more additional pivotal Phase 3 clinical trials, and/or other significant and time-consuming requirements related to clinical trials, non-clinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such additional data and information are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a drug product for marketing in the U.S., and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific patient populations and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA typically requires that certain contraindications, warnings or precautions be included in the product labeling, and may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which may involve clinical trials designed to further assess a drug's safety and/or

efficacy and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS if the FDA determines that a REMS is required. A REMS could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. For example, the FDA has required a REMS for ZULRESSO to mitigate the potential for harm associated with the risk of excessive sedation and loss of consciousness during the ZULRESSO infusion. As part of the REMS, administration of ZULRESSO is limited to healthcare settings that have been certified under a REMS program under the supervision of qualified staff, and patients who are prescribed ZULRESSO are required to enroll in a patient registry which may allow us to compile additional information to further our understanding of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during administration of ZULRESSO and management of the risk. Any limitations on approval, marketing or use for any of our products could restrict the commercial promotion, distribution, prescription or dispensing of those products. Product approvals may be withdrawn for non-compliance with regulatory requirements if problems occur following launch, or if the FDA determines that the product is no longer safe or effective.

### **Orphan Drug Designation**

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug product intended to treat a “rare disease or condition,” which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals in the U.S., but for which there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for this type of disease or condition will be recovered from sales of the product. If orphan product designation is sought, it must be requested before submitting an NDA for the drug for the proposed rare disease or condition. If the FDA grants orphan drug designation, the common name of the therapeutic agent and its designated orphan use are disclosed publicly by the FDA. Orphan product designation does not, by itself, convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other sponsors’ applications to market the same drug for the entire rare disease or condition for which the drug has been granted orphan drug designation for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Orphan exclusivity operates independently from other regulatory exclusivities and other protection against generic competition, including patents that we hold for our products. A sponsor of a product application that has received an orphan drug designation may also be granted tax incentives for clinical research undertaken to support the application. In addition, the FDA may coordinate with the sponsor on research study design for an orphan drug and may exercise its discretion to grant marketing approval on the basis of more limited product safety and efficacy data than would ordinarily be required, based on the limited size of the applicable patient population.

Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication than that for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor’s product for the same indication or disease. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. The FDA can revoke a product’s orphan drug exclusivity under certain circumstances, including when the holder of the approved orphan drug application is unable to assure the availability of sufficient quantities of the drug to meet patient needs. Orphan drug status in the EU has similar, but not identical, benefits.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term “same disease or condition” in the statute means the designated “rare disease or condition” and could not be interpreted by the FDA to mean the “indication or use.” Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the “indication or use.” Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

## Expedited Development and Review Programs

The FDA has several programs that are intended to expedite or facilitate the process for reviewing new drugs that are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition and, if approved, would provide meaningful therapeutic benefit over existing treatments. Fast Track designation and Breakthrough Therapy designation are two of these programs and apply to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug as a Fast Track product at any time during the development of the product and may request the FDA to designate the drug as a Breakthrough Therapy based on preliminary clinical evidence which meet the criteria outlined in the FDA's programs. Under the Fast Track or Breakthrough Therapy expedited programs, the FDA may review sections of the marketing application on a rolling basis before the complete NDA is submitted if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product submitted to the FDA for marketing, including under a Fast Track or Breakthrough Therapy program, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval.

Any product is eligible for priority review if it treats a serious condition and, if approved, would offer a significant improvement in the safety and effectiveness of treatment, diagnosis or prevention compared to marketed products. Significant improvement may be shown by evidence of increased effectiveness for the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months from the date of the NDA filing.

A product may also be eligible for accelerated approval if the product is intended to treat a serious or life-threatening illness and, if approved, would provide meaningful therapeutic benefit over existing treatments. Accelerated approval for a product means that it may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. If the FDA concludes that a drug shown to be effective can be safely used only if distribution or use is restricted, it will require such post-marketing restrictions, as it deems necessary to assure safe use of the drug, such as:

- distribution restricted to certain facilities or physicians with special training or experience; or
- distribution conditioned on the performance of specified medical procedures.

The limitations imposed would be commensurate with the specific safety concerns presented by the drug. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

With passage of FDORA, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to the FDA every six months (until the study is completed) and use expedited procedures to withdraw accelerated approval of an NDA or biologics license application, or BLA, if the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.

Fast Track designation, priority review, accelerated approval and Breakthrough Therapy designation do not change the standards for approval, but may expedite the development or approval process.



## **Pediatric Trials**

The Food and Drug Administration Safety and Innovation Act, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-Phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from non-clinical studies, early phase clinical trials, and/or other clinical development programs. The FDA, if it learns of new information, may also request that the sponsor amend the initial PSP. The FDA may send a Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required and have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation.

## **Post-Marketing Requirements**

Following approval of a new product, a pharmaceutical company and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the Internet. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. Further, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about approved products or products in development to payors, including unapproved uses of approved products.

Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional non-clinical studies and clinical trials. As with new NDAs, the review process is often significantly extended by FDA requests for additional information or clarification. Any distribution of prescription drug products and pharmaceutical samples must comply with the U.S. Prescription Drug Marketing Act and the Drug Supply Chain Security Act.

FDA regulations also require that approved products be manufactured in specific approved facilities and in accordance with cGMP. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. The discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including, among other things, recall or withdrawal of the product from the market.

Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, administrative enforcement, warning or untitled letters from the FDA, mandated corrective advertising or communications with doctors, and civil penalties or criminal prosecution, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

### **Other Regulatory Matters**

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the U.S., the Department of Health and Human Services; the U.S. Department of Justice; the DEA; the Consumer Product Safety Commission; the Federal Trade Commission; the Occupational Safety and Health Administration; the Environmental Protection Agency; and state and local governments.

In the U.S., a drug product approved by the FDA may also be subject to regulation under the CSA as a controlled substance. The CSA is administered by the DEA and establishes, among other things, certain registration, security, recordkeeping, reporting, import, export and other requirements for controlled substances. The CSA classifies controlled substances into five schedules: Schedule I, II, III, IV or V. FDA approved pharmaceutical products may be listed in Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. An approved drug product or drug candidate that has not yet been approved by the FDA may be subject to scheduling as a controlled substance under the CSA, depending on the drug's potential for abuse. For a drug approved by the FDA and determined to require control under the CSA, the CSA requires the DEA to issue an interim final order scheduling the drug within 90 days after the DEA receives notice from HHS that the FDA has approved the drug and the DEA receives a scientific and medical evaluation and scheduling recommendation from the Department of Health and Human Services, after it has been completed by the FDA. The FDA recommended, and the DEA adopted, that brexanolone be scheduled as a Schedule IV controlled substance.

In the U.S., arrangements and interactions with health care professionals, third-party payors, patients and others expose us to broadly applicable anti-fraud and abuse, anti-kickback, false claims and other health care laws and regulations. These broadly applicable laws and regulations may constrain the business or financial arrangements or relationships through which we sell, market and distribute our approved product and any future products that may obtain marketing approval. In the U.S., federal and state health care laws and regulations that may affect our operations include:

- The federal Anti-Kickback Statute, which makes it illegal for any person, including a company marketing a prescription drug (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, that is intended to induce or reward the referral of an individual or purchase, lease or order, or the arranging for or

recommending the purchase or order, of a particular item or service, for which payment may be made in whole or in part under a federal healthcare program, such as Medicare or Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and prescribers, patients, purchasers and formulary managers on the other. Liability under the Anti-Kickback Statute may be established without proving actual knowledge of the statute or specific intent to violate it. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors to the federal Anti-Kickback Statute protecting certain common business arrangements and activities from prosecution or regulatory sanctions, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration to those who prescribe, purchase, or recommend pharmaceutical and biological products, including certain discounts, or engaging such individuals as consultants, advisors, or speakers, may be subject to scrutiny if they do not fit squarely within an exemption or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants, charitable donations, product support and patient assistance. Violations of this law may be punishable by up to ten years in prison, criminal fines, damages, administrative civil money penalties, and the potential for exclusion from participation in federal healthcare programs.

- The federal civil False Claims Act, which prohibits anyone from, among other things, knowingly presenting, or causing to be presented claims for payment of government funds that are false or fraudulent, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or knowingly and improperly avoiding, decreasing or concealing an obligation to pay money to the federal government. Actions under the False Claims Act may be brought by the federal government or as a qui tam action by a private individual in the name of the government. Many pharmaceutical manufacturers have been investigated and have reached substantial financial settlements with the federal government under the civil False Claims Act for a variety of alleged improper activities. The government may deem companies to have “caused” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our activities relating to the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Penalties for a False Claims Act violation may include three times the actual damages sustained by the government, plus significant civil penalties for each separate false or fraudulent claim, and the potential for exclusion from participation in federal healthcare programs.
- Numerous federal and state laws, including state data breach notification laws, state health information and/or genetic privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act and the California Consumer Privacy Act), govern the collection, use, and disclosure and protection of health-related and other personal information. Failure to comply with these laws and regulations could result in government enforcement actions and create liability, private litigation, or adverse publicity. In addition, we or our collaborators may obtain health information from third parties, such as hospitals, healthcare professionals, and research institutions, that are subject to privacy and security requirements under the federal Health Insurance Portability and Accountability Act of 1996, and its implementing regulations, or collectively, HIPAA. HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their “business associates” – independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service for or on behalf of a covered entity. Although we are not directly subject to the HIPAA information privacy and security provisions – other than with respect to providing certain employee benefits – we could potentially be subject to criminal penalties if we or our agents knowingly obtain, use or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, HIPAA does not replace federal, state, or other laws that may grant individuals even greater privacy protections.
- The HIPAA fraud provisions, which impose criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors, and prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry, in connection with the delivery of or payment for healthcare benefits, items or services.

- The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, which requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare & Medicaid Services, or CMS, the agency that administers the Medicare and Medicaid programs, information related to direct or indirect payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. Applicable manufacturers also are required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives.
- Analogous state and local laws and regulations, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed under Medicaid and other state programs or, in several states, regardless of the payor. We also may become subject to other state laws that require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state laws that restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs; state laws that require drug manufacturers to report information related to clinical trials, or information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; state laws and local ordinances that require identification or licensing of sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Substantial resources are necessary to ensure that our business arrangements and interactions with health care professionals, third-party payors, patients and others comply with applicable health care laws and regulations. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law, and if we are found to be in violation of any of these laws or any other governmental regulations, we may be subject to significant civil, criminal and administrative penalties, imprisonment, damages, fines, exclusion from government funded health care programs such as Medicare and Medicaid, or the curtailment or restructuring of our operations. Any action against us for violation of these laws or regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business.

Numerous other laws may apply to our products. Pricing and rebate programs must comply with the Medicaid rebate requirements of the U.S. Omnibus Budget Reconciliation Act of 1990 and more recent requirements in the Patient Protection and Affordable Care Act, as amended, and its implementing regulations (collectively referred to herein as the ACA (addressed further below in the section on “U.S. Healthcare Reform”). If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. Many states impose various requirements on pharmaceutical manufacturers to report development costs and pricing information when prices are increased. Penalties for late or faulty reporting can be significant. Products must meet applicable child-resistant packaging requirements under the U.S. Poison Prevention Packaging Act. Manufacturing, sales, promotion and other activities are also potentially subject to federal and state consumer protection and unfair competition laws.

The handling of any controlled substances must comply with the CSA and Controlled Substances Import and Export Act.

The distribution of pharmaceutical products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. The failure to comply with any of these laws or regulatory requirements subjects firms to possible legal or regulatory action. Depending on the circumstances, failure to meet applicable regulatory requirements can result in criminal prosecution, fines or other penalties, injunctions, issuance of warning or untitled letters, recall or seizure of products, total or partial suspension of production, denial or withdrawal of product approvals, or refusal to allow a firm to enter into supply contracts, including government contracts. Federal regulators, state attorneys general, and plaintiffs’ attorneys have been and will likely continue to be active in this space. Any action against us for violation of

these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Prohibitions or restrictions on sales or withdrawal of future products marketed by us could materially affect our business in an adverse way.

Many of these laws differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Many of the state laws enable a state attorney general to bring actions and provide private rights of action to consumers as enforcement mechanisms. There is also heightened sensitivity around certain types of health information, such as sensitive condition information or the health information of minors, which may be subject to additional protections. Compliance with these laws is difficult, constantly evolving, and time consuming. Changes in statutes, regulations or the interpretation of existing laws or regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

### **U.S. Patent Term Restoration and Marketing Exclusivity**

Depending upon the timing, duration and specifics of the FDA approval of our drug candidates, if any, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, or the testing phase, plus the time between the submission date of an NDA and the approval of that application, or the approval phase. This patent term restoration period may be reduced by the FDA if it finds that applicant did not act with due diligence during the testing phase or the approval phase. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. PTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, if circumstances permit, we intend to apply for restoration of patent term for one of our then owned or licensed patents, if any, to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were, for example, to fail to apply within applicable deadlines, to fail to apply prior to expiration of relevant patents or otherwise to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our ability to generate revenues could be materially adversely affected.

Some of our products may also be entitled to certain non-patent-related data exclusivity under the FDCA. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA may not be submitted by another company for another drug containing the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA Orange Book by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a full NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. Three-year exclusivity prevents the FDA from approving ANDAs and 505(b)(2) applications that rely on the information that served as the basis of granting three-year exclusivity. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations, and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a

full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the non-clinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy. We have obtained five-year NCE exclusivity for brexanolone, and plan to seek NCE exclusivity for our current and future product candidates, if eligible.

## **European Union Drug Development**

In the European Economic Area, or EEA, our future products may also be subject to extensive regulatory requirements. As in the U.S., medicinal products can only be marketed if a marketing authorization from the competent regulatory authorities in the EU has been obtained.

Similar to the U.S., the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive, has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive in a manner that is often not uniform. This has led to variations in the rules governing the conduct of clinical trials in the individual EU Member States. Under the regime of the Clinical Trials Directive, before a clinical trial can be initiated, it must be approved in each EU Member State where there is a site at which the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the regime of the Clinical Trials Directive, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In order to streamline the regulation of clinical trials across the EU, the EU Parliament has adopted Regulation (EU) No 536/2014, or the EU Clinical Trials Regulation. The EU Clinical Trials Regulation, which repeals and replaces the Clinical Trials Directive, introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU, including a new coordinated procedure for authorization of clinical trials that is reminiscent of the mutual recognition procedure for marketing authorization of medicinal products, and increased obligations on sponsors to publish clinical trial results. The main characteristics of the regulation include: a streamlined application procedure through a single entry point, referred to as the “EU portal”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts.

The EU Clinical Trials Regulation became effective on January 31, 2022 and is applicable directly in all countries of the EEA (which is comprised of 27 Member States of the EU plus Norway, Iceland and Liechtenstein). The EU Clinical Trials Regulation allows for starting and conducting a clinical trial in accordance with the Clinical Trials Directive during a transitional period which ended on January 31, 2023. Clinical trials authorized under the Clinical Trials Directive before January 31, 2023 can continue to be conducted under the Clinical Trials Directive until January 31, 2025. Any application to transition ongoing trials from the Clinical Trials Directive to the new EU Clinical Trials Regulation will need to be submitted and authorized before the end of the transitional period. The EU Clinical Trials Regulation is intended to simplify and streamline the approval of clinical trials in the EEA.

In the EU, pediatric data or an approved Pediatric Investigation Plan, or PIP, or waiver, is required to have been approved by the European Medicines Agency, or EMA, prior to submission of a marketing authorization application to the EMA or the competent authorities of the EU Member States. In some EU countries, we may also be required to have an approved PIP before we can begin enrolling pediatric patients in a clinical trial.

## **European Union Drug Review and Approval and Post-marketing Requirements**

In the EEA (which is comprised of 27 Member States of the EU plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after a related marketing authorization has been granted. Marketing authorization for medicinal products can be obtained through several different procedures. These are through a centralized, mutual recognition procedure, decentralized procedure, or national procedure (if marketing authorization is sought for a single EU Member State). The centralized procedure allows a company to submit a single application to the EMA. If a related positive opinion is provided by the EMA, the European Commission will grant a centralized marketing authorization that

is valid in all EU Member States and three of the four European Free Trade Associations countries (Iceland, Liechtenstein and Norway), all of whom make up the EEA.

The UK withdrew from the EU on January 31, 2020, commonly referred to as Brexit. Marketing authorizations granted through the EU centralized procedure continue to be valid in Northern Ireland by virtue of the Northern Ireland Protocol, but such EU marketing authorizations are not valid in the rest of the UK (England, Wales and Scotland, or collectively Great Britain). EU marketing authorizations existing as at the end of the Brexit transition period on December 31, 2020 were automatically converted into Great Britain marketing authorizations as of January 1, 2021. Until the end of 2023, a marketing authorization for Great Britain can be applied for on an expedited timetable through the UK European Commission Decision Reliance Procedure, after having received a positive opinion from the EMA's Committee for Medicinal Products for Human Use. It is not yet known whether the UK European Commission Decision Reliance Procedure will remain available after 2023. A Great Britain marketing authorization can alternatively be applied for separately through the standard national level procedure.

The EU centralized procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance that is not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or for which grant of centralized marketing authorization is in the interest of patients in the EU.

The decentralized authorization procedure permits companies to file identical applications for authorization to several EU Member States simultaneously for a medicinal product that has not yet been authorized in any EU Member State. The competent authorities of a single EU Member State, the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant marketing authorization for their territories on the basis of this assessment. The only exception to this is where an EU Member State considers that there are concerns of potential serious risk to public health related to authorization of the product. In these circumstances, the matter is submitted to the Heads of Medicines Agencies for review. The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States.

The maximum timeframe for the evaluation of a marketing authorization application in the EU is 210 days, not including clock stops during which applicants respond to questions from the competent authority. The initial marketing authorization granted in the EU is valid for five years. The authorization may be renewed and valid for an unlimited period unless the national competent authority or the European Commission decides on justified grounds to proceed with one additional five-year renewal period. The renewal of a marketing authorization is subject to a re-evaluation of the risk-benefit balance of the product by the national competent authorities or the EMA.

The holder of an EU marketing authorization for a medicinal product must also comply with the EU's pharmacovigilance legislation. This includes requirements to conduct pharmacovigilance, or the assessment and monitoring of the safety of medicinal products.

Various requirements apply to the manufacturing and placing on the EU market of medicinal products. Manufacture of medicinal products in the EU requires a manufacturing authorization, and import of medicinal products into the EU requires a manufacturing authorization allowing for import. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, or APIs, including the manufacture of APIs outside of the EU with the intention to import the APIs into the EU. Similarly, the distribution of medicinal products within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. Marketing authorization holders and/or manufacturing authorization holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

In the EU, the advertising and promotion of medicinal products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities in connection with a marketing authorization approval. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. Breaches of the rules governing the promotion of medicinal products in the EU could be penalized by civil, criminal or administrative sanctions, which may include fines and imprisonment. These laws may further limit or restrict the advertising and promotion of medicinal products to the general public and may also impose limitations on promotional activities with healthcare professionals.

### **European Union Regulatory Data Exclusivity**

In the EU, innovative medicinal products that are subject to marketing authorization on the basis of a full dossier and do not fall within the scope of the concept of global marketing authorization qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The concept of global marketing authorization prevents the same marketing authorization holder or members of the same group, or companies that have concluded tacit or explicit agreements concerning the marketing of the same medicinal product, from obtaining separate data and market exclusivity periods for medicinal products that contain the same active substance. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced. However, the generic product or biosimilar products cannot be marketed in the EU for a further two years thereafter. The overall ten-year period may be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

### **European Union Orphan Designation and Exclusivity**

In the EU, orphan drug designations are granted by the European Commission based on a scientific opinion by the EMA's Committee for Orphan Medicinal Products in relation to medicinal products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU and in relation to which there exists no satisfactory method of diagnosis, prevention, or treatment (or the product would be a significant benefit to those affected). Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the medicinal product.

Orphan medicinal products are entitled to ten years of exclusivity in all EU Member States. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the product. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it is established that the criteria for orphan designation are no longer met, such as if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

In addition, grant of orphan designation by the European Commission also entitles the holder of this designation to financial incentives such as reduction of fees or fee waivers. Orphan drug designation must be requested before submitting an application for marketing authorization. Orphan drug designation does not, in itself, convey any advantage in, or shorten the duration of, the regulatory review and authorization process.



## **European Union Data Protection**

EU Member States and other jurisdictions where we may in the future operate have adopted data protection laws and regulations, which impose significant compliance obligations. For example, the General Data Protection Regulation, or GDPR, imposes strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the sharing of personal data with third parties, the transfer of personal data out of the EU, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for violations of the data protection obligations. Obligations also include the need to conclude arrangements with clinical trials sites concerning data processing activities. Data protection authorities from the different EU Member States may interpret the GDPR and applicable related national laws differently and impose requirements additional to those provided in the GDPR. In addition, guidance on implementation and compliance practices may be updated or otherwise revised, which adds to the complexity of processing personal data in the EEA.

In addition, the GDPR restricts the ability of companies to transfer personal data from the EEA to the U.S. and other countries, which may adversely affect our ability to transfer personal data or otherwise may cause us to incur significant costs to come into compliance with applicable data transfer impact assessments and implementation of legal data transfer mechanisms. One mechanism previously relied upon by U.S. companies for such transfers was the EU-U.S. Privacy Shield Framework, or Privacy Shield. However, in July 2020, the European Court of Justice ruled the Privacy Shield to be an invalid data transfer mechanism and confirmed that the European Commission's Standard Contractual Clauses, or the Model Clauses, remain valid. In June 2021, the European Commission published updated versions of the Model Clauses, which must be incorporated into new and existing agreements within prescribed timeframes in order to continue to lawfully transfer personal data outside of the EU. As a result, companies may no longer rely on the Privacy Shield as a basis on which to transfer personal data from the EU to the U.S. U.S.-based companies are permitted to rely on other authorized means and procedures to transfer personal data provided by the GDPR. The Model Clauses may also come under increased scrutiny as a result of the European Court of Justice's judgement in July 2020, though they remain the most common authorized procedure to transfer personal data out of the EU. Following the European Court of Justice's ruling, the European Data Protection Board issued a statement providing among other things that it is a primary responsibility of the exporter and the importer, when considering whether to rely on the Model Clauses to export data from the EU to third countries, to ensure that the importer maintains a level of protection that is essentially equivalent to that guaranteed by the GDPR in light of the EU Charter of Human Rights. Companies may need to revise the Model Clauses used in their contracts in light of the July 2020 judgement. Companies that have not taken steps to demonstrate that their Model Clauses and personal data recipients in the U.S. are suitable to transfer to receive the personal data may be subject to enforcement actions by competent authorities in the EU for failure to comply with related data privacy rules. In October 2022, President Biden issued an executive order to implement EU-U.S. data privacy safeguards. The European Commission is now expected to review the executive order and could propose an adequacy decision concerning the level of personal data protection in the U.S. under which personal data could flow freely from the EU to the U.S.

In addition, the privacy and data security landscape in the EU continues to remain in flux. The United Kingdom's exit from the EU, often referred to as Brexit, has created uncertainty with regard to future data protection regulation in the United Kingdom. The European Commission has adopted an adequacy decision concerning the level of data protection in the UK. Personal data may now flow freely from the EEA to the UK; however, the European Commission may suspend the adequacy decision if it decides that the UK no longer provides for an adequate level of data protection.

## **Rest of the World Regulation**

For other countries outside of the U.S., UK and EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Approval by a regulatory authority in one jurisdiction does not guarantee approval by comparable regulatory authorities in other jurisdictions. If we fail to comply with applicable foreign regulatory requirements applicable to a given country, we may not be able to obtain regulatory approval for our product candidates in such country if we choose

to seek such approval, or we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

## Coverage and Reimbursement

### U.S. Healthcare Reform

The containment of healthcare costs continues to remain a priority of federal and state governments, and the prices of drugs have been a focus in recent efforts. Changes in government legislation or regulation and changes in governmental health benefit programs' or commercial payors' policies governing reimbursement for our products, if successfully developed and approved, may reduce reimbursement of our products' costs to physicians, pharmacies, patients, and distributors. The U.S. federal government and state legislatures, as well as foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and utilization management requirements, such as requirements for substitution of generic products or therapeutic equivalents. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could limit our net revenue and results for products, if any, we commercialize in the future.

The pricing and reimbursement environment for our products may change in the future and become more challenging due to state and federal healthcare reform measures. The American Recovery and Reinvestment Act of 2009, or ARRA, for example, allocated new federal funding to compare the effectiveness of different treatments for the same condition. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are made to Congress. Although ARRA does not mandate the use of the results of comparative effectiveness studies for reimbursement purposes, it is not clear what effect, if any, the research will have on the sales of any products for which we receive marketing approval or on the reimbursement policies of public and private payors. It is possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of any product for which we receive marketing approval. For example, if third-party payors find our products not to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The ACA was a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals, the provision of subsidies to eligible individuals enrolled in plans offered on the health insurance exchanges, and the expansion of the Medicaid program. This law has substantially changed the way healthcare is financed by both governmental and private insurers and has significantly impacted the pharmaceutical industry. Changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, benefits for patients within a coverage gap in the Medicare Part D prescription drug program (commonly known as the "donut hole"), rules regarding prescription drug benefits under the health insurance exchanges, changes to the Medicaid Drug Rebate Program, expansion of the Public Health Service Act's 340B drug pricing program, or 340B program, and fraud and abuse enforcement. These changes have impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment for performance initiatives and improvements to the Medicare physician quality reporting system and feedback program.

One of the goals of ACA was to expand coverage for the uninsured while at the same time containing overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA increased minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program and extended manufacturers' Medicaid rebate liability to drugs dispensed to individuals who are enrolled in Medicaid managed care organizations. The ACA also requires manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to direct or indirect payments and other transfers of value to physicians and teaching hospitals, as well as ownership and investment interests held in the company by physicians and their immediate family members. Since 2022, applicable manufacturers also are required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified

nurse-midwives. Failure to submit required information may result in civil monetary penalties of \$1,000 to \$10,000 for each payment or ownership interest that is not timely, accurately, or completely reported (annual maximum of \$150,000), and \$10,000 to \$100,000 for each knowing failure to report (annual maximum of \$1 million).

Some states have elected not to expand their Medicaid programs by raising the income limit to 133% of the federal poverty level for the ACA expansion population, as is permitted under the ACA. For each state that does not choose to expand its Medicaid program, there may be fewer insured patients overall, which could impact sales of our products that are approved and that we successfully commercialize, and our business and financial condition. Where Medicaid patients receive insurance coverage under any of the new options made available through the ACA, the possibility exists that manufacturers may be required to pay Medicaid rebates on drugs used under these circumstances, a decision that could impact manufacturer revenues.

Certain provisions of the ACA have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the U.S. Tax Cuts and Jobs Act of 2017, signed into law in December 2017, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate.” We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to commercialize our product candidates, if approved.

Other legislative changes relating to reimbursement have been adopted in the U.S. since the ACA was enacted. For example, on August 2, 2011, the Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals for spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction, which triggered the legislation’s automatic reductions. In concert with subsequent legislation, this has resulted in aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2030 (with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, due to the COVID-19 pandemic). On December 10, 2021, President Biden signed a law that provided for 1% Medicare sequestration in the second quarter of 2022 and the full 2% sequestration thereafter until 2030. To offset the temporary suspension during the COVID-19 pandemic, in 2030, the sequestration will be 2.25% for the first half of the year, and 3% in the second half of the year. The Infrastructure Investment and Jobs Act extended sequestration and increased it to 4% for the first six months of fiscal year 2031 before dropping to 0% for the remainder of fiscal year 2031. As long as these cuts remain in effect, they could adversely impact payment for any products we may commercialize in the future. We expect that additional federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, and in turn could significantly reduce the projected value of certain development projects and reduce our profitability.

Further, on August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022, or IRA, which, among other things, established a Medicare Part B inflation rebate scheme, under which, generally manufacturers will owe rebates if the average sales price of a Part B drug increases faster than the pace of inflation. Failure to timely pay a Part B inflation rebate is subject to a civil monetary penalty. The IRA also establishes a Medicare Part D inflation rebate scheme, under which generally manufacturers will owe rebates if the average manufacturer price of a Part D drug increases faster than the pace of inflation. The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologics without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price, starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. The IRA further makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs, and a change in manufacturer liability under the program that could negatively affect the profitability of our product candidates, if successfully developed and approved. Congress continues to examine various policy proposals that may result in pressure on the prices of prescription drugs in the government health benefit programs. The IRA or other legislative change could impact the market conditions for our product candidates.

Additional legislative changes, regulatory changes, or guidance could be adopted, which may impact potential marketing approvals and reimbursement for our product candidates, if approved. For example, there has been increasing legislative, regulatory, and enforcement interest in the U.S. with respect to drug pricing practices. There have been several Congressional inquiries and proposed and enacted federal and state legislation and regulatory initiatives designed to, among other things, bring more transparency to product pricing, evaluate the relationship between pricing and

manufacturer patient programs, and reform government healthcare program reimbursement methodologies for drug products. Individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including by requiring pharmaceutical manufacturers to report to state agencies when they introduce new drugs to market with prices over a certain threshold, or when they increase the price of a drug over a certain threshold. If healthcare policies or reforms intended to curb healthcare costs are adopted, the prices that we charge for any approved products may be limited, our commercial opportunity may be limited and/or our revenues from sales of our product and any future products, if approved, may be negatively impacted.

It is possible that the above-mentioned measures, as currently enacted or may be amended in the future, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, and new payment methodologies and additional downward pressure on coverage and payment and the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of additional cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products. We cannot be sure whether additional legislative changes will be enacted in the U.S. or outside of the U.S., or whether regulatory changes, guidance or interpretations will be changed, or what the impact of such changes on our product candidates, if any, may be.

### **Pharmaceutical Pricing and Reimbursement**

Sales of ZULRESSO, zuranolone, if approved, and any other product candidates we successfully develop in the future depend on the availability and extent of coverage and reimbursement from third-party payors, which are increasingly reducing reimbursements for medical products and services. Decreases in third-party reimbursement for our products or a decision by a third-party payor not to cover a product or to manage utilization by, for example, requiring prior authorization, could reduce physician usage of our products and have a material adverse effect on our sales, results of operations and financial condition. In the U.S., healthcare providers are reimbursed for covered services and products through Medicare, Medicaid, and other government healthcare programs, as well as through commercial insurance and managed healthcare organizations. No uniform policy of coverage and reimbursement for drug products exists. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be set because the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for determining the reimbursement amount for the drug product. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will each be made on a payor-by-payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

We participate in the Medicaid Drug Rebate Program and other governmental programs. The Medicaid Drug Rebate Program and other governmental programs impose obligations to report certain pricing data to the federal government as well as other compliance obligations. Other programs impose limits on the price we are permitted to charge certain entities for our products. Statutory and regulatory changes or other agency action regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of our products for which we receive regulatory approval and could negatively impact our results of operations or expand our rebate liability. For example, effective in April 2022, Congress expanded the availability of postpartum coverage under Medicaid and the Children's Health Insurance Program (CHIP).

Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being available for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data we report on a monthly and quarterly basis to CMS, the federal agency that administers the Medicare and Medicaid programs. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity in the U.S. in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. Where our average manufacturer price increases faster than the pace of inflation, we may be subject to an additional rebate in the amount that our average manufacturer price has exceeded the pace of inflation. Currently, the rebate is capped at 100 percent of the average manufacturer price, but, effective January 1, 2024, this cap on the rebate will be removed, and our rebate liability could increase accordingly.

The ACA (addressed further above in the section on “U.S. Healthcare Reform”) made significant changes to the Medicaid Drug Rebate Program, and CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate Program under the ACA. On December 31, 2020, CMS issued a final regulation that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements (beginning in 2022); and provide definitions for “line extension,” “new formulation,” and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula (beginning in 2022). Our failure to comply with these price reporting and rebate payment options, as well as pharmaceutical benefit manager “accumulator” programs, could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the 340B drug pricing program in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the Health Resources and Services Administration, or HRSA, requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B “ceiling price” for the manufacturer’s covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The ACA expanded the list of covered entities to include certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, but exempts “orphan drugs” from the ceiling price requirements for these covered entities. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and, in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Changes to the definition of average manufacturer price and the Medicaid Drug Rebate amount also could affect our 340B ceiling price calculations and negatively impact our results of operations.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that are found to have knowingly and intentionally overcharged covered entities, which became effective on January 1, 2019. It is unclear how HRSA will apply its enforcement authority under the regulation. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis, and HRSA then publishes them to covered entities. Moreover, under a final regulation effective January 13, 2021, HRSA newly established an administrative dispute resolution, or ADR, process for claims by covered entities that a manufacturer has engaged in overcharging, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that could be appealed only in federal court. HRSA has recently issued a proposed rule to modify the ADR process, which could impact the procedures that are used to determine whether we owe additional 340B discounts. An ADR proceeding could subject a manufacturer to onerous procedural requirements and result in additional liability.

Federal law also requires that a company that participates in the Medicaid Drug Rebate Program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Starting in 2023, manufacturers must pay refunds to Medicare for single source drugs or biologics, or biosimilar

biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages, for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Manufacturers that fail to pay refunds could be subject to civil monetary penalties of 125 percent of the refund amount.

Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our approved products and the resulting Medicare payment rate, and could negatively impact our results of operations. Also, the Medicare Part B drug payment methodology is subject to change based on legislation enacted by Congress.

Congress also could enact additional changes that affect our overall rebate liability and the information we report to the government as part of price reporting calculations, which could impact the market conditions for our products. We further expect continued scrutiny on government price reporting and pricing more generally from Congress, agencies, and other bodies, and are seeing an increase in state interest in price reporting, transparency, and other policies to address drug pricing concerns.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. The Medicaid rebate amount will be computed each quarter based on our submission to CMS of our current average manufacturer prices and best prices for the quarter. If we become aware that our Medicaid reporting for a prior period was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for a period not to exceed three years from the period in which the data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program. Any corrections to our rebate calculations could result in an overage or underage in our rebate liability for past quarters, depending on the nature of the correction. Price recalculations also may affect the ceiling price at which we are required to offer our products to covered entities under the 340B program, and may require us to issue refunds to 340B covered entities, which can be costly and burdensome.

Further, the IRA establishes Medicare Part B and Part D inflation rebate schemes (the first Part B inflation rebate period is in first quarter 2023; the first Part D inflation rebate period is in fourth quarter 2022 through third quarter 2023) and a drug price negotiation program, with the first negotiated prices to take effect in 2026. It also makes several changes to the Medicare Part D benefit, including the creation of a new manufacturer discount program in place of the current coverage gap discount program (beginning in 2025). Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with the new Part D manufacturer drug discount program.

We could be held liable for errors associated with our submission of pricing data. Civil monetary penalties can be applied if we are found to have made a misrepresentation in the reporting of our average sales price for each misrepresentation and for each day in which the misrepresentation was applied, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. In addition to retroactive rebates and the potential for 340B program refunds, if we are found to have knowingly submitted false average manufacturer price or best price information to the government, or to have misrepresented that information, we may be liable for significant civil monetary penalties per item of false information. Our failure to submit monthly/quarterly average manufacturer price and best price data on a timely basis could result in a significant civil monetary penalty per day for each day the information is late beyond the due date. Such failures also could be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program, or, if we fail to comply with 340B program requirements, HRSA could decide to terminate our 340B program participation agreement. In the event that CMS terminates our rebate agreement or HRSA terminates our 340B program participation agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs.

CMS and the Office of Inspector General have pursued manufacturers that were alleged to have failed to report these data to the government in a timely manner. Governmental agencies may also make changes in program interpretations, requirements or conditions of participation, some of which may have implications for amounts previously estimated or paid. We cannot guarantee that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by the Department of Veterans Affairs, or VA, Department of Defense, or DoD, Public Health Service, and Coast Guard (collectively, the Big Four agencies) and certain federal grantees, we are required to participate in the VA Federal Supply Schedule, or FSS, pricing program, established under Section 603 of the Veterans Health Care Act of 1992. Under this program, we are obligated to make our “covered” drugs (*i.e.*, innovator drugs and biologics) available for procurement on an FSS contract and charge a price to the Big Four agencies that is no higher than the Federal Ceiling Price, or FCP, which is a price calculated pursuant to a statutory formula. The FCP is derived from a calculated price point called the “non-federal average manufacturer price”, or Non-FAMP, which we are required to calculate and report to the VA on a quarterly and annual basis. Pursuant to applicable law, knowing provision of false information in connection with a Non-FAMP filing can subject a manufacturer to significant civil monetary penalties for each item of false information. The FSS contract also contains extensive disclosure and certification requirements. In addition, Section 703 of the National Defense Authorization Act for FY 2008, requires us to pay quarterly rebates to DoD on utilization of covered drugs that are dispensed through DoD’s Tricare network pharmacies to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP for the calendar year that the product was dispensed. If we overcharge the government in connection with the FSS contract or Tricare Retail Pharmacy Rebate Program, whether due to a misstated FCP or otherwise, we will be required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and any response to government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU Member States have the power to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. An EU Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved. Historically, products launched in the EU do not follow price structures of the U.S., and generally prices tend to be significantly lower.

In various EU Member States, we expect to be subject to continuous cost-cutting measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including countries representing major markets. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. On January 31, 2018, the European Commission presented a proposal for a regulation on health technologies assessment. The proposal was adopted in December 2021 and will apply as of January 2025. This EU HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas.

## Employees and Human Capital

Our mission to pioneer solutions to deliver life-changing brain health medicines so every person can thrive depends on our ability to attract, develop, engage, and retain the industry's highest quality talent across all dimensions of diversity. This understanding guides our approach to recruiting, managing and supporting our human capital resources. At Sage, we strive for a best-in-class working culture and a spirit of collaboration and inclusivity with a goal of supporting our team members and their families while we work to achieve our mission and evolve our business and culture as we grow. At Sage, we believe every voice matters and every contribution counts.

**General Information.** As of February 8, 2023, we employed 689 full-time employees, including 360 in research and development and 329 in selling, general and administrative and no part-time employees. Approximately 33 of our employees hold M.D. or Ph.D. degrees. We have never had a work stoppage, and none of our employees are represented by a labor organization or under any collective-bargaining arrangements. We consider our employee relations to be good.

### ***Diversity, equity, and inclusion***

We are committed to taking action to integrate diversity, equity, inclusion, and equal opportunity to foster a diverse workforce, sense of belonging and innovative thinking. We have four core areas of focus:

- **Experience:** Foster a diverse and inclusive culture that enables a sense of belonging and innovative thinking.
- **Talent:** Recruit and develop diverse, high-performing individuals and teams.
- **External:** Identify and partner with diverse community organizations and vendors to increase diversity in our ecosystem.
- **Patients:** Continue to grow and nurture long-term and transparent relationships to ensure diverse voices are represented.

Our commitment to diversity, equity, and inclusion is a core focus of our leadership team: nine of our seventeen leadership team members are women and/or from diverse racial and ethnic groups. As of year-end 2022, approximately 63% of our U.S. workforce identified as female and 30% identified as racially or ethnically diverse.

### ***Compensation, Benefits and Ongoing Professional Development***

Our vision is to fearlessly lead the way to create a world with better brain health, which requires everyone to consistently give their best. We aim to spur every single employee on to realize their true potential. To do this, we appreciate what it takes to be at one's best, which is why we prioritize the health and well-being of all team members. To promote our employees' continued well-being and development, we offer a variety of inclusive benefits and opportunities. We offer comprehensive work-life and income protection benefits, including health, dental, vision, life insurance, disability and retirement savings programs, paid time off and family leave, family planning, mental health days, caregiving support, a "be well" subsidy, technology benefits, tuition reimbursement and an employee assistance program. We continue to prioritize the needs of our employees through a robust listening strategy and are focused on assessing and responding to evolving needs.

Our employees are encouraged to take advantage of an array of professional and career development resources delivered through a variety of venues, including continued learning courses, online learning, company-wide coaching, podcasts, and leadership circles. We believe our investment in learning and growth gives us a competitive edge and our strategies are focused on optimal performance, ongoing professional growth, and future of work capabilities, with the following areas of focus:

- **Critical Leadership Capabilities:** Build a culture where leaders drive inclusion, performance, curiosity, and personal and professional growth.
- **Create a change agile and integrated organization:** Maximize our ability to collaborate and forge new pathways in the face of change.



- **Strengthen our commitment to personal and professional growth:** Increase engagement and retention through learning investment in individual employees.

We are committed to fostering an environment in which everyone feels valued, respected, and empowered to contribute and provided access to the resources and opportunities to do their best work, while we strive to make a positive difference for patients and their families.

### **Corporate Information**

We commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, we changed our name to Sage Therapeutics, Inc. under our Second Amended and Restated Certificate of Incorporation. Our mailing address and executive offices are located at 215 First Street, Cambridge, Massachusetts and our telephone number at that address is (617) 299-8380. We maintain an Internet website at the following address: [www.sagerx.com](http://www.sagerx.com). The information on our website is not incorporated by reference in this Annual Report or in any other filings we make with the Securities and Exchange Commission, or SEC.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Securities Exchange Act of 1934, as amended. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding us and other issuers that file electronically with the SEC. The SEC's Internet website address is <http://www.sec.gov>.

## Item 1A. Risk Factors

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10-K, or Annual Report, and in our other public filings before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. If any such risks or uncertainties actually occur, our business, financial condition or operating results could differ materially from the plans, projections and other forward-looking statements included in this Annual Report, including in the foregoing Business section and later in the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and elsewhere in this report and in our other public filings and public statements. The trading price of our common stock could decline due to any of these risks, and as a result, our stockholders may lose all or part of their investment.*

### **Risks Related to Product Development, Regulatory Approval and Commercialization**

***Our future business prospects depend heavily on our ability, with our collaboration partner, Biogen, to gain regulatory approval of zuranolone (SAGE-217) in the U.S. as a treatment for major depressive disorder, or MDD, and postpartum depression, or PPD, and to successfully commercialize zuranolone in those indications, if approved. While our NDA for zuranolone is currently under review, we cannot be certain that the design and results of our development program for zuranolone will be sufficient to obtain regulatory approval of zuranolone for the treatment of MDD or PPD on the timelines we expect or at all. Even if we receive regulatory approval of zuranolone in MDD and PPD, our commercialization efforts with respect to zuranolone may not be successful.***

Our future business prospects depend heavily on our ability, along with our collaboration partner, Biogen, to gain regulatory approval of zuranolone in the U.S. as a treatment for MDD and PPD.

Our NDA seeking approval of zuranolone for the treatment of both MDD and PPD was accepted for filing by the U.S. Food and Drug Administration, or FDA, and granted priority review in February 2023, with a Prescription Drug User Fee Act, as amended, or PDUFA, target action date for the NDA of August 5, 2023. The FDA may not approve zuranolone as a treatment for MDD and/or PPD on the timelines we expect, or at all. The FDA may require additional trials or data to approve zuranolone as a treatment for MDD and/or PPD, any of which may significantly delay and put at risk our efforts to obtain approval and may not be successful. The FDA may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract for the manufacture of zuranolone do not conform to applicable requirements, including current Good Manufacturing Practices, or cGMPs. The FDA may find deficiencies in the conduct of clinical trials or nonclinical studies or in the preparation, collection or analysis of data from clinical and non-clinical studies submitted in our NDA. If our NDA for zuranolone is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee. The FDA may also approve zuranolone, but only for one of the indications described in our NDA or for only a specific subset of patients with MDD or PPD, or may impose other restrictions, such as limitations or restrictions in the approved label such as a boxed warning, contraindications or a REMS requirement. The FDA may not meet expected review timelines or may elect to extend the timeframe for their review, or there may be delays at any point in the regulatory review cycle that negatively impact our plans and expectations, including anticipated launch timelines and plans in MDD or PPD. Other decisions or actions of the FDA or other regulatory agencies may also adversely affect the zuranolone program, our plans, progress or results and the potential product profile and success of zuranolone. Even if zuranolone is approved for marketing, it may not have the profile or market acceptance we expect in clinical practice after launch or the unmet need for new treatment options in MDD may not be as we significant as we expect or we may encounter reimbursement-related or other market-related issues in the commercialization of zuranolone. We and our collaborator may never be able to successfully commercialize zuranolone in the approved indications or to meet our expectations with respect to timing and revenues or profits from sales of such product.

***Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop, gain regulatory approval of and commercialize our current and future product candidates beyond zuranolone. We cannot be certain that we will be able to initiate planned clinical trials, to complete ongoing clinical trials or to***

***announce results of such trials with respect to any of our other product candidates, on the timelines we expect or at all, or that the results of our clinical trials or other activities under our development programs will be positive. We cannot be certain that we or our collaborators will be able to advance such product candidates into additional trials or to successfully develop, obtain regulatory approval for, or successfully commercialize any of our such product candidates, if approved.***

Our future business prospects depend heavily on our ability, alone or through our collaborations, to successfully develop and gain regulatory approval of our current and future product candidates beyond zuranolone. Drug development and obtaining regulatory approval for a product involves a long, expensive and uncertain process, involving a high degree of risk.

Before obtaining regulatory approvals for the commercial sale of any product candidate, non-clinical studies and clinical trials must demonstrate that the product candidate is safe and effective for use in each target indication. We or our collaborators, as applicable, may not be able to demonstrate the efficacy and safety of any of our other current product candidates or any future product candidate at each stage of clinical development or we may encounter other issues with any clinical trials or non-clinical studies required for regulatory submissions. Success in non-clinical studies or in earlier clinical trials or interim results of clinical trials may not be repeated or observed in ongoing, future or completed studies or trials involving the same compound or other product candidates. Some or all of our or our collaborators' clinical trials may fail to meet their primary or key secondary endpoints, raise safety issues or generate mixed results. For example, in December 2019, we announced that the MOUNTAIN Study, a Phase 3 clinical trial of zuranolone for the treatment of MDD, did not meet its primary endpoint. We may find that studying alternate formulations of our product candidates or doses that achieve higher or lower patient exposure may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results. For example, in our ongoing dose-ranging study of SAGE-324, the KINETIC 2 Study, we are evaluating multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies. We might decide to evaluate different doses, formulations, and durations of dosing for any of our product candidates with other studies or programs in the future. The results of clinical trials or non-clinical studies of our product candidates at any stage may not support further development or may not be sufficient to file for and obtain regulatory approval on the timelines we expect or at all. Other decisions or actions of the FDA or other regulatory agencies may affect our plans, progress or results.

Changes in formulation or the need to refine or scale-up the manufacturing process as we do for any of our product candidates could also delay development or require us to conduct additional clinical trials or non-clinical studies or conduct post-approval analyses, or could lead to different results than achieved with the earlier formulation or processes. We or our collaborators may not be able to initiate or complete our clinical trials or announce results from our clinical trials on the timelines we expect. We or our collaborators may experience slower than expected activation of sites or enrollment and randomization of patients in our clinical trials, particularly in clinical trials where an in-patient stay or frequent site visits are required, the patient population is small, enrollment criteria are more selective than historically used, there are existing therapies, where other companies are running large clinical trials, or where relevant clinical sites or our vendors are experiencing healthcare staffing shortages or significant turnover. There is also the potential for slower than expected clinical site initiation, delays or problems in analyzing data, the potential need for additional analysis or data or the need to enroll additional patients, or other unexpected issues such as adverse events in any of our clinical trials. These types of delays or issues could lead to delays in the completion of a trial and announcement of results.

Our ongoing and planned development activities may be negatively impacted by a number of factors, including the downstream effects of the COVID-19 pandemic. Widespread healthcare and vendor staffing shortages and increased competition for patients and clinical sites may make it difficult to enroll patients in our clinical trials and/or identify and activate participating clinical sites for our trials, may cause other delays at clinical trial sites and/or vendors, and may increase the rates of patients withdrawing from our clinical trials following enrollment. Some clinical sites may decline or delay participation in our trials due to capacity and resource constraints, given the increase in the number of clinical trials being conducted as pandemic-related restrictions have lifted. These factors may substantially slow clinical site identification and activation and enrollment in our clinical trials, or cause us to pause trials, which may, in each case, significantly impact our ability to meet our expected timelines, budgets, or other plans. For example, as a result of a slower than anticipated pace of enrollment, we now expect to complete enrollment in our KINETIC 2 Study of SAGE-324 in late 2023, rather than in late 2022 as we had initially projected.

In response to these challenges during the COVID-19 pandemic, we or our clinical sites implemented measures to help minimize the number of visits a clinical trial participant is required to make to a site, including by limiting or modifying clinical trial procedures and visits for data collection, and some clinical sites imposed other restrictions or limitations on key clinical trial activities such as restrictions related to monitoring of the sites by clinical research organizations. Some of these restrictions and limitations could be implemented again in the future, including in connection with the emergence of new COVID-19 strains. Limitations or modifications to study procedures, study visits or data collection, restrictions on key clinical trial activities such as monitoring or auditing, or other restrictions that may affect data analysis activities may require additional assessment and evaluation from institutional review boards; negatively impact the integrity or completeness of our trial data, the powering of a trial, the integrity or relevance of clinical study endpoints; or impact the timing of availability of results.

The drug development process can take many years, and may include post-marketing studies and surveillance, which will require the expenditure of substantial resources. Of the large number of drugs in development in the U.S., only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, even if we have the requisite financial resources, when needed, to continue to fund our development efforts, we cannot assure you that any of our current or future product candidates will be successfully developed or commercialized either in the U.S. or in any country outside the U.S. Even if we or our collaborators conduct the trials required by or discussed with the FDA, the FDA may ultimately decide that the design, number and type of trials, number of patients studied or results, even if positive, are not sufficient to file for or gain regulatory approval of any of our product candidates in the indications we study, or do not support the safety or efficacy or our intended profile for the product.

Even if we or a collaborator of ours gains approval of any of our current or future product candidates, we and our collaborator may never be able to successfully commercialize such new product in the approved indications or meet our expectations with respect to timing and revenues or profits from sales of such product.

***We may never be able to generate meaningful revenues from sales of ZULRESSO® (brexanolone) CIV injection at levels or on timing necessary to support our investment and goals.***

Our first product, ZULRESSO, was approved by the FDA in March 2019 as a treatment for PPD in adults, and was made commercially available in June 2019. We may never be able to generate meaningful revenues from sales of ZULRESSO or revenues at levels or on timing necessary to support our investment and goals. Our revenues from sales of ZULRESSO have been negatively impacted by significant barriers arising from the complex requirements for treatment and by the direct and indirect impacts of the COVID-19 pandemic. Some or all of these factors are expected to continue to impact revenues negatively in the future.

ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO is approved for administration only in a medically-supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategy, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat women with PPD are complex and time-consuming. These actions include becoming REMS-certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor-by-payor basis under commercial coverage. These requirements have created significant barriers to treatment for women with PPD. We expect

these barriers will continue to negatively impact ZULRESSO revenue growth, but we do not know the extent of the anticipated impact. These barriers were compounded by the COVID-19 pandemic and continue to be impacted by its related disruptive effects on the U.S. healthcare system, and other changes to the macroeconomic environment.

The spread of COVID-19 in the U.S. resulted in a significant number of sites of care pausing, limiting or delaying treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe that, at certain points during the COVID-19 pandemic, concerns about exposure to the virus or its variants caused a significant and sustained reduction in the number of women with PPD seeking treatment with ZULRESSO and in the number of physicians willing to prescribe it, and that difficulties in accessing treatment with ZULRESSO have now been compounded by healthcare staffing shortages and other changes to the macroeconomic environment. Given the ongoing disruption to the healthcare system in the U.S., including as a result of staffing shortages, we cannot predict for how long and to what extent ZULRESSO sales will be adversely impacted by these factors.

Our commercial efforts for ZULRESSO, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach will continue to substantially limit the revenue opportunity for ZULRESSO, and may make it difficult for us to achieve revenue growth and meet our revenue goals. Given this approach, the number of new healthcare settings that become treating sites for ZULRESSO, if any, is also expected to be limited. We may also find that certain healthcare settings that have in the past been active treating sites may not be willing to remain infusion-ready as a result of the complex requirements related to administration of ZULRESSO and compliance with the REMS, related limitations and restrictions, or because of actual or perceived difficulties obtaining satisfactory reimbursement or limitations on coverage and reimbursement or for other reasons, including staffing shortages. Healthcare settings that are active treating sites may also limit capacity used for ZULRESSO infusions.

We continue to encounter other issues and challenges in commercializing ZULRESSO and generating revenues, including:

- Some women with PPD who need treatment find it too onerous to undergo an infusion or to be treated at a certified healthcare setting overnight for the length of stay required for treatment, or to be enrolled in the registry that is part of the REMS process or may be concerned about the risk of excessive sedation and sudden loss of consciousness.
- More healthcare providers than we expected have been unwilling to accept ZULRESSO as a treatment paradigm for women with PPD and this may continue; we believe this unwillingness is due primarily to the product profile and reimbursement challenges associated with ZULRESSO.
- We compete with lower cost antidepressants.
- Given the mode of administration, the nature of the REMS and the current limitation on the administration of ZULRESSO to a medically-supervised healthcare setting certified under the REMS, use of ZULRESSO in the U.S. has been focused primarily on women with more severe symptoms of PPD, and we expect that to continue.
- We may be unable to fully comply with our obligations under the ZULRESSO REMS, which include auditing of healthcare settings, collection and analysis of required data, and other requirements, to the satisfaction of the FDA, or the FDA may require modifications to or additional restrictions under the ZULRESSO REMS.
- If zuranolone is successfully approved for PPD and commercialized, it could further limit our commercial opportunity for ZULRESSO.

We also expect to continue to encounter challenges related to coverage and reimbursement of ZULRESSO. These include restrictions related to the severity of PPD cases for which ZULRESSO will be reimbursed, requirements that other treatments be used prior to ZULRESSO, or other limitations in the scope, breadth, availability or amount of reimbursement covering ZULRESSO or the infusion. For example, the availability, terms and timing of coverage for ZULRESSO by state Medicaid systems is expected to continue to vary significantly by state, and we encounter states that impose significant coverage restrictions or lengthy delays on reimbursement of ZULRESSO. Similarly, certain healthcare settings or patients may determine that the financial burdens of treatment are not acceptable. A number of healthcare

settings that are willing to administer ZULRESSO to women with PPD who have commercial insurance do not currently treat Medicaid patients, which adversely affects our ability to generate revenue from ZULRESSO.

Any of these issues could impair our ability to generate revenues or to meet our expectations with respect to the amount or timing of revenues. Any issues or hurdles related to our commercialization efforts may materially adversely affect our business, results of operations, financial condition and prospects and could lead us to make significant further changes to the scope and nature of our efforts. There is no guarantee that we will be successful in our commercialization efforts with respect to ZULRESSO, or that we will be able to generate meaningful revenues or revenues at the levels or on the timing necessary to support our investment and goals.

***ZULRESSO, zuranolone, and our other current or future product candidates and any future products, if successfully developed and approved, may cause undesirable side effects that limit their commercial profile; delay or prevent further development or regulatory approval; cause regulatory authorities to require labeling statements, such as boxed warnings or a REMS; or result in other negative consequences.***

We may observe undesirable side effects or other potential safety issues in nonclinical studies, in clinical trials at any stage of development of our product candidates, as part of an expanded access program, if initiated for any of our products or product candidates, in commercial use or in post-approval studies of any approved product. Clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, certain side effects of ZULRESSO, zuranolone, any other current or future product candidates, or any future products, if successfully developed and approved, may only be uncovered with a larger number of patients exposed to the product. Those side effects could be serious or life-threatening. If we or others identify undesirable side effects caused by ZULRESSO, zuranolone, any other existing or future product candidate or any future approved product:

- regulatory authorities may withdraw, withhold or limit their approval of such products;
- the FDA or regulatory authorities outside the U.S. may impose a clinical hold or partial clinical hold prior to the initiation of development or during development of our product candidates which could cause us or our collaborators to have to stop, delay or restrict further development; or we or our collaborators may, even without a clinical hold, decide to interrupt, delay or halt existing non-clinical studies and clinical trials or stop development;
- we may have difficulty enrolling patients in our clinical trials and completing such trials on the timelines we expect or at all, or we may have to conduct additional non-clinical studies or clinical trials as part of a development program;
- if an NDA for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;
- we or our collaborators may not be able ultimately to demonstrate, to the satisfaction of the FDA or other regulatory authorities, that our product candidates are safe and that the benefits outweigh the safety risks, and the FDA or applicable foreign regulatory authorities may not approve the product candidate;
- regulatory authorities may require the addition of labeling statements, such as a boxed warning or additions to an existing boxed warning, or a contraindication, including as a result of inclusion in a class of drugs for a particular disease, or may require a REMS, or modifications to an existing REMS;
- we or our collaborators may be required to change the way such products are distributed or administered, conduct post-approval studies or change the labeling of the products;
- we or our collaborators may be subject to regulatory investigations and government enforcement actions;
- we or our collaborators may decide to remove such products from the marketplace;
- we or our collaborators could be sued and held liable for injury caused to individuals exposed to or taking our products or product candidates; and

- our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected products, could substantially increase the risks and costs of developing our product candidates or commercializing our products, and could significantly adversely impact our ability and that of our collaborators to successfully develop, gain regulatory approval for, and commercialize our current product candidates or future products and generate revenues.

***Obtaining regulatory approval to market any of our product candidates is a complex, lengthy, expensive and uncertain process, and the FDA and regulatory authorities outside of the U.S. may delay, limit or deny approval of zuranolone or any of our other product candidates for many reasons. Any setback or delay in obtaining regulatory approval for zuranolone or any of our other product candidates or in our ability to commence marketing of our products, if approved, may have a material adverse effect on our business and prospects.***

We are not permitted to market any of our product candidates in the U.S. until we or our collaborators receive approval of an NDA from the FDA or in any foreign countries until we or our collaborators receive the requisite marketing approval from such countries. Obtaining approval of an NDA in the U.S. or marketing approval in any country outside the U.S. is a complex, lengthy, expensive and uncertain process. The FDA and regulatory authorities outside the U.S. may delay, limit or deny approval of zuranolone or any of our other product candidates for many reasons, including, among others:

- we or our collaborators may not be able to demonstrate, to the satisfaction of the FDA or other regulatory authorities, that our product candidates are safe and effective in any indication and that the benefits outweigh the safety risks;
- the results of our non-clinical studies and clinical trials may be negative, or may not meet the level of statistical or clinical significance or other criteria required by the FDA or regulatory authorities outside the U.S. for marketing approval;
- the FDA or regulatory authorities outside the U.S. may impose a clinical hold or partial clinical hold prior to the initiation of development or during development of our product candidates which could cause us to have to stop, delay or restrict further development;
- the FDA or regulatory authorities outside the U.S. may disagree with our interpretation of data from our non-clinical studies and clinical trials, or may not accept data generated at one or more of our sites conducting non-clinical studies or clinical trials which may cause the study or trial to fail;
- the FDA or regulatory authorities outside the U.S. may determine that the number, design, size, conduct, implementation or result of our non-clinical studies or clinical trials is inadequate for regulatory approval or that changes in dosing or drug formulation used in our non-clinical studies or clinical trials require additional trials or studies, even if the regulatory authorities have previously reviewed and commented on the design and details of our plans;
- the FDA or regulatory or other government authorities outside the U.S. may require that we or our collaborators conduct additional non-clinical studies and clinical trials prior to approval or post-approval;
- the FDA or applicable foreign regulatory authorities may not approve the formulation, labeling or specifications of any of our product candidates;
- if an NDA for any of our product candidates is reviewed by an advisory committee of the FDA, the advisory committee may recommend against approval of the application or may recommend that the FDA require, as a condition of approval, additional non-clinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions, and the FDA may ultimately agree with the recommendations of the advisory committee;
- the FDA or applicable foreign regulatory authorities may approve a product candidate for which we or our collaborators are seeking regulatory approval for a more limited patient population than expected or with substantial use restrictions;
- as was the case with ZULRESSO, the FDA may require a REMS as a condition of approval or post-approval for our product candidates, or may modify an existing REMS;

- the FDA or applicable foreign regulatory authorities may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including cGMPs; or
- the FDA or applicable foreign regulatory agencies may change their approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize or delay our or our collaborators' ability to obtain regulatory approval for and successfully market zuranolone or our other product candidates. Even if we or our collaborators receive marketing approval for zuranolone or any of our other product candidates, regulatory or other governmental authorities may still impose significant restrictions, including restrictions on the indicated use or marketing, or may impose ongoing requirements for potentially costly post-approval studies. For example, the FDA has imposed post-approval obligations in connection with approval of ZULRESSO. We may not be able to fulfill these obligations in accordance with the FDA's timelines, or at all. We expect the FDA to recommend scheduling with respect to zuranolone, and the FDA may also recommend scheduling with respect to any of our other current or future product candidates. In such event, as was the case with ZULRESSO, prior to a product launch, the U.S. Drug Enforcement Administration, or DEA, will need to determine the controlled substance schedule of the product, taking into account the recommendation of the FDA. The timing of the scheduling process would delay our ability to market any product candidate that is successfully developed and approved.

We have been granted priority review of our NDA seeking approval of zuranolone for the treatment of MDD and PPD. We may seek priority review of future NDA submissions with the FDA, if our development efforts with respect to other product candidates are successful, but the FDA may not grant such priority review. Even if the FDA grants priority review for an NDA, the FDA may not meet the applicable review timelines or may elect to extend the timeframe for their review. Delays, resource constraints, and other disruptions at the FDA and other agencies may slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, the U.S. government has shut down several times in recent history and certain regulatory agencies, including the FDA, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs in the future, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Fast Track and Breakthrough Therapy designations from the FDA or PRIority Medicines, or PRIME, designation from the European Medicines Agency, or EMA, do not necessarily lead to a faster development pathway or regulatory review process, and do not increase the likelihood of regulatory approval. The FDA may withdraw Fast Track designation or Breakthrough Therapy designation, and the EMA may withdraw PRIME designation, if the relevant agency believes that the designation is no longer supported by data from our clinical development programs.

***The COVID-19 pandemic, its related downstream effects, and changes to the macroeconomic environment have adversely impacted and may continue to adversely impact our business, including our sales of ZULRESSO and our initiation, conduct and completion of non-clinical studies and clinical trials.***

The COVID-19 pandemic in the U.S. resulted in a significant number of sites of care pausing treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe, at certain points during the pandemic, concerns about exposure to the virus or its variants caused a significant and sustained reduction in the number of women with PPD seeking treatment with ZULRESSO and in physicians willing to prescribe it, and that difficulties in accessing treatment with ZULRESSO have since been compounded by healthcare staffing shortages and other changes to the macroeconomic environment. Given the ongoing disruption to the healthcare system in the U.S., including as a result of staffing shortages, we cannot predict for how long and to what extent ZULRESSO sales will be adversely impacted by these factors.



As a result of the COVID-19 pandemic, its downstream effects, and changes to the macroeconomic environment we could observe delays or other disruptions that may negatively impact our ongoing and planned development activities, including the timing of initiation and completion of non-clinical studies and clinical trials or the integrity, completeness or usefulness of the data we collect in those studies or trials. These delays and disruptions may include:

- delays or difficulties in qualifying clinical sites and in clinical site activation, or the diversion of other healthcare resources and personnel, due to healthcare and vendor staffing shortages or as a result of recommended or required precautions or limitations that could be implemented in the future;
- delays or difficulties in enrolling patients in our clinical trials, including, for example, with respect to recruiting older patients as we saw in certain clinical trials at certain times during the pandemic, or an increase in the number of patients withdrawing from our clinical trials prior to completion as a result of concerns about potential future variants of COVID-19 or as a result of recommended or required precautions or limitations intended to curb the spread of the virus, or the potential that patients in our trials may have or contract COVID-19 or potential future variants of the virus which may impact the trial results;
- delays or disruptions in non-clinical studies due to precautions taken by contract research organizations, or CROs, or other vendors in response to potential future restrictions recommended or imposed by federal, state or local authorities;
- limitations or modifications to study procedures, the number and type of study visits or data collection or data analysis activities, or other restrictions on other key clinical trial activities such as monitoring and auditing, in response to potential variants of COVID-19 or as a result of future restrictions imposed or recommended by federal, state or local governments;
- interruption or delays in the operations of the FDA and foreign regulatory agencies, including as a result of staffing shortages or other resource constraints, which may impact timelines for initiation of clinical trials, amendments of protocols, inspections of manufacturing facilities and review of regulatory submissions;
- interruption of, or delays in, availability of supplies of our product candidates if the COVID-19 pandemic continues in surges or recurs in waves for an extended period, including the potential for shortages of raw materials, other drugs or materials used in our clinical trials, or staff available to our contract manufacturing organizations or other vendors in the supply chain or as the result of restrictions or limitations in their businesses or activities; and
- limitations on employee resources that would otherwise be focused on the conduct of our non-clinical studies and clinical trials, including due to illness as a result of potential future waves of variants of COVID-19.

Additionally, future surges of COVID-19 may cause economic disruptions and may in the future adversely impact the capital markets and make additional capital unavailable to us on acceptable terms, or at all if we were to seek it. There may also be other long-term negative effects of the COVID-19 pandemic that may negatively affect general economic conditions and adversely impact our ability to access the capital markets in the future.

***The number of people with the diseases and disorders for which our products and product candidates are targeted may be smaller than we expect or our other assumptions with respect to the potential markets for our products and product candidates may not be correct and the markets may be significantly smaller than we expect.***

Our first product, ZULRESSO, has been approved in the U.S. for the treatment of PPD in adults. We completed a rolling submission of an NDA to the FDA seeking approval of zuranolone for the treatment of MDD and PPD in December 2022. We are developing SAGE-324 as a potential oral therapy for neurological conditions, such as essential tremor, epilepsy and Parkinson's disease. We are developing SAGE-718 as a potential treatment for cognitive dysfunction associated with Huntington's disease, Parkinson's disease and Alzheimer's disease. There is no precise method of establishing the actual number of patients with any of these disorders in any geography over any time period. With respect to PPD, MDD, essential tremor and the other indications for which we are developing, or plan to develop, our product candidates, we estimate the prevalence of the disease or disorder, and our estimates as to prevalence, including the assumptions we apply in determining our estimate, may not be accurate. In each case, there is a range of estimates in the published literature and in marketing studies, which include estimates within the range that are lower than our estimates. For example, our estimates of the prevalence of PPD are higher than estimates reported in some of the published literature and results obtained from certain studies analyzing claims databases. We believe these differences may be the result of variations in analytical methodologies and possibly under-diagnosis of PPD as a result of lack of screening and under-reporting and some patients being reluctant to seek treatment in clinical practice. The actual number of patients with PPD,

MDD, essential tremor, Huntington's disease, Parkinson's disease, Alzheimer's disease, or any other indication for which we elect to pursue development of our product candidates may, however, be significantly lower than we believe. Even if our prevalence estimates are correct, any approved product that we develop may only be indicated for or used by a subset of patients with the relevant disease or disorder. Our assumptions and estimates about the market for ZULRESSO and the potential market for zuranolone and our other current and future product candidates may not be accurate. In the event the number of patients with the diseases and disorders we are studying is significantly lower than we expect, we or our collaborators may have difficulties in enrolling patients in our clinical trials which may delay or prevent development of our product candidates. If our prevalence estimates with respect to any indication or our other market assumptions are not accurate, the markets for any approved product for these indications may be smaller than we anticipate, which could limit our revenues and our ability to achieve profitability or to meet our expectations with respect to the level and timing of revenues or profits.

***Positive results from non-clinical studies and clinical trials of our product candidates are not necessarily predictive of the results of later non-clinical studies and clinical trials of our product candidates in the same indications or other indications. Interim results from non-clinical studies and clinical trials may not be predictive of results of such non-clinical studies or clinical trials once completed. If we cannot replicate the positive results from our earlier non-clinical studies and clinical trials of our product candidates in our later non-clinical studies and clinical trials in the same indications or other indications, or we cannot replicate our interim results in our completed non-clinical studies and clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.***

Positive results from non-clinical studies and clinical trials of our product candidates may not necessarily be predictive of the results we or our collaborators may obtain from subsequent non-clinical studies or clinical trials using the same product candidate or other product candidates. For example, unlike earlier trials of zuranolone in MDD and PPD, the Phase 3 MOUNTAIN Study evaluating zuranolone in patients with MDD did not meet its primary endpoint. We or our collaborators may find that ongoing or future clinical trials of zuranolone or any of our other product candidates may also fail to meet their primary endpoints. Similarly, interim results from non-clinical studies and clinical trials may not be predictive of results of a non-clinical study or clinical trial once completed.

We or our collaborators may also observe safety issues in clinical trials or non-clinical studies of our product candidates that we or they did not observe or appreciate in earlier stage clinical studies or non-clinical studies, or a different rate or severity of events, including as a result of an increase in dosing or in frequency or duration of dosing, studying a different patient population or different indication than previously studied, or administering a product candidate with a concomitant medication. For example, in our ongoing dose-ranging study of SAGE-324, we are evaluating multiple doses, including the same maximum dose of SAGE-324 that we evaluated in prior studies. Any of these studies may result in unexpected adverse events or raise other safety issues or may otherwise generate negative results.

The results from non-clinical animal models may not be replicated in clinical trials. Many product candidates, including many targeting central nervous system disorders, with promising non-clinical profiles have failed to demonstrate similar safety, non-toxicity and efficacy in humans.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later-stage clinical trials after achieving positive results in earlier-stage development, and we cannot be certain that we will not face similar setbacks. Many drugs have failed to replicate efficacy and safety results in larger or more complex later stage trials. Moreover, non-clinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in non-clinical studies and clinical trials nonetheless failed to obtain FDA approval. If we or our collaborators fail to produce positive results in our ongoing and planned non-clinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially adversely affected.

***Failures or delays in the commencement, enrollment or completion of our ongoing and planned clinical trials of our current and future product candidates could cause us not to meet our expected timelines or result in increased costs to***

*us, and could delay, prevent or limit our ability to gain regulatory approval of any such product candidate and to generate revenue from resulting products, if any.*

Successful completion of clinical trials at each applicable stage of development is a prerequisite to submitting an NDA to the FDA or equivalent filings outside the U.S. and, consequently, the ultimate approval and commercial marketing of any of our product candidates for the indications in which we develop them. We do not know whether any of our ongoing clinical trials will be completed, and results announced, or whether future trials will begin, as planned or expected, if at all, as the commencement, enrollment and completion of clinical trials and announcement of results can be delayed or prevented for a number of reasons, including, among others:

- denial by the FDA or other regulatory authority of permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or placement of one or more clinical trials on full or partial clinical hold;
- delay or inability to satisfy the requirements of the FDA to commence clinical trials, including chemistry, manufacturing and control, or CMC, requirements, or to file or receive approvals of additional investigational new drug applications, or INDs, that may be required;
- delay or inability to satisfy the requirements for clinical trials conducted in the EU, if applicable, pursuant to Regulation (EU) No 536/2014, or the EU Clinical Trials Regulation;
- negative or inconclusive results from our ongoing non-clinical studies or clinical trials;
- challenges in identifying, recruiting, enrolling and retaining patients to participate in clinical trials;
- challenges in qualifying and activating clinical trial sites, including due to capacity and resource constraints and attrition at sites, and potential delays at clinical trial sites;
- the impact of the COVID-19 pandemic and its downstream effects, and/or the impact of other macroeconomic and geopolitical conditions;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- inadequate quantity or quality of supplies of a product candidate or other materials necessary to conduct clinical trials;
- difficulties obtaining Institutional Review Board, or IRB, approval, and equivalent approval for sites outside the U.S., to conduct a clinical trial at a prospective site or sites;
- delays or problems in analyzing data, or the need for additional analysis or data or the need to enroll additional patients;
- the occurrence of serious adverse events or unexpected drug-related side effects experienced by patients in a clinical trial or unexpected results in ongoing non-clinical studies;
- delays in validating endpoints utilized in a clinical trial;
- the FDA or applicable regulatory authorities outside the U.S. disagreeing with our clinical trial design and our interpretation of data from clinical trials, or changing the requirements for approval even after the regulatory authority has reviewed and commented on the design for our clinical trials; and
- reports from non-clinical or clinical testing of other therapies that raise safety or efficacy concerns.

In addition, a clinical trial may be suspended or terminated by us, the FDA or other regulatory authorities, the IRB or Ethics Committee, or EC, at the sites where the IRBs or ECs are overseeing a clinical trial, or recommended for termination or suspension by a data and safety monitoring board overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

- inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a partial or full clinical hold;
- unforeseen safety issues, including any that could be identified in our ongoing non-clinical studies, or adverse side effects or lack of effectiveness identified in ongoing clinical trials;
- changes in government regulations or administrative actions; and
- problems with clinical supply materials.

Additionally, changes in regulatory requirements or guidance or unanticipated events during our non-clinical studies and clinical trials may force us or our collaborators to amend non-clinical studies and clinical trial protocols or the applicable regulatory authorities may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. If we or our collaborators experience delays completing, or if we or our collaborators terminate, any of our non-clinical studies or clinical trials, or if we or our collaborators are required to conduct additional non-clinical studies or clinical trials, the development pathway, and ultimately the commercial prospects, for our product candidates may be harmed and our ability to generate product revenue from resulting products, if any, will be delayed.

***We or our collaborators may never seek or receive regulatory approval to market any of our products or product candidates outside of the U.S., or receive pricing and reimbursement outside the U.S. at acceptable levels.***

We or our collaborators may not seek, or may seek but never receive, regulatory approval to market our products or product candidates outside of the U.S. or in any particular country or region. In order to market any product outside of the U.S., we or our collaborators must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional non-clinical studies or clinical trials, additional work related to manufacturing and analytical testing on controls, and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in other countries. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the U.S. as well as other risks. In particular, in many countries outside of the U.S., products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval may require additional studies and data, and can result in substantial delays in bringing products to market in such countries and such investment may not be justified from a business standpoint given the market opportunity or level of required investment. Even if we or our collaborators generate the data and information which we believe may be sufficient to file an application for regulatory approval of any of our products or product candidates in a region or country outside the U.S., the relevant regulatory agency may find that we did not meet the requirements for approval, or even if our application is approved, we may have significant post-approval obligations.

Even if we or our collaborators are able to successfully develop our product candidates and obtain marketing approval in a country outside the U.S., we or they may not be able to obtain pricing and reimbursement approvals in such country at acceptable levels or at all, and any pricing and reimbursement approval we or they may obtain may be subject to onerous restrictions such as caps, rebates or other hurdles or restrictions on reimbursement. Failure to obtain marketing and pricing approval in countries outside the U.S. without onerous restrictions or limitations related to pricing, or any delay or other setback in obtaining such approval, would impair our ability or that of our collaborators to market our product candidates successfully or at all in such foreign markets. Any such impairment would reduce the size of our potential market or revenue potential, which could have a material adverse impact on our business, results of operations and prospects.

Any setback or delay in obtaining regulatory approval or commencing marketing, if approved, for our product candidates in a country or region outside the U.S. where we or our collaborators have decided it makes business sense to proceed may have a material adverse effect on our business and prospects.

***We rely completely on third-party suppliers to manufacture commercial supplies of ZULRESSO and clinical drug supplies for our product candidates, and we intend to rely on third parties to produce commercial supplies of zuranolone, if approved, and non-clinical, clinical and commercial supplies of our approved products and product candidates in the future.***

We do not currently have, nor do we plan to acquire or develop, the infrastructure or capability internally to manufacture supplies of ZULRESSO for commercial use, or of zuranolone or any of our other existing or future product candidates, for use in the conduct of our clinical trials and non-clinical studies or for future commercial use, and we rely completely on third-party suppliers for both active drug substances and finished drug products.

We rely on our contract manufacturers for commercial supplies of active drug substance, finished drug product and packaged and labeled product with respect to ZULRESSO. We also rely on our contract manufacturers to manufacture sufficient quantities of zuranolone to produce validation batches, and, if zuranolone is approved by the FDA, to manufacture commercial supplies of active drug substance, finished drug product and packaged and labeled product. We also rely on our contract manufacturers to manufacture sufficient quantities of SAGE-324, SAGE-718, SAGE-689 and our other product candidates for ongoing and planned clinical trials and non-clinical studies and expect to rely on them to scale our manufacturing processes for future clinical trials, if our development efforts are successful. We expect our contract manufacturers to comply with cGMPs in the manufacture of our products. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must typically complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including cGMPs, after we submit the relevant NDA or equivalent foreign regulatory submission to the applicable regulatory agency, which we expect to occur in connection with our NDA for zuranolone for the treatment of MDD and PPD, which is under review by the FDA. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, and pass regulatory inspections, on the timelines we expect or at all, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities with respect to our products. For example, if the FDA were to find deficiencies in connection with a pre-approval inspection related to our zuranolone NDA submission, the FDA could issue a Form 483 documenting one or more deficiencies, require we provide and comply with a corrective action plan, or determine that our NDA is not approvable in its then-current form.

In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our third-party contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our third-party contract manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our products and product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would significantly adversely delay or impact our commercialization efforts for any approved product and our ability to develop and obtain regulatory approval for our product candidates. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information. Also, if a natural disaster were to interrupt or halt production of our drug substance or drug product at one of our third-party contract manufacturers, or cause the loss of batches, we could encounter a supply shortage or face significant costs to rebuild our supply.

We have long-term supply agreements with our contract manufacturers with respect to ZULRESSO drug substance and drug product. We have an inventory of ZULRESSO drug product and drug substance in place to help mitigate any potential supply risks, but there is no guarantee that this inventory will be adequate. We have a long-term supply agreement with our contract manufacturer for zuranolone drug product, but we do not have a long-term supply agreement with any of our contract manufacturing organizations, or CMOs, for zuranolone drug substance and do not have arrangements in place for either long-term supply or redundant supply of drug substance or drug product for SAGE-324 or SAGE-718. Each batch of drug substance and drug product for our product candidates, with the exception of zuranolone drug product, is individually contracted through a purchase order governed by master service and quality agreements.

If our existing CMOs for our other product candidates are not willing to enter into long-term supply agreements, or are not willing or are unable to supply drug substance or drug product to us, we could be required to engage new contract manufacturers who would need to scale up the manufacturing process before we would be able to use the drug product or

drug substance they manufacture for clinical trials or for future commercialization, if we are successful and gain approval. In addition, any contract manufacturer will need to complete validation batches, pass an inspection by the FDA and other applicable foreign regulatory agencies, and be approved by regulatory authorities as our manufacturer before we would be able to use drug product or drug substance they manufacture for commercial purposes, which could result in significant delays or gaps in product availability. We plan to continue to rely upon contract manufacturers to manufacture commercial quantities of our products, if approved. If we are unable to maintain arrangements for third-party manufacturing, or are unable to do so on commercially reasonable terms, or are unable to obtain timely regulatory approvals in connection with our contract manufacturers, we may not be able to successfully commercialize any approved product or successfully complete development of our current or future product candidates.

***Zuranolone, if approved, or any other future products, if our ongoing development efforts are successful, may not achieve broad market acceptance or reimbursement at sufficient levels, which would limit the revenue that we generate from its sales.***

The commercial success of zuranolone, if approved by the FDA, or any of our other current or future product candidates, if successfully developed and approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance among healthcare professionals, patients, policy-makers and healthcare payors, and reimbursement at sufficient levels.

The availability of coverage and adequacy of reimbursement is essential for most patients to be able to access and afford treatments. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Government authorities, including the Centers for Medicare & Medicaid Services, or CMS, an agency within the Department of Health and Human Services, or HHS, in the U.S., and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Payors may adopt restrictions on coverage for any of our products, including zuranolone, if approved, such as requiring patients to try other lower cost therapies prior to reimbursing our product, requiring patients to meet severity or other criteria more restrictive than the approved label for our product, or requiring onerous and time-consuming prior authorization procedures, or they may limit the amount of reimbursement. These restrictions or limitations might impede appropriate use of our product for the approved indication. Restrictions and limitations on reimbursement or delays in obtaining coverage may vary significantly among payors and payor types. As a result, there is significant uncertainty related to third-party payor coverage and reimbursement of zuranolone, if approved, or any of our other future product candidates, if successfully developed and approved. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is a covered benefit under its health plan; safe, effective and medically necessary; appropriate for the specific patient; cost-effective; and neither experimental nor investigational. Regulatory approvals, pricing and reimbursement for drug products vary widely from country to country.

The inability of us or our collaborators to promptly obtain and maintain coverage and adequate reimbursement rates from both government-funded and private payors for zuranolone, if approved, and any other approved products that we develop could have a material adverse effect on our operating results, our ability to successfully commercialize our products, our ability to raise capital and our overall financial condition. Even if coverage is provided, we may not be able to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor can be an expensive and time-consuming process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. The industry competition to be included in third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement, often leads to downward pricing pressures on pharmaceutical products. In addition, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Increasingly, third-party payors

are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply when such metrics are not submitted accurately and on a timely basis. Before granting reimbursement approval, payors may require us to demonstrate that our product candidates, in addition to treating the target indications, also provide incremental health benefits to patients or healthcare costs savings. If zuranolone receives regulatory approval, we plan to pursue a value-based agreement strategy with payors. Payors may not be receptive to the use of value-based agreements or may not agree with our approach and such a strategy may not increase market acceptance or access. If we believe a value-based agreement strategy will not be successful we may change our approach. We cannot be sure that adequate coverage or reimbursement will be available for zuranolone or any other product candidate that we or our collaborators commercialize.

Market acceptance with respect to zuranolone, if approved, or any of our other product candidates that we successfully develop will depend on a number of factors, including, among others:

- the efficacy and safety of our products as demonstrated in clinical trials;
- the potential and perceived advantages and limitations of our products over current or future alternative treatment options, including in the case of zuranolone, if approved, the availability of lower cost antidepressants;
- the incidence and severity of any side effects of the products;
- limitations or warnings contained in the labeling approved for our products by the FDA or other applicable regulatory authorities;
- the clinical indications and size of patient populations for which our products are approved;
- the convenience, benefit, ease and availability of alternative treatments already approved or expected to be commercially launched in the near future;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, and our ability to increase awareness of our approved products through marketing efforts;
- the strength and effectiveness of our sales, marketing and distribution strategies and support or that of our collaborators;
- publicity concerning our products or competing products and treatments;
- pricing and cost effectiveness; or
- the availability of sufficient third-party coverage or reimbursement, and the willingness of patients to pay out-of-pocket in the absence of such coverage or reimbursement, including in the case of ZULRESSO for both the product and the cost of the infusion.

Our efforts to change the treatment paradigm for a given disorder or to educate the medical community and third-party payors about the benefits of any current or future products, to the extent permitted, including zuranolone for the treatment of MDD and PPD, if approved in those indications, may require significant resources and may never be successful. If zuranolone, if approved, or any other product candidates that may be approved in the future, do not achieve an adequate level of acceptance by patients, physicians, healthcare settings and payors, or reimbursement at reasonable levels, or if the patient population for which any such product is approved is smaller than we expect, we may not generate sufficient revenue from our products to become or remain profitable or to adequately fund operations or may not do so to the degree or on the timelines we expect.

***Even if marketing approval is granted for a product, we may face significant post-marketing obligations and future development and regulatory difficulties.***

Regulatory authorities may impose significant and potentially costly post-marketing obligations with respect to approval of any product, including post-marketing studies, additional CMC work and additional pediatric studies. For example, the FDA has imposed post-marketing commitments with respect to approval of ZULRESSO, and we may encounter issues or delays in the conduct of these post-marketing commitments or we may generate unexpected results.

In the event we or our collaborators elect, or are required, to proceed with pediatric studies of any of our product candidates in any indication, regulatory authorities may also require additional non-clinical studies or clinical trials be completed prior to commencement of such pediatric studies.

As was the case with brexanolone, the FDA may recommend controlled substance scheduling for our current or future product candidates, including zuranolone, if approved. In such event, the DEA will need to determine the controlled substance schedule taking into account the recommendation of the FDA. If products are determined to be controlled substances, the manufacturing, shipping, storing, selling and using of the products will be subject to an additional regulation. Distribution, prescribing and dispensing of these drugs are also regulated. Because of their restrictive nature, these laws and regulations could limit commercialization of our product candidates containing controlled substances. Failure to comply with these laws and regulations could also result in withdrawal of our DEA registrations, disruption in manufacturing and distribution activities, consent decrees, criminal and civil penalties and state actions, among other consequences. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. Brexanolone is currently regulated as a Schedule IV controlled substance. Other Schedule IV controlled substances include sedative hypnotics such as benzodiazepines.

ZULRESSO is, and any future approved products will also be, subject to ongoing FDA requirements governing the labeling, packaging, storage and promotion of the product and record-keeping and submission of safety and other post-market information. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks, safety and efficacy in pediatric populations or alternate doses or dose regimens.

The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. For example, the FDA has required a REMS for ZULRESSO. Any REMS required by the FDA may lead to increased costs to assure compliance with the REMS and with additional post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. In addition, if we are unable to comply with the ZULRESSO REMS or any REMS imposed for a future product, we may face additional restrictions, limitations or substantial penalties, any of which may materially adversely affect our business and results of operations.

We, our collaborators and the third-party manufacturers of our drug substance and drug products and our respective facilities are subject to extensive regulations in the manufacture of our products and product candidates, including GMP, and are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMPs and other regulations. If we, our collaborators or a regulatory agency discover problems with our approved products or product candidates such as poor control of production processes or other problems with the facility where our products are manufactured or in the manufacturing process, introduction of contaminants, or adverse events of unanticipated severity or frequency, a regulatory agency may impose restrictions on our products, the manufacturer or us or our collaborators, including requiring withdrawal of such products from the market or suspension of manufacturing. If we, our collaborators, our approved products, our product candidates, or the manufacturers for our products or product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw marketing approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications submitted by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.



***Competing therapies may exist or could emerge that adversely affect the amount of revenue we are able to generate from the sale of ZULRESSO, zuranolone, if approved, or any of our other current or future product candidates, if successfully developed and approved.***

The biopharmaceuticals industry is highly competitive. There are many public and private companies, universities, governmental agencies and other research organizations actively engaged in the research and development of products that may be similar to our products or product candidates or address similar markets. It is probable that the number of companies seeking to develop products and therapies similar to our products or targeting similar indications will increase. Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. We expect competition in the indications we are pursuing will focus on efficacy, safety, convenience, availability, and price. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are perceived to be safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Currently, there are no pharmacological therapies specifically approved for the treatment of PPD other than ZULRESSO. Current standard of care for PPD commonly consists of psychotherapy; however, patients with moderate or severe PPD are often prescribed antidepressant medications such as selective serotonin reuptake inhibitors, or SSRIs, and serotonin and norepinephrine reuptake inhibitors, or SNRIs.

Our most advanced product candidate is zuranolone, for which we filed an NDA with the FDA seeking approval for the treatment of MDD and PPD. Patients with MDD are typically treated with a variety of antidepressant medications, including SSRIs, SNRIs and atypical antipsychotics. If approved, zuranolone may also face competition for the treatment of MDD from AXS-05, a combination formulation of an NMDA receptor antagonist, dextromethorphan, with bupropion, an FDA-approved antidepressant affecting norepinephrine and dopamine, which such combination formulation was approved in August 2022 by the FDA for the treatment of MDD in adults. Zuranolone, if approved, may also face competition from esketamine, which is approved for the treatment of treatment-resistant depression and depressive symptoms in adults with MDD with acute suicidal ideation or behavior, and from cariprazine, which was recently approved for the adjunctive treatment of MDD in patients who are receiving ongoing antidepressant therapy. A number of other companies are developing product candidates intended for the treatment of MDD. Furthermore, if zuranolone is successfully approved for PPD and commercialized, it could further limit our commercial opportunity for ZULRESSO.

In the field of neuroactive steroids focused specifically on modulation of GABA<sub>A</sub> receptors, we also face competition from a number of companies, including Marinus Pharmaceuticals, Inc., or Marinus. In March 2022, Marinus announced that the FDA had approved ganaxolone, a known GABA<sub>A</sub> positive allosteric modulator neuroactive steroid, to treat seizures associated with CDKL5 deficiency disorder, a rare, genetic epilepsy. Other GABA<sub>A</sub> competitors include darigabat, which is being developed by Cerevel Therapeutics, Inc. for the treatment of epilepsy and panic disorder.

SAGE-324, a novel GABA<sub>A</sub> receptor positive allosteric modulator, is in Phase 2 development for essential tremor. If successfully developed and approved as a treatment for essential tremor, SAGE-324 will face competition from current first-line treatments which include  $\beta$ -adrenergic blocker propranolol and anticonvulsant primidone. Other companies are also developing potential treatments for essential tremor, including a T-type calcium channel modulator that Jazz Pharmaceuticals, Inc. is currently evaluating in Phase 2b development and a Phase 2 T-type calcium channel modulator being developed by Praxis.

A number of companies are working to develop products designed to modulate the NMDA receptor. Aptinyx Inc. has two Phase 2 NMDA receptor modulators in development for multiple indications, targeting two indications each, including NYX-458 being developed for the treatment of cognitive impairment in Parkinson's disease. Novartis AG, following its acquisition of Cadent Therapeutics, Inc., is also developing its own NMDA receptor positive allosteric modulator, CAD-9303, which is currently being investigated in cognitive impairment associated with schizophrenia. In addition, Vaccinex, Inc. is evaluating VX15/2503, a monoclonal antibody against the protein semaphorin 4D (SEMA4D),

as a treatment for cognitive impairment in Huntington's disease. Several companies have developed or are developing products for the treatment of Alzheimer's disease.

***Our existing collaborations with Biogen and Shionogi, and any future collaborations, may not lead to the successful development or regulatory approval of product candidates or commercialization of products. Our collaborators may have competing priorities, conflicting incentives, or different views than us on key decisions, including appropriate program spending, that may hamper or delay our development and commercialization efforts or increase our costs. Our business may be adversely affected if any of our collaborators fails to perform its obligations or terminates our collaboration, or if we are not able to establish future collaborations that we believe to be important to our business on commercially reasonable terms.***

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates in some or all markets.

Our existing and future collaborations, if any, may not lead to the successful development and commercialization of any products. Our collaborators face both the same challenges and hurdles that we would face in the development and commercialization of product candidates if we were engaged in the activities solely ourselves, as well as additional challenges related to operating under a collaboration. For example, we have entered into a collaboration and license agreement with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, collectively with BIMA, Biogen, to jointly develop and commercialize zuranolone and SAGE-324 in the U.S. and granting Biogen rights to develop and commercialize those product candidates in the rest of the world other than Japan, Taiwan and South Korea, or the Shionogi Territory, in the case of zuranolone. We have a separate collaboration with Shionogi & Co., Ltd., or Shionogi, under which we granted rights to Shionogi for the development and commercialization of zuranolone in the Shionogi Territory. The efforts under these collaborations may not be successful and we may never receive any additional milestone payments, profit-share revenue or royalty payments from Biogen or Shionogi. In addition, under most collaborations, including our existing collaborations, a certain degree of control in decision-making is transferred to or shared with our collaborators. Our collaborators may use their decision-making authority to make decisions that could delay, decrease the potential of, or otherwise adversely impact, development and commercialization of our product candidates. Similarly, where we share decision-making authority, the need to gain alignment on decisions may slow or impede advancement of our programs and cause us not to be able to meet our timelines or achieve our goals. Our collaborators may have competing priorities or different incentives that cause them to divert resources away from our collaboration, or we may not agree on appropriate spending levels, which could hamper our overall development and commercialization efforts or increase our overall spending. Our collaborators may independently develop, or develop with a competitor, competitive products or may believe that product candidates being evaluated in the collaboration could be competitive with the collaborator's own products. In the case of the collaboration with Biogen, both companies have agreed to certain exclusivity provisions for certain products in specified indications which may limit certain development opportunities outside the collaboration. In addition, if we depend on collaborators for capabilities and funding for major product development efforts globally or in key territories then our business may be adversely affected if our collaborator fails to perform its obligations under the agreement or the collaboration terminates. Disputes may also arise with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all.

***We may not be successful in our efforts to identify or discover additional product candidates beyond our existing product candidates or to file investigational new drug, or IND, applications for clinical development of new compounds at the rate we expect, or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

The success of our business depends upon our and our collaborators' ability to successfully develop, gain approval of and commercialize products based on our current product candidates and on our ability to generate new compounds for development in the future and to successfully complete the non-clinical work necessary to file INDs to pursue clinical development of such new compounds. Our research programs may fail to generate new compounds that meet the standards for non-clinical development, and, if even we are successful in generating such compounds, we may not be able to produce the non-clinical and other data necessary to support IND applications for clinical development, in each case in the number or at the rate we expect or at all for a number of reasons. For example, we may not be able to identify a sufficient number of new targets in areas of interest to us. Our research methodology may be unsuccessful in generating a sufficient number of new compounds appropriate for non-clinical testing in the target areas we identify. Even if we generate new compounds in areas of interest to us, we may determine that those compounds are not appropriate for non-clinical development, or we may generate data in non-clinical development that do not support IND filings for clinical development. We may not have, or devote, sufficient technical, financial, and human resources to our research efforts at the various stages needed to identify targets, generate compounds, conduct non-clinical studies and prepare INDs. Additional potential product candidates may be shown to have harmful side effects or may not have a positive risk/benefit profile or may have other characteristics that may make the product candidates not appropriate for further development or unlikely to receive marketing approval. Further, even if we generate new compounds in areas of interest, we may determine that those compounds are not worth pursuing for strategic reasons, including new legislation that may impact the viability of commercializing such compounds, if approved.

Because we have limited financial and management resources, we focus on a limited number of clinical and research programs and product candidates and are currently focused on certain brain health disorders. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful and may not yield any commercially viable drugs. Our resource allocation decisions may cause us to fail to capitalize on other viable opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain such sole development and commercialization rights. If any of these events occur, it may have a material adverse effect on our business.

***We rely, and expect that we will continue to rely, on third parties to conduct any clinical trials for our product candidates. If these third parties do not successfully carry out their contractual duties, comply with applicable standards and meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our products, if approved, and our business could be substantially harmed.***

We do not have the ability to independently conduct clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct clinical trials of our product candidates. We enter into agreements with third-party CROs to provide monitors for and to manage data for our ongoing clinical trials. We rely heavily on these parties for execution of clinical trials for our product candidates and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these clinical trials and the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

- have staffing difficulties and shortages, attrition of experienced staff, and other resource constraints;
- fail to comply with contractual obligations;
- fail to comply with current Good Clinical Practices, or GCPs, or experience other regulatory compliance issues;

- undergo changes in priorities or become financially distressed;
- form relationships with other entities, some of which may be our competitors; or
- be impacted by the downstream effects of the COVID-19 pandemic, including changes to the macroeconomic environment in ways that adversely affect our business.

These factors may materially adversely affect the willingness or ability of third parties to conduct our clinical trials, and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. We, clinical investigators, and our CROs are required to comply with regulations and guidelines, including GCPs, for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for any product candidates in clinical development or where clinical trials are being conducted. If we or our CROs or contract manufacturers fail to comply with these regulations or if the quality or accuracy of the clinical data obtained is compromised due to the failure to adhere to our clinical protocols or other regulatory requirements or for other reasons, and we are unable to rely on clinical data collected, we may be required to repeat clinical trials or extend the duration of, or increase the size of our clinical trials. This would delay the regulatory approval process, and could also subject us to enforcement action up to and including civil and criminal penalties. If any of our relationships with third-party CROs terminate or if a CRO needs to be replaced, we may not be able to enter into arrangements with alternative CROs in a timely manner or at all. Any of these issues could significantly delay or prevent regulatory approval of our product candidates and require significantly greater expenditures. In such an event, we believe that our financial results might be harmed, our costs could increase and our ability to generate revenue from products beyond ZULRESSO could be delayed.

***As our development and commercialization efforts advance, we expect to continue to significantly develop and expand our company, and we may encounter difficulties in managing this development and expansion, which could disrupt our operations.***

Given the complexity and level of activities and resources that are necessary to develop and commercialize pharmaceutical products, we have been growing and expanding our company and, if our planned development and regulatory efforts are successful, we expect to continue to need to significantly increase our number of employees and the scope of our operations. For example, to commercialize any future products, we will need to recruit and train additional qualified sales personnel, and continue to implement and improve our managerial, operational and financial systems. We may not be able to effectively manage any expansion of our operations or recruit and train additional qualified personnel. This may result in weaknesses in our infrastructure and give rise to operational mistakes or delays, loss of business opportunities, loss of employees and reduced productivity among remaining employees. If our management is unable to effectively manage any potential significant expansion, our expenses may increase more than expected, and our ability to successfully develop and gain regulatory approval of our product candidates and generate or increase our revenue, if such product candidates are approved, could be reduced and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize any future products that we successfully develop, and to compete effectively will depend, in part, on our ability to effectively manage the potential future expansion of our company.

***Our future success depends on our ability to attract, retain and motivate qualified personnel.***

To accomplish our objectives, we require a strong management team with expertise in research and development, clinical development and commercialization. Although we have entered into employment agreements with each of our executive officers, each of them is employed “at will” and may terminate his or her employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. Recruiting and retaining qualified personnel is critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. Failure to succeed in clinical trials or in obtaining regulatory approval may make it more challenging to recruit and retain qualified personnel. If we are

unable to continue to attract and retain high quality personnel, our development efforts, commercialization activities, business, financial condition, results of operations and growth prospects could be adversely affected.

***We face potential product liability exposure, and, if claims are brought against us, we may incur substantial liability.***

The sale of ZULRESSO and any future approved products and use of our product candidates in clinical trials will expose us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers or others using, prescribing, selling or otherwise coming into contact with our products and product candidates. For example, we may be sued if any product or product candidate allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing, sale or commercial use. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, including as a result of interactions with alcohol or other drugs, knowledge of risks, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection laws. If we become subject to product liability claims and cannot successfully defend ourselves against them, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in, among other things:

- withdrawal of patients from our clinical trials, or difficulty in enrolling clinical trials;
- substantial monetary awards to patients or other claimants;
- decreased demand for our approved products;
- damage to our reputation and exposure to adverse publicity;
- increased FDA warnings on product labels;
- litigation costs;
- distraction of management's attention from our primary business;
- loss of revenue; and
- withdrawal of products from the market or our inability to successfully gain approval of product candidates.

We maintain product liability insurance coverage with a \$20.0 million annual aggregate coverage limit. Nevertheless, our insurance coverage may be insufficient to reimburse us for any expenses or losses we may suffer. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses, including if insurance coverage becomes increasingly expensive. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. The cost of any product liability litigation or other proceedings, even if resolved in our favor, could be substantial, particularly in light of the size of our business and financial resources. A product liability claim or series of claims brought against us could cause our stock price to decline and, if we are unsuccessful in defending such a claim or claims and the resulting judgments exceed our insurance coverage, our financial condition, business and prospects could be materially adversely affected.

***If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.***

The Medicaid Drug Rebate Program, which we participate in, and other governmental programs impose obligations to report pricing figures to the federal government, require us to pay rebates and participate in discount programs. Other programs impose limits on the price we are permitted to charge certain entities for ZULRESSO or for any future products for which we receive regulatory approval. Statutory and regulatory changes or binding guidance regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of ZULRESSO or any future products for which we receive regulatory approval and could negatively impact our results of operations. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results. The Patient Protection and Affordable Care Act, as amended, referred to herein as the ACA, and regulations promulgated thereunder could affect our obligations in ways we cannot anticipate.

Pricing and rebate calculations vary among products and programs. The calculations are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. If we become obligated to restate or recalculate the amounts we report under these programs, our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and our price discounts and rebates could be increased. Additionally, we could be held liable for errors associated with our submission of pricing data under the Medicaid Drug Rebate Program and other federal or state drug pricing programs, including retroactive rebates and program refunds, and if we are found to have knowingly submitted false average manufacturer price or best price information to the government, civil monetary penalties per item of false information. Certain failures to submit required data could result in a civil monetary penalty for each day the information is late beyond the due date and be grounds for CMS to terminate our Medicaid drug rebate agreement, pursuant to which we participate in the Medicaid program, or, if we fail to comply with 340B program requirements, the Health Resources and Services Administration, or HRSA, could decide to terminate our 340B program participation agreement. In the event that CMS terminates our rebate agreement or HRSA terminates our 340B program participation agreement, no federal payments would be available under Medicaid or Medicare Part B for our covered outpatient drugs. We are also subject to civil monetary and other penalties applicable to the drug pricing negotiation program and Part B and Part D inflation rebate programs, as discussed further below under the risk factor entitled “*Healthcare regulations aimed at reducing healthcare costs may have a material adverse effect on our business or results of operation.*”

***We are subject to other laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

We are subject to a number of healthcare and other statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we currently or may in the future conduct our business.

Our current or future interactions and arrangements with third-party payors, healthcare providers, patients, healthcare settings, and others who play a role in the recommendation, prescription, reimbursement and administration of ZULRESSO and will play a similar role with respect to zuranolone, if approved and any of our other future product candidates, if successfully developed and approved, are governed in part by broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute ZULRESSO or expect to market, sell and distribute any future approved products. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly (including any kickback, bribe or certain rebates), in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. This statute has been interpreted to apply to arrangements between pharmaceutical companies on the one hand, and prescribers, purchasers and formulary managers, among others, on the other.
- The federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties. Pharmaceutical companies have been prosecuted under the False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product, among other activities. In addition, the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes privacy, security and breach reporting obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information upon covered entities subject to the rule.
- The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.
- The federal transparency requirements, sometimes referred to as the “Sunshine Act”, under the ACA require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to HHS information related to physician payments and other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations were extended to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.
- Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.
- Various federal and state health information and data protection laws and regulations, and similar types of laws outside the U.S., govern the collection, use, disclosure and protection of health-related and other personal information by us and our collaborators.

Ensuring that our future practices and business arrangements comply with applicable healthcare laws and regulations is costly. It is possible that governmental authorities will conclude that our business practices and arrangements do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our practices or operations, including activities conducted by our commercial team or other of our employees, consultants or vendors, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations and materially adversely affect our business and financial condition. We may also be substantially negatively impacted if governmental authorities conclude that the business practices of one of our collaborators does not comply with applicable laws. If any of the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We and our employees are also subject to other statutes and regulations related to our business, including: regulations imposed by the FDA and applicable non-U.S. regulators, as previously discussed; anti-bribery and anti-corruption laws and regulations applicable to activities outside the U.S.; rules on reporting financial and other information or data timely and accurately; and rules related to insider trading.

Although we have adopted a code of conduct and have an active compliance program, it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may be ineffective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure by our employees to comply with these laws or regulations.

***Data collection is governed by restrictive regulations governing the use, processing, and cross-border transfer of personal information.***

We must comply with numerous federal, state and non-U.S. laws which govern the privacy and security of health and other personal information. As described above, to the extent applicable to our business activities, HIPAA imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. In addition, when we conduct clinical trials in the U.S., any personal information that is collected in connection with these trials also is regulated by the Federal Policy for the Protection of Human Subjects (the Common Rule) which creates obligations for our company when conducting these trials.

We plan to enroll subjects in our ongoing or future clinical trials in the European Union, or EU, or other countries. When we do so, we may be subject to additional privacy restrictions, including restrictions relating to the collection, use, storage, transfer, and other processing of personal data, including personal health data, regarding these individuals. Clinical trial activities in the EEA, for example, are governed by the General Data Protection Regulation, or GDPR, in relation to the processing of personal data. The GDPR imposes several requirements on companies that process personal data, strict rules on the transfer of personal data out of the EEA, including to the U.S., and fines and penalties for failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR in some situations. The obligations under the GDPR may be onerous and adversely affect our business, financial condition, results of operations and prospects. Compliance with the GDPR is a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities. The issues related to the transfer of personal data are subject to substantial uncertainty at this time, and there can be no reasonable level of confidence that any such data transfers will be found to be consistent with EU law if they are challenged. The United Kingdom's, or UK's, exit from the EU, often referred to as Brexit, has created uncertainty with regard to future data protection regulation in the United Kingdom. The European Commission has adopted an adequacy decision concerning the level of data protection in the UK. Personal data may now flow freely from the EEA to the UK; however, the European Commission may suspend the adequacy decision if it decides that the UK no longer provides for an adequate level of data protection. Similar laws exist in many other countries around the world, and these laws (which are evolving and expanding) create complicated and potentially inconsistent obligations that may impact our business.

We are also subject to the California Consumer Privacy Act, or CCPA, which creates individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact our business activities. The CCPA also has been amended through a recent referendum in California that creates additional obligations that went into effect on January 1, 2023. In November 2020, California voters approved the California Privacy Rights Act, or CPRA, ballot initiative which introduced significant amendments to the CCPA and established and funded a dedicated California privacy regulator, the California Privacy Protection Agency, or the CPPA. New implementing regulations will be issued under the CPRA that may lead to new or additional obligations for us. Failure to comply with the CCPA may result in, among other things, significant civil penalties and injunctive relief, or statutory or actual damages. In addition, California residents have the right to bring a private right of action in connection with certain types of incidents. These claims may result in significant liability and damages. At least four states have passed similar general privacy legislation that may impact our business activities in the future, and additional states are evaluating similar kinds of general privacy legislation. In addition, there are substantial efforts at the federal level to pass a national data privacy law that may impact our business activities. The uncertainty, ambiguity, complexity and potential inconsistency surrounding the implementation and interpretation of CCPA and other enacted or potential laws in other states and at the federal level exemplify the vulnerability of our business to the evolving regulatory environment related to the privacy, security and confidentiality of personal data and protected health information. We may be subject to fines, penalties, or private actions in the event of non-compliance with such laws. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. We have implemented processes to manage compliance with the CCPA and continue to assess the impact of the CPRA, and other federal and state legislation, on our business as additional information and guidance becomes available.

In addition to the foregoing, any breach of privacy laws or data security laws, particularly resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and



financial condition. As a data controller, we will be accountable for any third-party service providers we engage to process personal data on our behalf, including our CROs. There is no assurance that privacy and security-related safeguards we implement will protect us from all risks associated with the third-party processing, storage and transmission of such information. In certain situations, both in the U.S. and in other countries, we also may be obligated as a result of a security breach to notify individuals and/or government entities about these breaches.

Additionally, in October 2022, President Joe Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The European Commission initiated the process to adopt an adequacy decision for the EU-U.S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may impact our activities with companies in the EU, and any potential future business operations in the EU.

***The FDA and other regulatory and enforcement agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, we may become subject to significant liability.***

The FDA and other regulatory and enforcement agencies strictly regulate the promotional claims that may be made about prescription products, and enforce laws and regulations prohibiting the promotion of unapproved, or "off-label" uses. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the approved labeling of the product. If we are found to have promoted off-label uses for any product, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has taken steps to restrict promotional activities of those companies. Pharmaceutical companies have also been prosecuted and incurred significant civil, criminal and administrative penalties, damages, fines under the False Claims Act in connection with their alleged off-label promotion of drugs. Any promotion of the off-label use of ZULRESSO, zuranolone, if approved, or any of our other future approved products by us or any of our employees could subject us to significant liability, which would materially adversely affect our business and financial condition.

***Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens, price controls, reimbursement issues and other risks and uncertainties, and could negatively impact our U.S. business.***

Our future profitability may depend, in part, on our ability, ourselves or through our collaborators, to commercialize our products and product candidates in foreign markets.

The pricing of prescription pharmaceuticals in foreign markets is subject to foreign governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

In some countries, including Member States of the EU, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. There can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In the U.S., recent legislative and administrative policies and proposals signal a desire to lower drug prices in the U.S. As a result, we or our collaborators outside the U.S. in the future may be limited in the prices we are able to charge for our products in the U.S. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our collaborators and the potential profitability of our products in those countries would be negatively affected.

Commercializing our products and product candidates in foreign markets would subject us to additional risks and uncertainties, including:

- our inability to directly control commercial activities to the extent we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, including the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- reduced protection of intellectual property rights, and the existence of additional potentially relevant third-party intellectual property rights, in some foreign countries; and
- foreign currency exchange rate fluctuations.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs. For example, Brexit has already and may continue to adversely affect European and/or worldwide regulatory conditions. Brexit could continue to lead to legal uncertainty and potentially divergent national laws and regulations in the EU and the United Kingdom, including those related to the pricing of prescription pharmaceuticals, as the United Kingdom determines which EU laws to replicate or replace, which could impair our ability to transact business in the EU and the United Kingdom in the future, if we elect to seek to commercialize any of our products there.

### **Risks Related to Our Intellectual Property Rights**

***If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.***

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We may also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents, should they issue; preserve the confidentiality of our trade secrets; and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents. For example, the U.S. Patent and Trademark Office, or U.S. PTO, has issued a final rejection against one of our patent applications claiming one of our proprietary GABA<sub>A</sub> positive allosteric modulator compounds, asserting a lack of novelty and non-obviousness. We are in the process of challenging the rejection, and may not be successful in overturning the rejection.

We may be unable to obtain issued patents covering our proprietary compounds. We cannot provide any assurances that any of our issued patents will be enforceable, or include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, the issued patent and patent applications that provide coverage for ZULRESSO only cover particular formulations and particular methods of using such formulations to treat depressive disorders such as PPD and MDD. As a result, such issued patent and any patent that may issue from such patent applications, would not prevent third-party competitors from creating, making and marketing alternative formulations of brexanolone that fall outside the scope of the patent claims or from practicing alternative methods. Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have

filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, derivation proceedings, *ex parte* reexamination, or *inter partes* review proceedings, post-grant review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. For example, our granted European patent covering brexanolone i.v. has been opposed by a third party, and the opposition proceedings are ongoing. Thus, any patents, should they issue, that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding or a derivation proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. Furthermore, though a patent, if it were to issue, is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability, and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues, and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods.

We also may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the U.S., and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales if any of our product candidates are approved in those countries. Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming, and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering our product or product candidates is invalidated or found unenforceable, our financial position and results of operations may be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations may also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our pending patent applications, if issued as a patent, will include claims having a scope sufficient to protect our current product candidates or any other products or product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to generate significant revenue from sales of ZULRESSO or any of our product candidates, if successfully developed and approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our pending patent applications and any patents that may issue in the future;

- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe any patents that may be issued to us;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents, if issued or as issued, will provide us with a competitive advantage and be found ultimately to be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe upon the patents or proprietary rights of others.

We may rely upon unpatented trade secrets and depend on unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our CROs, collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

***We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing ZULRESSO, zuranolone, if approved, and our other product candidates, if successfully developed and approved.***

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties. The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our products or product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop our current product candidates and commercialize ZULRESSO and any future products, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications which may later result in issued patents that our product or product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Patent litigation is costly and time-consuming. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim were successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product or product candidates. In the case of

trademark claims, if we are found to be infringing, we may be required to redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, CROs, outside scientific collaborators, and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign to us any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution or another party.

Most of our employees have also been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. We may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees which could have a materially adverse effect on our business.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.***

The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other formalities and provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful.***

Even if the patent applications we own or license are issued, competitors may infringe these patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents should be interpreted narrowly and do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings or derivation proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

***Issued patents covering our product or any of our product candidates could be found invalid or unenforceable if challenged in court.***

If we or one of our collaborators or licensors initiated legal proceedings against a third party to enforce a patent, if and when issued, covering our product or any of our product candidates, the defendant could counterclaim that the patent covering our product or any of our product candidates is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness, lack of written description, or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *ex parte* reexamination, *inter partes* review, derivation proceedings or interferences and equivalent proceedings in foreign jurisdictions, e.g., opposition or revocation proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. For example, our granted European patent covering brexanolone i.v. has been opposed by a third party, and the opposition proceedings are ongoing. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on the applicable product or product candidates. Such a loss of patent protection would have a material adverse impact on our business.

***We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

Filing patent applications and prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the U.S., assuming that rights are obtained in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications.

Competitors may use our technologies in jurisdictions where we do not pursue patent protection. They may pursue and obtain their own patent protection to develop their own products. Further, they may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology and pharmaceuticals. For example, a 2022 report from the Office of the U.S. Trade Representative identified a number of countries, including India and China, where challenges to the procurement and enforcement of patent rights have been reported. Several countries, including India and China, have been listed in the report every year since 1989. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights in such jurisdictions. Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could, among other things, result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***For ZULRESSO and certain of our product candidates, we are dependent on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing certain of our products or product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our products, product candidates or technology from third parties or, in certain cases, we fail to meet certain development deadlines, we could lose license rights that are important to our business.***

We are a party to a number of license agreements under which we are granted rights to intellectual property that are important to our business and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. If we fail to obtain a license, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- our right to sublicense patent and other rights to third parties under licenses or collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully commercialize the relevant product or to successfully develop and commercialize the affected product candidates.

We have entered into several licenses to support our various programs. We may enter into additional licenses to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payment, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, the licensor may allege that we have breached our license agreement, and may accordingly seek to terminate our license. In addition, future licensors may decide to terminate their licenses with us at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop a product candidate or commercialize a product, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms, our business could materially suffer.

***Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.***

Some of the intellectual property rights we have licensed may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. For example, some of the intellectual property rights licensed to us under the license agreement with The Regents of the University of California may have been generated using U.S. government funds. As a result, the U.S. government may have certain rights to intellectual property embodied in our current product or current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if the government determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified



time limits. In addition, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

If we enter into future arrangements involving government funding, and we discover compounds or product candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

***If we do not obtain new chemical entity or other types of marketing and data exclusivity for our product candidates and if we do not obtain additional protection under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments, and similar foreign legislation by extending the patent terms of our product candidates, our business may be materially harmed.***

Marketing exclusivity provisions under the Federal Food, Drug, and Cosmetic Act, or FDCA, can delay the submission or the approval of certain marketing applications by other companies for a product with the same active moiety as a product we sell or may in the future sell. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity, or NCE. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovator drug or for another indication, where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for a full NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication or condition of use. We have obtained NCE exclusivity for brexanolone and plan to seek NCE exclusivity for our current and future product candidates. There is no guarantee that our product candidates will qualify for marketing or data exclusivity under these provisions or that such exclusivity for any of our products will alone be sufficient for our business. The applicable five-year and three-year exclusivity periods of NCE or data exclusivity under the FDCA will not delay the submission or approval of a full NDA.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own or license may be eligible for limited patent term restoration in the future under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. Even if, at the relevant time, we have a valid issued patent covering our product, we may not be granted an extension if we were to fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, and we do not have any other exclusivity, our competitors may obtain approval of competing products following our patent expiration and our business, financial condition or results of operations could be adversely affected.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

Our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the U.S. has recently enacted wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, in March 2012, in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the U.S. Supreme Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, in June 2013, in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. In June 2014, in *Alice Corporation Pty. Ltd. v. CLS Bank International, et al.*, a case involving patent claims directed to a method for mitigating settlement risk, the U.S. Supreme Court held that the patent eligibility of claims directed to abstract ideas, products of nature, and laws of nature should be determined using the same framework set forth in *Prometheus*. The U.S. PTO has issued a set of guidelines setting forth procedures for determining subject matter eligibility of claims directed to abstract ideas, products of nature, and laws of nature in line with the *Prometheus*, *Myriad*, and *Alice* decisions. The guidance does not limit the application of *Myriad* to DNA but, rather, applies the decision to other natural products. The full impact of these decisions on our business is not yet known.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

***With passage of the CREATES Act, we are exposed to possible litigation and damages by competitors. In addition, existing statutes, including the CREATES Act, and proposed legislation in Congress, if passed into law, could limit the patent exclusivity on our products or facilitate earlier entry of generic competition.***

Under the CREATES Act, legislation intended to facilitate the development of generic and biosimilar products, we are exposed to possible litigation and damages by competitors who may claim that we are not providing sufficient quantities of our approved products on commercially reasonable, market-based terms for testing in support of their ANDAs and 505(b)(2) applications. Such litigation would subject us to additional litigation costs, damages and reputational harm, which could lead to lower revenues. Increased risk of generic competition with ZULRESSO, zuranolone, if approved, and any of our other product candidates, if approved, including as a result of the CREATES Act, could impact our ability to maximize product revenue.

In addition, members of Congress have proposed numerous legislative initiatives aimed at limiting the patent exclusivity on drug products or facilitating earlier entry of generic versions of approved drugs. Examples of bills that have been proposed include a bill that, if passed, would create a presumption of invalidity for patents beyond the first patent covering a drug product thus shifting the burden to the innovator to prove that these subsequent patents are separately patentable inventions, distinct from the first patent; a bill that, if passed, would empower the Federal Trade Commission to investigate whether large patent portfolios covering a drug product constitute an anti-competitive practice and to file antitrust lawsuits in such instances; and a bill that, if passed, would limit the availability of a 30-month stay on approval by the FDA of a generic version of a drug to only those instances where the ANDA litigation involves a composition of

matter patent claiming the drug substance. Such legislation, if passed into law, could adversely affect ZULRESSO or any future products or result in earlier entry into the market of generic versions of our drugs.

## **Risks Related to our Industry**

### ***Healthcare regulations aimed at reducing healthcare costs may have a material adverse effect on our business or results of operations.***

There have been, and likely will continue to be, legislation and legislative, administrative and regulatory proposals in the U.S., both at the federal and state level, and in many foreign jurisdictions, aimed at reducing healthcare costs. The implementation of cost containment measures, drug pricing controls or other reforms could have an adverse effect on our revenue from ZULRESSO, zuranolone, if approved, or from the sales of any other products that are successfully developed and approved, and may limit our ability to achieve profitability.

For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, provided a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% (pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D (subsequently modified by the IRA, as discussed below).

Certain provisions of the ACA have been subject to judicial challenges as well as efforts to modify them or to alter their interpretation or implementation. For example, the U.S. Tax Cuts and Jobs Act of 2017, signed into law in December 2017, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." We expect that the ACA, its implementation, efforts to challenge or modify the ACA or its implementing regulations, or portions thereof, and other healthcare reform measures that may be adopted in the future, could have a material adverse effect on our industry generally and on our ability to commercialize our product candidates, if approved.

There has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs, including under Medicare and Medicaid, which may potentially impact negotiations on pricing and discounts with commercial payers, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. There have been multiple Congressional and administrative efforts to address drug pricing, including the Inflation Reduction Act of 2022, or IRA. It is unclear whether any other legislation or public policy will come to pass, and if so, what effect it could have on our business.

The IRA was signed into law by President Biden in August 2022. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for certain outpatient prescription drug coverage, as well as Medicare Part B. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare, with negotiated prices subject to a cap and first set to take effect in 2026; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (the first Part B inflation rebate period is in first quarter 2023; the first Part D inflation rebate period is fourth quarter 2022 through third quarter 2023); and replaces the Part D coverage gap discount program with a new Part D discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years of these programs. Manufacturers may be subject to civil monetary penalties for certain violations of the negotiation and inflation rebate provisions and an excise tax during a noncompliance period under the negotiation program.

Specifically, with respect to price negotiations, Congress authorized CMS to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. Drugs may be selected for negotiation only once they are at least seven years post-approval (such that they will be nine years post approval when first subject to the maximum negotiated price) and biologics may be selected for negotiation 11 years post approval (such that they will be 13 years post-approval when first subject to the maximum negotiated price). It does not apply to drugs and biologics that have been approved for a single rare disease or condition. We could be at risk of government action if, in the future, any of our products are the subject of Medicare price negotiations. In that event, the outcome of the Medicare price negotiations, which will be made publicly available, may also impact negotiations on pricing and discounts with commercial payers. These risks as to pricing may further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if the pricing of any of our products are the subject of Medicare price negotiations. As a result, these risks may also impact the development decisions we make with respect to our products.

Further, the IRA subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the IRA by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The IRA also requires manufacturers to pay rebates for drugs reimbursed under Medicare Part D whose price increases exceed inflation and caps Medicare out-of-pocket drug costs beginning in 2025, at \$2,000 a year, subject to an adjustment for inflation thereafter. Drug manufacturers may also be subject to civil monetary penalties with respect to their compliance with these programs. In addition, the IRA potentially raises risks related to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or “catastrophic period” of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by eliminating the coverage gap starting in 2025, reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and imposing price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

It is unclear how the IRA will be implemented. We further cannot predict with certainty what impact the IRA or any other federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition. There may be additional Congressional and administrative efforts to address drug pricing.

At the state level, legislatures have increasingly passed legislation and agencies have implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and price transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at containing or lowering the cost of healthcare or limiting exclusivity periods for pharmaceutical products. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for ZULRESSO and for zuranolone, if approved, or any of our other product candidates, if approved;
- our ability to receive or set a price that we believe is fair for our products;
- our ability to generate revenue and achieve or maintain profitability;
- the amount of taxes that we are required to pay; and
- the availability of capital.

We expect that the measures discussed above, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, lower reimbursement, and new payment methodologies. This could lower the price that we receive for any approved product. Any denial in coverage or reduction in reimbursement from Medicare or other government-funded programs may result in a similar denial or reduction in payments from private payors, which may prevent us from being able to generate sufficient revenue from sales of ZULRESSO, successfully commercialize zuranolone or any other products if approved in the future, and achieve profitability.

***Our internal computer systems or networks, or cloud platforms or those of our collaborators, our third-party CROs or our other contractors, consultants or service providers, may fail or suffer security breaches, which could result in a material disruption of our development programs, compromise personal or sensitive information related to our business, or cause us to incur significant liabilities which could adversely impact our business.***

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business, and despite the implementation of security measures, our internal computer systems and those of our collaborators, our third-party CROs and our other contractors, consultants and service providers are vulnerable to cyber security threats, including damage from unauthorized access, theft, natural disasters, terrorism, war, telecommunication and electrical failures, and system malfunction, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, viruses, worms, denial-of-service attacks, supply chain attacks, social engineering schemes and other means to affect service reliability and threaten the confidentiality, integrity and availability of information). If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs or cause us to have liability for disclosure of personal information of our customers. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory submission and approval efforts and significantly increase our costs to recover or reproduce the data, if possible. To the extent that any disruption, disaster or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed or prevented.

We could be required to expend significant amounts of money and other resources to respond to these threats or breaches and to repair or replace information systems or networks or cloud platforms. We also could suffer financial loss or the loss of valuable confidential information. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive acts or practices in violation of Section 5(a) of the Federal Trade Commission Act, or the FTC Act. The Federal Trade Commission, or the FTC, expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards. The guidance of the FTC for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule, which establishes national standards for covered entities to protect individuals' electronic personal health information. The HIPAA Security Rule requires covered entities to have appropriate administrative, physical and technical safeguards to help ensure the confidentiality, integrity, and security of electronic protected health information. With respect to privacy, the FTC also sets expectations that companies honor the privacy promises made to individuals about how the company handles consumers' personal information. Any failure to honor promises, such as the statements made in a privacy policy or on a website, may also constitute unfair or deceptive acts or practices in violation of the FTC Act. While we do not intend to engage in unfair or deceptive acts or practices, the FTC has the power to enforce promises as it interprets them, and events that we cannot fully control, such as data breaches, may be result in FTC enforcement. Enforcement by the FTC under the FTC Act can result in civil penalties or enforcement actions.

Although we develop and maintain systems and controls designed to prevent these events from occurring and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes are costly and require ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, we cannot guarantee that our, or our third-party CROs' or our other contractors', consultants' or service providers' security measures will be sufficient to prevent data loss and other security

breaches. Despite our efforts, the possibility of these events occurring cannot be eliminated entirely and there can be no assurance that any measures we take will prevent cyber-attacks or security breaches that could adversely affect our business, including security breaches that may remain undetected for extended periods of time, which can substantially increase the potential for a material adverse impact resulting from the breach.

### **Risks Related to Our Financial Position and Need for Capital**

***We are a biopharmaceutical company that has not generated significant revenue to date. We have incurred significant operating losses since our inception, and anticipate that we will incur losses for the foreseeable future.***

We are a biopharmaceutical company with only one approved product, and only began generating revenue from product sales in the second quarter of 2019. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk.

We have funded our operations to date primarily through proceeds from sales of common stock, including the sale of stock to BIMA; redeemable convertible preferred stock prior to our initial public offering and, to a lesser extent, the issuance of convertible notes. From our inception through December 31, 2022, we had received aggregate net proceeds of \$2.8 billion from such transactions. We also received \$1.0 billion in upfront payments under our collaborations with Biogen and Shionogi. As of December 31, 2022, our cash, cash equivalents and marketable securities were \$1.3 billion. We have incurred net losses in each year since our inception, except for net income of \$606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen. Our net loss was \$532.8 million for the year ended December 31, 2022, and our accumulated deficit was \$2.0 billion as of December 31, 2022.

Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We expect our research and development expenses and selling, general and administrative expenses to increase, particularly as we advance planned and ongoing clinical trials for SAGE-718 and SAGE-324 and prepare for the potential commercial launch of zuranolone, including in support of permitted pre-launch and launch-readiness activities associated with zuranolone. In addition, if we obtain marketing approval for zuranolone or any of our other current or future product candidates beyond ZULRESSO, we would expect to incur significant sales, marketing and outsourced-manufacturing expenses. We incur significant legal and accounting costs associated with operating as a public company. We expect to continue to incur additional significant and increasing operating losses for the foreseeable future. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate product revenue and/or revenue from our collaborations on a sustained basis. We began to generate revenue from product sales in the second quarter of 2019 in conjunction with launch of our first product, ZULRESSO, which commenced in June 2019. We expect that our revenue opportunity for ZULRESSO will continue to be limited. Our ability to generate significant product revenue from any future approved product depends on a number of factors, including, but not limited to:

- our ability to successfully obtain marketing approval of zuranolone in the U.S. for the indications and on the timelines we expect;
- our ability to initiate and successfully complete all efficacy and safety clinical trials and non-clinical studies required to file for, and obtain, U.S. and foreign marketing approval for our other product candidates; and our ability to file for and receive marketing approval to commercialize our product candidates, if successfully developed; and
- with respect to zuranolone, if approved, and any other approved product, our ability, alone or with collaborators, to commercialize the product by developing and effectively deploying a sales force, and to achieve market

acceptance and satisfactory reimbursement of such product in the medical community, with patients and with third-party payors.

If we are unable to generate significant product revenue and/or revenue from our collaborations on a sustained basis, we will not become profitable, and may be unable to continue operations without continued funding.

***We may need to raise additional funding at some point in the future, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted.***

We are currently commercializing ZULRESSO, have filed for marketing approval of zuranolone in the U.S. for the treatment of adults with MDD and PPD, have begun our permitted pre-launch and launch-readiness activities associated with the potential approval of zuranolone, and are advancing our other product candidates through non-clinical and clinical development. Commercializing a product and developing additional small molecule products are expensive. We expect our research and development expenses and selling, general and administrative expenses to increase, particularly as we advance planned and ongoing clinical trials for SAGE-718 and SAGE-324 and prepare for the potential commercial launch of zuranolone, including in support of permitted pre-launch and launch-readiness activities associated with zuranolone. We expect we will require additional capital in the future to fund operating needs. We may need to raise additional funds sooner if we choose to pursue additional indications and/or geographies for our product candidates, conduct additional clinical trials for indications we are already pursuing beyond the anticipated trials, identify new potential opportunities or otherwise expand our activities more rapidly than we presently anticipate.

As of December 31, 2022, our cash, cash equivalents and marketable securities were \$1.3 billion. We expect that our existing cash, cash equivalents and marketable securities, in addition to anticipated funding from our ongoing collaborations, excluding revenues and milestones, will be sufficient to fund our anticipated level of operations through 2024. Our current operating plan does not contemplate other development activities we may pursue or that all of the currently planned activities will proceed at the same pace, or that all of the activities will be fully initiated or completed during that time. We may use available capital resources sooner than we expect under our current operating plan. In addition, our operating plan may change. We may need or choose to seek additional funds sooner than planned, through equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances, licensing arrangements and arrangements involving other rights or a combination of these or other approaches. In any event, we anticipate we will require additional capital to expand future development efforts for, obtain regulatory approval for, and to commercialize our product candidates. If current or future economic conditions impact capital markets for an extended period, or if our business prospects are impaired or the capital markets disrupted for any other reason, additional capital may not be available to us on acceptable terms, or at all. Failure to obtain capital if and when needed may force us to delay, limit or terminate our product development efforts or other operations. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations.

We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. In the event we receive negative data from our key clinical programs or encounter other major setbacks in our development or regulatory activities or in our commercialization efforts, our stock price is likely to decline which would make a future financing more difficult and potentially more dilutive to our existing stockholders. For example, after the announcement of the topline results of the Phase 3 MOUNTAIN Study of zuranolone on December 5, 2019, our stock price declined significantly. In addition, future global economic uncertainty, reduced liquidity, capital market disruptions, and other macroeconomic or geopolitical conditions may potentially make it more difficult for us to raise additional funds on favorable terms. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders. The issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The incurrence of indebtedness would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business.

We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, the ownership interest of our stockholders in our company will be diluted. Debt financing, if available, would increase our fixed payment obligations and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved product, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

### **Risks Related to Our Common Stock**

#### ***Market volatility may affect our stock price and the value of an investment in our stock.***

The market price for our common stock, similar to that of other biopharmaceutical companies, is volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

- the success or failure of our efforts to: receive FDA approval of our NDA for zuranolone for the treatment of MDD and PPD on a timely basis or at all;
- the results of our commercialization efforts with respect to zuranolone, if approved, and our ability to attain commercial success;
- plans for, progress of, timing of, changes to, delays in or results from clinical trials or non-clinical studies of any of our product candidates, including positive or negative key data from such studies or clinical trials, serious adverse events arising in the course of development, or any delays or major announcements related to such studies or trials;
- the success or failure of any regulatory activities with respect to our other existing or future product candidates beyond zuranolone;
- announcements of new products, technologies, commercial relationships, acquisitions, collaborations or other events by us or our competitors;
- the success or failure of our therapies;
- regulatory or legal developments in the U.S. and other countries;
- adverse developments with respect to our intellectual property portfolio or failure to obtain or loss of exclusivity;
- failure of our future product candidates, if successfully developed and approved, to achieve commercial success;
- fluctuations in stock market prices and trading volumes of similar companies;
- the state of the U.S. and world economies, general market conditions and overall fluctuations in U.S. equity markets, including as a result of U.S. or world events;
- changes in healthcare laws affecting pricing, reimbursement or access;
- variations in our quarterly operating results;
- changes in our financial guidance or securities analysts' estimates of our financial performance;



- changes in accounting principles;
- our ability to raise additional capital and the terms on which we can raise it;
- the impact of the COVID-19 pandemic and its downstream effects, as well as other macroeconomic trends and geopolitical events;
- sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;
- additions or departures of key personnel;
- discussion of us or our stock price by the press and by online investor communities; and
- other risks and uncertainties described in these risk factors.

***We have broad discretion in how we use our existing cash and the proceeds from potential future follow-on public offerings, and may not use such cash and proceeds effectively, which could affect our results of operations and cause our stock price to decline.***

We have considerable discretion in the use of our cash and the application of the net proceeds from potential future follow-on public offerings. We may use cash and net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from any potential future follow-on offerings in a manner that does not produce income or that loses value.

***Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, even one that may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include a classified board of directors, a prohibition on actions by written consent of our stockholders and the ability of our board of directors to issue preferred stock without stockholder approval. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

***Future sales of our common stock may cause our stock price to decline.***

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock, and impair our ability to raise adequate capital through the sale of additional equity securities. For example, the 6,241,473 shares of our common stock purchased by BIMA were subject to an 18-month lockup period, which expired on June 30, 2022, after which BIMA is able to sell a certain amount of its shares, subject to certain sales and volume limitations, or, if BIMA requests registration of its shares pursuant to its registration rights, without such sales and volume limitations. Following a second 18-month period, which expires December 31, 2023, BIMA will be able to sell shares without limitation.

**Item 1B. Unresolved Staff Comments**

None.

**Item 2. Properties**

Our corporate headquarters are located in Cambridge, Massachusetts. We lease 63,017 square feet of office space in a multi-tenant building pursuant to a lease dated as of December 2011, as amended in March 2019, that will expire on August 31, 2024.

In May 2016, we entered into a lease, as amended in April 2018, under which we rent 40,419 square feet of additional office space in a separate multi-tenant building in Cambridge, Massachusetts. The term for this lease will expire on August 31, 2024.

We have entered into other non-material leases and may lease additional space prior to the expiration of our leases to meet the needs of the business.

**Item 3. Legal Proceedings**

We may from time to time become involved in legal proceedings relating to claims arising from our ordinary course of business, including claims related to contracts, employment arrangements, operating activities, intellectual property or other matters. We are not currently subject to any legal proceeding that we believe would have a material adverse impact on our financial position, results of operations or cash flows or other material legal proceeding.

**Item 4. Mine Safety Disclosures**

Not applicable.

**Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities****Market Information**

On July 18, 2014, our common stock began trading on the Nasdaq Global Market under the symbol “SAGE”. Prior to that time, there was no public market for our common stock.

**Stockholders**

As of February 8, 2023, there were six stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

**Performance Graph**

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since January 1, 2018 through December 31, 2022, to two indices: the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes an initial investment of \$100 on December 31, 2017 in our common stock, the stocks comprising the Nasdaq Composite Index, and the stocks comprising the Nasdaq Biotechnology Index. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.



\* \$100 invested on December 31, 2017 in stock or index.

The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Annual Report into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

**Dividend Policy**

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

**Issuer Purchases of Equity Securities**

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

**Item 6. [Reserved]**

## Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K, for the year ended December 31, 2022, or Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. We caution you that forward-looking statements are not guarantees of future performance, and that our actual results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate, may differ materially from the results discussed or projected in the forward-looking statements contained in this Annual Report. We discuss risks and other factors that we believe could cause or contribute to these potential differences elsewhere in this Annual Report, including under Part I, Item 1A, "Risk Factors" and under "Cautionary Note Regarding Forward-Looking Statements" in this Annual Report. In addition, even if our results of operations, financial condition and liquidity, and the developments in our business and the industry in which we operate are consistent with the forward-looking statements contained in this Annual Report, they may not be predictive of results or developments in future periods. We caution readers not to place undue reliance on any forward-looking statements made by us, as such statements speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, or SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.*

*Information pertaining to fiscal year 2020 was included in the Company's Annual Report on Form 10-K for the year-ended December 31, 2021, on pages 89 through 110, under Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations," which was filed with the SEC on February 24, 2022.*

### Overview

We are a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. We are currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry. Our focus as a company is on brain health, and we are currently targeting two critical central nervous system, or CNS, receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of GABA<sub>A</sub> receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders.

Our first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. for the treatment of postpartum depression, or PPD, in adults. We launched ZULRESSO commercially in the U.S. for the treatment of PPD in June 2019. ZULRESSO may only be administered in qualified, medically-supervised healthcare settings. Brexanolone is chemically identical to allopregnanolone, a naturally occurring neuroactive steroid that acts as a positive allosteric modulator of GABA<sub>A</sub> receptors.

We also are developing a portfolio of other novel compounds that target GABA<sub>A</sub> receptors including our most advanced product candidate, zuranolone (SAGE-217). Zuranolone is a novel oral compound for the treatment of major depressive disorder, or MDD, and PPD. In December 2022, we, and our collaboration partner, Biogen, completed submission of a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, seeking approval of zuranolone for the treatment of both MDD and PPD. The NDA was accepted for filing and granted priority review by the FDA in February 2023, with a Prescription Drug User Fee Act, as amended, or PDUFA, target action date of August 5, 2023. The FDA granted Fast Track designation to zuranolone for the treatment of PPD in early 2022 and previously granted zuranolone Breakthrough Therapy designation and Fast Track designation to zuranolone for the treatment of MDD. Zuranolone is a neuroactive steroid that, like brexanolone, is a positive allosteric modulator of GABA<sub>A</sub> receptors, targeting both synaptic and extrasynaptic GABA<sub>A</sub> receptors. We may in the future develop zuranolone for other affective disorders.

To date, we have completed six pivotal clinical trials of zuranolone, four in MDD and two in PPD. The completed pivotal trials evaluating zuranolone for the treatment of PPD and three of the four completed pivotal trials evaluating

zuranolone for the treatment of MDD met their primary endpoints. We announced results from the following clinical trials of zuranolone in either 2021 or 2022:

- **SKYLARK Study (completed)**

In June 2022, we announced that the SKYLARK Study, a Phase 3 placebo-controlled clinical trial evaluating a two-week course of zuranolone 50 mg in women with PPD, met its primary and all key secondary endpoints.

- **CORAL Study (completed)**

In February 2022, we announced that the CORAL Study, a placebo-controlled Phase 3 clinical trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with a newly administered open-label standard antidepressant therapy, or ADT, compared with open-label standard of care ADT co-initiated with placebo, as an acute rapid response treatment in patients with MDD, met its primary endpoint and key secondary endpoint.

- **WATERFALL Study (completed)**

In June 2021, we announced that the WATERFALL Study, a pivotal, Phase 3, double-blind, randomized, placebo-controlled clinical trial evaluating the efficacy and safety of zuranolone 50 mg in adults aged 18 to 64 years with MDD, met its primary endpoint.

- **SHORELINE Study (ongoing)**

In March and December 2021, we reported positive topline 12-month data from both the 30 mg cohort and a portion of the 50 mg cohort of the SHORELINE Study, an open-label Phase 3 clinical trial of zuranolone in MDD, which is designed to evaluate the safety, tolerability, and need for repeat dosing of zuranolone in adults for up to one year. Enrollment in the 50 mg cohort of the study has been completed and the study is ongoing.

We are jointly developing zuranolone and another of our late-stage compounds, SAGE-324, in the U.S. with Biogen MA Inc., or BIMA, and Biogen International GmbH, or, together with BIMA, Biogen, under a collaboration and license agreement, or the Biogen Collaboration Agreement, that became effective in December 2020.

Under the Biogen Collaboration Agreement, we will also jointly commercialize products containing zuranolone, which we refer to as Licensed 217 Products, and products containing SAGE-324, which we refer to as Licensed 324 Products, with Biogen in the U.S. if our development efforts are successful. We refer to the Licensed 217 Products and Licensed 324 Products collectively as the Licensed Products. In addition, we have granted Biogen sole rights to develop and commercialize the Licensed Products outside the U.S., other than in Japan, Taiwan and South Korea, or the Shionogi Territory, with respect to zuranolone, where we have granted such rights to Shionogi & Co., Ltd., or Shionogi. We refer to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the Biogen Territory.

We also have a collaboration agreement with Shionogi for the development of zuranolone in the Shionogi Territory. In September 2021, Shionogi reported completion of a Phase 2 clinical trial of zuranolone for the treatment of patients with moderate to severe MDD in Japan, which Shionogi reported achieved its primary endpoints. Shionogi has also reported that it is conducting two Phase 3 trials of zuranolone for the treatment of patients with moderate to severe MDD as a monotherapy and as an add-on to other antidepressants, and announced that, pending results from these trials, it is aiming to submit an NDA to the Pharmaceuticals and Medical Devices Agency in Japan in the first quarter of 2024 seeking approval of zuranolone for the treatment of MDD.

SAGE-324 is a novel GABA<sub>A</sub> receptor positive allosteric modulator intended for chronic oral dosing. In April 2021, we and Biogen announced that our placebo-controlled Phase 2 KINETIC Study evaluating SAGE-324 for the treatment of adults with essential tremor had achieved its primary endpoint. We are currently enrolling patients with essential tremor in a Phase 2b dose-ranging clinical trial of SAGE-324, known as the KINETIC 2 Study. In May 2022, we also initiated an open-label Phase 2 clinical trial designed to evaluate the long-term safety and tolerability of SAGE-324 in patients with essential tremor, with incidence of treatment-emergent adverse events as the primary endpoint. This is intended to be a multi-year clinical trial, and will initially be open to rollover patients from other SAGE-324 clinical trials in patients with essential tremor, including the KINETIC 2 Study. We believe SAGE-324 also has potential for the treatment of a number

of other neurological conditions, including epilepsy and Parkinson's disease. Additional development plans for SAGE-324 will be determined as part of our strategic collaboration with Biogen.

Our second area of focus for development is novel compounds that target the NMDA receptor. Our lead product candidate selected in this area is SAGE-718, an oxysterol-based positive allosteric modulator of the NMDA receptor, which we are exploring in certain cognition-related disorders associated with NMDA receptor dysfunction, including cognition dysfunction associated with diseases such as Huntington's disease, Parkinson's disease and Alzheimer's disease.

The FDA has granted SAGE-718 Fast Track designation as a potential treatment for patients with Huntington's disease. SAGE-718 is currently being studied in three ongoing clinical trials in patients with Huntington's disease cognitive impairment:

- **DIMENSION Study**

In February 2022, dosing commenced in the DIMENSION Study, a double-blind placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment. The DIMENSION Study is designed to evaluate the efficacy of once-daily dosed SAGE-718 over three months.

- **SURVEYOR Study**

In March 2022, we initiated the SURVEYOR Study, a placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with Huntington's disease cognitive impairment, with a healthy volunteer component, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.

- **PURVIEW Study**

In December 2022, we initiated the PURVIEW Study, a Phase 3 open-label study to evaluate the long-term safety and tolerability of SAGE-718 in patients with Huntington's disease cognitive impairment.

We are also evaluating SAGE-718 for the treatment of cognitive issues associated with Parkinson's disease and Alzheimer's disease. In May 2021, we announced results from the first part of a Phase 2a open-label study of SAGE-718 evaluating patients with mild cognitive impairment due to Parkinson's disease, known as the PARADIGM Study. Data from the PARADIGM Study showed that SAGE-718 had a positive impact on multiple domains of cognition, including executive function and learning and memory. As expected, no appreciable effect was observed on measures of simple attention or reaction time in keeping with the profile of SAGE-718 based on data to date. We have completed a four-week dosing cohort in the PARADIGM Study to gather additional data in the Parkinson's disease patient population and presented results in October 2022. In March 2022, we initiated a double-blind, placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease, known as the PRECEDENT Study. The PRECEDENT Study is designed to evaluate the safety and efficacy of SAGE-718 in patients with mild cognitive impairment due to Parkinson's disease over 42 days, followed by a controlled follow-up period.

In December 2021, we reported topline data from a Phase 2a open-label clinical trial of SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease, known as the LUMINARY Study. Data from the LUMINARY Study showed treatment with SAGE-718 resulted in consistent improvement across multiple tests of executive performance, as well as improvement on key tests of learning and memory. SAGE-718 has been well-tolerated in studies to date. In December 2022, we initiated the LIGHTWAVE Study, a randomized placebo-controlled Phase 2 clinical trial of SAGE-718 in patients with mild cognitive impairment and mild dementia due to Alzheimer's disease.

We have other programs at earlier stages of development with a focus on both acute and chronic brain health disorders. We expect to continue our work on allosteric modulation of the GABA<sub>A</sub> and NMDA receptor systems in the brain. The GABA<sub>A</sub> and NMDA receptor systems are broadly accepted as impacting many psychiatric and neurological disorders, spanning disorders of mood, seizure, cognition, anxiety, sleep, pain, and movement, among others. We believe that we may have the opportunity to develop molecules from our internal portfolio with the goal of addressing a number of these disorders in the future. We also believe that we may have the opportunity to use our scientific approach to explore targets beyond the GABA<sub>A</sub> and NMDA receptor systems and to develop compounds in areas of unmet need outside of brain health.

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO, in June 2019. In the fourth quarter of 2020, we recorded revenue from the strategic collaboration with and stock purchase by Biogen.

We have incurred net losses in each year since our inception, except for net income of \$606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement, and we had an accumulated deficit of \$2.0 billion as of December 31, 2022. Our net losses were \$532.8 million and \$457.9 million for the years ended December 31, 2022 and 2021, respectively. These losses have resulted principally from costs incurred in connection with research and development activities and selling, general and administrative costs associated with our operations and our commercial build. We expect to incur significant expenses and increasing operating losses for the foreseeable future.

We expect that our expenses will increase in the foreseeable future in connection with our ongoing activities, including if and as we:

- continue our development efforts for zuranolone, including work to complete the open-label SHORELINE Study of zuranolone in MDD; advance our permitted pre-launch and launch-readiness activities with respect to zuranolone, and commercialize zuranolone in MDD and PPD, if approved; and potentially advance the development of zuranolone in additional indications as part of our strategic collaboration with Biogen;
- continue our commercialization efforts with respect to ZULRESSO for the treatment of PPD in the U.S., with a primary focus on geographies that have existing, active ZULRESSO treating sites;
- complete the ongoing and planned clinical trials of SAGE-324 as part of our strategic collaboration with Biogen;
- complete ongoing and planned clinical trials of SAGE-718;
- support our collaboration with Biogen with respect to zuranolone and SAGE-324 in the U.S., and support Biogen's development of zuranolone and SAGE-324 in Biogen's licensed territories outside the U.S. and Shionogi's development of zuranolone in the Shionogi Territory;
- advance our earlier-stage compounds;
- continue our research and development efforts to evaluate the potential for our existing product candidates for the treatment of additional indications or in new formulations;
- identify new targets, and generate and test new compounds and product candidates, with a focus on indications where we believe we can make well-informed, rapid go/no-go decisions, with the goal of developing a diversified portfolio of assets with differentiated features;
- prepare and file NDAs with the FDA and conduct permitted pre-launch activities with respect to any of our other product candidates that we believe have been successfully developed;
- commercialize any product candidates for which we obtain regulatory approval, including the manufacture of commercial supplies;
- continue to add personnel at the appropriate time, as our efforts and activities progress, including personnel to support ongoing zuranolone commercialization efforts, such as launch planning, permitted payor engagements, scientific exchange, disease awareness education, and ongoing product development, and to support launch of zuranolone in MDD and PPD, if approved;
- evaluate the market potential and regulatory pathways for our product candidates beyond zuranolone and SAGE-324 in the European Union and other jurisdictions outside the U.S., and determine how best to move forward where and when it may make business and strategic sense;
- continue to build, maintain, defend, leverage, and expand our intellectual property portfolio, including by utilizing the strengths of our proprietary chemistry platform and scientific know-how to expand our portfolio of new chemical entities to lessen our long-term reliance on the success of any one program and to facilitate long-term growth; and



- continue to explore opportunities to establish licenses, collaborations or other agreements or alliances with other biotechnology and pharmaceutical companies, at the appropriate time, where we believe a collaboration will add significant value to our efforts, including through capabilities, infrastructure, speed or financial contributions, or to acquire new compounds, product candidates or products if we believe such opportunities will help us achieve our goals or meet other strategic objectives.

Until such time that we can generate significant revenue on a sustained basis from product sales and/or from collaborations, if ever, we expect to finance our operations primarily through a combination of revenue, equity or debt financings and other sources, including our collaborations with Biogen and Shionogi and potential future collaborations. We may not be successful in our commercialization of ZULRESSO, zuranolone, if approved, or any other product, and may not generate meaningful revenue or revenue at the levels or on the timing necessary to support our investment and goals. We may never successfully complete development of any of our current or future product candidates, successfully file for or obtain necessary regulatory approval for such product candidates, or achieve commercial viability for any resulting approved product. We may not obtain or maintain adequate patent protection or other exclusivity for our products or product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. Our inability to raise capital if and when needed would have a negative impact on our financial condition and on our ability to pursue our business strategy. Arrangements with our existing collaborators have required us to relinquish rights to certain of our technologies or product candidates, and any future collaborations may require us to relinquish additional rights. We will need to generate significant revenue to achieve profitability, and we may never do so.

We expect that our existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to anticipated funding from our ongoing collaborations, excluding revenues and milestones, will enable us to fund our operating expenses and capital expenditure requirements through 2024. See “—Liquidity and Capital Resources”.

### Revenue

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO as a treatment for PPD, in June 2019.

Our revenue from sales of ZULRESSO has been negatively impacted by significant barriers arising from the complex requirements for administration of the treatment and by the COVID-19 pandemic. ZULRESSO is administered as a continuous infusion given over two and a half days. Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness during the ZULRESSO infusion, ZULRESSO must be administered only in a medically-supervised healthcare setting that has been certified under a Risk Evaluation and Mitigation Strategies, or REMS, program and meets the other requirements of the REMS program, including requirements related to monitoring of the patient during the infusion. The actions required for a healthcare setting to be ready and willing to treat women with PPD are complex and time-consuming. These actions include: becoming REMS-certified; achieving formulary approvals; establishing protocols for administering ZULRESSO; and securing satisfactory reimbursement. Sites must often negotiate reimbursement on a payor-by-payor basis under commercial coverage. These requirements are expected to continue to limit future ZULRESSO revenue growth.

These barriers have been compounded by the COVID-19 pandemic, its related disruptive effects on the U.S. healthcare system, and other changes to the macroeconomic environment. The spread of COVID-19 in the U.S. resulted in a significant number of sites of care pausing, limiting or delaying treatment of new patients with ZULRESSO and potential new sites of care pausing site activation activities for a period of time. We believe that, at certain points during the pandemic, concerns about exposure to the virus or its variants caused a significant and sustained reduction in the number of women with PPD seeking treatment with ZULRESSO and in the number of physicians willing to prescribe it, and that difficulties in accessing treatment with ZULRESSO have since been compounded by healthcare staffing shortages and other changes to the macroeconomic environment. Given the ongoing disruption to the healthcare system in the U.S., including as a result of staffing shortages, we cannot predict for how long and to what extent ZULRESSO sales will be adversely impacted by these factors.

Our ZULRESSO commercial operations, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We expect that this approach to our commercial efforts will continue to substantially limit the revenue opportunity for ZULRESSO.

We expect that ZULRESSO revenues are likely to fluctuate quarter to quarter. We will not generate revenue from other products unless and until we or any of our collaborators successfully develop, obtain regulatory approval of, and commercialize one of our current or future product candidates. If we enter into additional collaboration agreements with third parties for our product candidates, we may generate revenue from those collaborations. We expect that revenue, if any, that we may generate under our existing or future collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services, milestone payments, royalties paid to us and our share of collaboration profits or losses resulting from sales of any commercialized products, and other payments.

In June 2018, we entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of MDD and other potential indications in the Shionogi Territory. Under the terms of the agreement, Shionogi is responsible for all clinical development, regulatory filings and commercialization and manufacturing of zuranolone for MDD, and potentially other indications, in the Shionogi Territory. In October 2018, we also entered into a supply agreement with Shionogi under which we supply Shionogi with zuranolone clinical material. To date, revenue from our collaboration with Shionogi has come from an initial, upfront license fee upon execution of the collaboration agreement of \$90.0 million, which was recorded as collaboration revenue in the year ended December 31, 2018, and for the supply of active pharmaceutical agreement, or API, for Shionogi's clinical trials.

In November 2020, we entered into the Biogen Collaboration Agreement with Biogen for the development, manufacture and commercialization of the Licensed Products. In connection with the execution of the Biogen Collaboration Agreement, we also entered into a stock purchase agreement for the sale and issuance to BIMA of

6,241,473 shares of our common stock for aggregate consideration of \$650.0 million. The Biogen Collaboration Agreement became effective in December 2020, and the sale of the common stock under the stock purchase agreement closed on December 31, 2020. As a result of the purchase of common stock by BIMA, Biogen has become a related party of ours. Under the terms of the Biogen Collaboration Agreement, we will jointly develop and, if successful, jointly commercialize the Licensed Products in the U.S., and Biogen solely will develop and commercialize the Licensed Products in the Biogen Territory. We and Biogen have agreed to share equally all costs for activities, as well as the profits and losses, upon FDA approval of the Licensed Products, under the Biogen Collaboration Agreement solely for the U.S. Biogen is solely responsible for all costs for activities under the Biogen Collaboration Agreement in the Biogen Territory. Biogen will be the principal and record sales of SAGE-217 products globally. We will be the principal and record sales of SAGE-324 products in the U.S. and Biogen will record sales of SAGE-324 Products in the Biogen Territory. In the year ended December 31, 2020, we recorded collaboration revenue – related party of \$1.1 billion, consisting of an upfront payment of \$875.0 million plus \$232.5 million in excess proceeds from the equity investment under the stock purchase agreement, when measured at fair value. For further discussion regarding the accounting for the Biogen Collaboration Agreement, refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

### **Collaborative Arrangements**

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of Accounting Standards Codification, or ASC, Topic 808, *Collaborative Arrangements*, or Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of ASC Topic 606, *Revenue from Contracts with Customers*, or Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step revenue recognition model and present the arrangement as collaboration revenue in the consolidated statements of operations and comprehensive income (loss).

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship, instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate. For further discussion regarding the accounting for collaborative arrangements, refer to Note 6, *Collaboration Agreements*, in the accompanying Notes to Consolidated Financial Statements appearing elsewhere in this Annual Report.

### **Cost of Goods Sold**

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party manufacturing costs, packaging services, freight, third-party royalties payable on our net product revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the high-single digit to low-double digits percentage range for the foreseeable future. We expect to utilize zero-cost inventory with respect to ZULRESSO for an extended period of time.

## Operating Expenses

Our operating expenses consist primarily of costs associated with research and development activities and selling, general and administrative activities.

### Research and Development Expenses

Research and development expenses, which consist primarily of costs associated with our product research and development efforts, are expensed as incurred. Research and development expenses consist primarily of:

- personnel costs, including salaries, benefits, stock-based compensation and travel expenses, for employees engaged in research and development functions;
- expenses incurred under agreements with contract research organizations, or CROs, and sites that conduct our non-clinical studies and clinical trials;
- expenses associated with manufacturing materials for use in non-clinical studies and clinical trials and developing external manufacturing capabilities;
- costs of outside consultants engaged in research and development activities, including their fees and travel expenses;
- other expenses related to our non-clinical studies and clinical trials and expenses related to our regulatory activities, including the rolling NDA submission for zuranolone for the treatment of MDD and PPD which we completed in December 2022, as well as preparation for a potential FDA Advisory Committee meeting in connection with such filing;
- payments made under our third-party license agreements; and
- a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. Payments to or reimbursements from Biogen related to the co-development and co-manufacturing activities are accounted for as an increase to or reduction of research and development expense. During the years ended December 31, 2022 and 2021, we recorded net reimbursement of \$73.2 million and \$79.8 million, respectively, from Biogen that was deducted from our research and development expenses because we incurred a greater amount of these expenses than Biogen.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We have been developing our product candidates and focusing on other research and development programs, including exploratory efforts to identify new compounds, target validation for identified compounds and lead optimization for our earlier-validated programs. Our direct research and development expenses are tracked on a program-by-program basis, and consist primarily of external costs, such as fees paid to investigators, central laboratories, CROs and contract manufacturing organizations, in connection with our non-clinical studies and clinical trials; third-party license fees related to our product candidates; and fees paid to outside consultants who perform work on our programs. We do not allocate employee-related costs and other indirect costs to specific research and development programs because these costs are deployed across multiple product programs under research and development and, as such, are separately classified as unallocated or stock-based compensation in research and development expenses.

Research and development activities are central to our business. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will

continue to increase in the foreseeable future as we continue or initiate clinical trials and non-clinical studies for certain product candidates and pursue later stages of clinical development of our product candidates.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates. The duration, costs, and timing of clinical trials and development of our product candidates will depend on a variety of factors, including:

- the scope, size, rate of progress, and expense of our ongoing as well as any additional clinical trials, non-clinical studies, and other research and development activities;
- future results of ongoing, planned or future clinical trials and non-clinical studies;
- decisions by regulatory authorities related to our product candidates;
- uncertainties in clinical trial enrollment rate or design;
- significant and changing government regulation; and
- the receipt and timing of regulatory approvals, if any.

In addition, the COVID-19 pandemic and its downstream effects, such as healthcare and vendor staffing shortages and disruption to the U.S. healthcare system, and/or the impact of other macroeconomic and geopolitical conditions, may also negatively impact our ongoing and planned development activities and increase our research and development costs. Concerns, precautions and restrictions, staffing shortages, or other changes to the macroeconomic environment, or from continuing concerns about the COVID-19 pandemic, may substantially slow clinical site identification and activation and enrollment in our clinical trials, may impair or delay the conduct, auditing, monitoring, or completion of our trials, may impair or impede the timeliness and completion of our data collection and analysis efforts or the integrity of our data, or may cause us to pause trials, in each case which may significantly impact our ability to meet our expected timelines or cause us to change our plans and may significantly increase our research and development costs. For example, we have experienced slower than anticipated recruitment in certain clinical trials, including our ongoing KINETIC 2 Study of SAGE-324 in patients with essential tremor, for which we now expect to complete enrollment in late 2023, rather than in late 2022 as we had initially projected.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate or for regulatory approval, or if we experience significant delays in enrollment in any of our clinical trials or need to enroll additional patients, we could be required to expend significant additional financial resources and time on the completion of clinical development.

Any failure to complete any stage of the development of any potential product candidates in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with not completing our programs on schedule, or at all, and the potential consequences of failing to do so, are set forth in Part I, Item 1A of this Annual Report under the heading “Risk Factors”.

### **Selling, General and Administrative Expenses**

Selling, general and administrative expenses consist primarily of personnel costs, including salaries, benefits and travel expenses for our executive, finance, business, commercial, corporate development and other administrative functions, and stock-based compensation expense. Selling, general and administrative expenses also include professional fees for expenses incurred under agreements with third parties relating to the commercialization of ZULRESSO; permitted pre-launch and launch-readiness activities related to zuranolone; public relations, audit, tax and legal services, including legal expenses to pursue patent protection of our intellectual property; and a portion of our information technology, facilities and other related expenses, including rent, depreciation, maintenance of facilities, insurance and supplies.

Our ongoing commercial efforts with respect to ZULRESSO, including our account management field-based team and sales representatives, are primarily focused on geographies that have existing, active ZULRESSO treating sites. We

expect to continue to incur significant commercialization expenses, including payroll and related expenses, to support our ongoing commercial activities associated with ZULRESSO. We expect that selling, general and administrative expenses will increase significantly in the future as we prepare for potential commercialization of zuranolone, engage in permitted pre-approval activities, recruit, train, and retain a direct sales force and commercialize zuranolone, if approved, and as we progress development efforts of our other current or future product candidates and commercialize those products, if successfully developed and approved. We expect to continue to incur significant expenses associated with general operations, including costs related to accounting and legal services, director and officer insurance premiums, facilities and other corporate infrastructure and office-related costs, such as information technology costs.

We consider the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as we and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. Payments to or reimbursements from Biogen related to the co-commercialization activities are accounted for as an increase to or reduction of selling, general and administrative expense. During the years ended December 31, 2022 and 2021, we recorded net reimbursement of \$2.2 million and \$11.3 million, respectively, from Biogen that was deducted from our selling, general and administrative expenses because we incurred a greater amount of these expenses than Biogen.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the U.S. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amount of assets, liabilities, revenue, costs and expenses, and related disclosures. We believe that the estimates and assumptions involved in the accounting policies described below may have the greatest potential impact on our consolidated financial statements and, therefore, consider these to be our critical accounting policies. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions. While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

#### ***Revenue Recognition***

We generate revenue from the sale of ZULRESSO, which was approved by the FDA in March 2019 and we subsequently began selling in June 2019, and from collaboration and supply agreements with our collaborators. To date, revenue from collaboration agreements has come from initial, upfront payments allocated to licenses of intellectual property delivered to our collaborators and from the supply of material for clinical trials under a supply agreement.

Under ASC Topic 606, *Revenue from Contracts with Customers*, or Topic 606, an entity recognizes revenue when or as performance obligations are satisfied by transferring control of promised goods or services to a customer, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. We assess if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

For contracts determined to be within the scope of Topic 606, we assess whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether

such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

We allocate the transaction price (the amount of consideration we expect to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognize the associated revenue when (or as) each performance obligation is satisfied. Our estimate of the transaction price for each contract includes all variable consideration to which we expect to be entitled.

#### *Collaboration and License Revenue*

In assessing whether a promised good or service is distinct in the evaluation of a collaboration or license arrangement subject to Topic 606, we consider factors such as the research, manufacturing and commercialization capabilities of the collaboration partner, and the availability of the associated expertise in the general marketplace. We also consider the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, we are required to combine that good or service with other promised goods or services until we identify a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices, or SSP, on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, we may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. We validate the SSP for performance obligations by evaluating whether changes in the key assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, we estimate the amount of consideration to which we will be entitled in exchange for transferring the promised goods or services to a customer. We determine the amount of variable consideration by using the expected value method or the most likely amount method. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, we adjust consideration for the effects of the time value of money if the timing of payments provides us with a significant benefit of financing. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. We assessed our arrangements with Shionogi and Biogen and concluded that a significant financing component does not exist for either arrangement. For arrangements with licenses of intellectual property that include sales-based royalties or milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties or milestone payments relate, we recognize royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty or milestone payment has been allocated has been satisfied.

We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is

based on the use of an output or input method. Revenue from our collaboration agreement with Shionogi has come from initial, upfront consideration upon execution of the agreement and for the supply of drug product for Shionogi clinical trials. Revenue from our collaboration agreement with Biogen has come from initial, upfront consideration related to the execution of the Biogen Collaboration Agreement. For additional information, refer to Note 6, *Collaboration Agreements*, to our consolidated financial statements appearing elsewhere in this Annual Report.

#### *Product Revenue, Net*

We recognize product revenues, net of variable consideration related to certain allowances and accruals that are determined using the expected value method, in our consolidated financial statements at the point in time when control transfers to the customer, which is typically when the product has been delivered to the customer's location. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. Our only performance obligation identified for ZULRESSO is to deliver the product to the location specified by the customer's order. We record shipping and handling costs associated with delivery of product to our customers within selling, general and administrative expenses on our consolidated statements of operations and comprehensive income (loss). We expense incremental costs of obtaining a contract as incurred if the expected amortization period of the asset would be less than one year. If we were to incur incremental costs with an amortization period greater than a year, such costs would be capitalized as contract assets, as they are expected to be recovered, and would be expensed by amortizing on a systematic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. We did not have any contract assets (unbilled receivables) at December 31, 2022, as customer invoicing generally occurs before or at the time of revenue recognition. We did not have any contract liabilities at December 31, 2022, as we did not receive any payments in advance of satisfying our performance obligations to our customers. Amounts billed or invoiced that are considered trade accounts receivable are included in prepaid expenses and other current assets on the consolidated balance sheets. As of December 31, 2022 and 2021, the Company had not provided any allowance for bad debts against the trade accounts receivable, and the amount of trade accounts receivable was not significant.

We record reserves, based on contractual terms, for the following components of variable consideration related to product sold during the reporting period, as well as our estimate of product that remains in the distribution channel inventory of our customers at the end of the reporting period. On a quarterly basis, we update our estimates, if necessary, and record any material adjustments in the period they are identified.

*Chargebacks:* We estimate chargebacks from our customers who directly purchase the product from us for discounts resulting from contractual commitments to sell products to eligible healthcare settings at prices lower than the list prices charged to our customers. Customers charge us for the difference between what they pay to us for the product and the selling price to the eligible healthcare settings. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at the end of each reporting period that we expect will be sold to eligible healthcare settings, and chargebacks that customers have claimed, but for which we have not yet issued a credit.

*Government Rebates:* We are subject to discount obligations under government programs, including Medicaid. We record reserves for rebates in the same period the related product revenue is recognized, resulting in a reduction of ZULRESSO product revenue and a current liability that is included in accrued expenses on our consolidated balance sheets. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

*Trade Discounts and Allowances:* We generally provide customary invoice discounts on ZULRESSO sales to our customers for prompt payment and we pay fees for sales order management, data, and distribution services. We estimate our customers will earn these discounts and fees and deduct these discounts and fees in full from gross ZULRESSO revenue and accounts receivable at the time we recognize the related revenue.

*Financial Assistance:* We provide voluntary financial assistance programs to patients with commercial insurance that have coverage and reside in states that allow financial assistance. We estimate the financial assistance amounts for ZULRESSO and record any such amounts within accrued expenses on the consolidated balance sheets. The calculation of the accrual for financial assistance is based on an estimate of claims and the cost per



claim that we expect to receive using demographics for patients who have registered and been approved for assistance. Any adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included as a component of accrued expenses on the consolidated balance sheets.

*Product Returns:* Consistent with industry practice, we offer product return rights to customers for damaged, defective or expiring product, provided it is within a specified period around the product expiration date as set forth in our return goods policy. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reserve within accrued expenses on our consolidated balance sheets. Product returns have been not significant to date and are not expected to be significant in the future.

### ***Collaborative Arrangements***

We analyze our collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, *Collaborative Arrangements*, or Topic 808. This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, we first determine which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, we apply the five-step model described above and presents the arrangement as collaboration revenue in the consolidated statements of operations and comprehensive income (loss).

For collaboration arrangements that are within the scope of Topic 808, we evaluate the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense, in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel and vendors to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research and development services on our behalf;
- other providers in connection with clinical trials;
- vendors in connection with non-clinical development activities; and
- vendors related to product manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. There may be instances in

which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. When determining accruals, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting expenses that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

### **Stock-Based Compensation**

We recognize compensation expense for stock-based awards, including grants of stock options and restricted stock units, granted to employees, non-employee directors and non-employee consultants based on the estimated fair value on the date of grant, over the requisite service period. We recognize stock-based compensation expense for only the portion of awards that are expected to vest.

For awards that vest upon achievement of a performance condition, we recognize compensation expense when achievement of the performance condition is met or during the period from which meeting the condition is deemed probable until the expected date of meeting the performance condition, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

The fair value of each stock option grant is estimated using the Black-Scholes option-pricing model. Effective January 1, 2020, we began using the historical volatility of only our common stock, as there is adequate historical data for the duration of the expected term.

The expected term of the stock options granted to employees, non-employee directors and non-employee consultants by us has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" stock options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the date of grant for time periods approximately equal to the expected term of the award. The expected dividend yield is zero, based on the fact that we have never paid cash dividends and do not expect to pay any cash dividends in the foreseeable future.

We also apply a forfeiture rate in order to calculate stock-based compensation expense. Expected forfeitures are based on our historical experience and management's expectations of future forfeitures. To the extent actual forfeitures differ from the estimates, the difference is recorded as a cumulative adjustment in the period in which the estimates are revised.

The fair value of each stock option granted under our equity plans has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected dividend yield	0%	0%	0%
Expected volatility	73%	76%	78%
Risk-free interest rate	2.49%	0.63%	0.97%
Expected term	6.03 years	5.92 years	5.98 years

These assumptions represented our best estimates, but the estimates involve inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates when valuing our stock options, our stock-based compensation expense could be materially different. In developing a forfeiture rate estimate for pre-vesting forfeitures, we have considered our historical experience of actual forfeitures. In the future, if our actual forfeiture rate is materially different from our estimate, then our stock-based compensation expense could be significantly different from what we have recognized in the current period.

As of December 31, 2022, we had unrecognized stock-based compensation expense related to our outstanding and unvested time-based stock option awards of \$61.0 million, which is expected to be recognized over the remaining weighted average vesting period of 2.94 years.

As of December 31, 2022, 650,000 performance-based stock options were both outstanding and unvested, the total unrecognized stock-based compensation expense related to these awards was \$8.2 million and the timing of recognition of this stock-based compensation expense is subject to our judgment as to when the performance conditions are considered probable of being achieved.

As of December 31, 2022, 160,403 time-based restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was \$5.0 million.

As of December 31, 2022, 1,255,078 performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was \$62.4 million.

### ***Recently Issued Accounting Pronouncements***

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is set forth in Note 2, Summary of Significant Accounting Policies, to the consolidated financial statements appearing elsewhere in this Annual Report.

## **Results of Operations**

### ***Comparison of the Years Ended December 31, 2022 and 2021***

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	<u>Year Ended December 31,</u>		<u>Increase (Decrease)</u>
	<u>2022</u>	<u>2021</u> (in thousands)	
Product revenue, net	\$ 7,686	\$ 6,308	\$ 1,378
Operating costs and expenses:			
Cost of goods sold	813	553	260
Research and development	326,163	283,166	42,997
Selling, general and administrative	227,699	183,498	44,201
Total operating costs and expenses	554,675	467,217	87,458
Loss from operations	(546,989)	(460,909)	(86,080)
Interest income, net	14,190	2,883	11,307
Other income, net	15	134	(119)
Net loss	<u>\$ (532,784)</u>	<u>\$ (457,892)</u>	<u>\$ (74,892)</u>

### ***Product Revenue, Net***

During the years ended December 31, 2022 and 2021, we recognized \$7.7 million and \$6.3 million, respectively, of net product revenue related to sales of ZULRESSO. Sales allowances and accruals consisted of chargebacks, discounts, distribution fees and patient financial assistance, and were not significant during either year.

### ***Collaboration Revenue***

During the years ended December 31, 2022 and 2021, we recognized no collaboration revenue from our agreement with Shionogi or collaboration revenue – related party from our agreement with Biogen.

We expect that revenue, if any, that we may generate under our collaboration agreements will fluctuate from quarter to quarter as a result of the timing and amount of license fees, payments for clinical materials or manufacturing services,

milestone payments, royalties paid to us and our share of collaboration profits or losses resulting from sales of any commercialized products, and other payments. We have the potential to receive milestone payments totaling \$225.0 million related to the first commercial sale of zuranolone in MDD and PPD in the U.S., if zuranolone is approved for marketing. For further discussion regarding our collaboration agreements with Shionogi and Biogen and the accounting for revenue from collaboration agreements, refer to Note 2, *Summary of Significant Accounting Policies*; and Note 6, *Collaboration Agreements* in the Notes to Consolidated Financial Statements, appearing elsewhere in this Annual Report.

### **Cost of Goods Sold**

During the years ended December 31, 2022 and 2021, cost of goods sold was \$0.8 million and \$0.6 million, respectively, and is made up of direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party manufacturing costs, packaging services, freight, third-party royalties payable on our net product revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. Prior to receiving initial FDA approval for ZULRESSO in March 2019, we manufactured ZULRESSO inventory to be sold upon commercialization and recorded \$8.9 million related to this inventory build-up as research and development expense. As a result, the manufacturing costs related to the ZULRESSO inventory build-up incurred before FDA approval were already expensed in a prior period and are therefore excluded from the cost of goods sold for the years ended December 31, 2022 and 2021. We estimate that our cost of goods sold as a percentage of net product revenue will remain in the high-single digit to low-double digits percentage range for the foreseeable future. We expect to utilize zero-cost inventory with respect to ZULRESSO for an extended period of time.

### **Research and Development Expenses**

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Increase (Decrease)
	2022	2021	
	(in thousands)		
zuranolone (SAGE-217)	\$ 93,440	\$ 122,256	\$ (28,816)
SAGE-324	31,496	18,771	12,725
SAGE-718	45,862	25,440	20,422
Other research and development programs	72,575	59,633	12,942
Unallocated expenses	130,129	87,168	42,961
Stock-based compensation	25,888	49,746	(23,858)
Net reimbursement from Biogen	(73,227)	(79,848)	6,621
	<u>\$ 326,163</u>	<u>\$ 283,166</u>	<u>\$ 42,997</u>

Research and development expenses for the year ended December 31, 2022 were \$326.2 million, compared to \$283.2 million for the year ended December 31, 2021. The increase of \$43.0 million was primarily due to the following:

- a decrease of \$28.8 million in expenses for development of zuranolone, primarily due to completion of the WATERFALL Study and the CORAL Study;
- an increase of \$12.7 million in expenses for development of SAGE-324, primarily due to activities directed towards the conduct of Phase 2 clinical trials which were initiated during 2021 and 2022;
- an increase of \$20.4 million in expenses for development of SAGE-718, primarily due to activities directed towards the conduct of Phase 2 clinical trials which were initiated during 2021 and 2022;
- an increase of \$12.9 million in expenses for other research and development programs, primarily due to increased work on early-stage research programs;
- an increase of \$43.0 million in unallocated expenses, primarily due to an increase in the hiring of employees and corporate infrastructure costs, such as information technology costs, to support the growth in our operations;

- a decrease of \$23.9 million in non-cash stock-based compensation expense. The decrease was primarily due to grants of stock options with high exercise prices that became fully vested before or during the year ended December 31, 2022, resulting in less expense than in the year ended December 31, 2021. The decrease was also due to the recognition of \$9.8 million of expense related to performance-based vesting criteria during the year ended December 31, 2021. No expense was recognized related to the achievement of performance-based vesting criteria during the year ended December 31, 2022; and
- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement decreased by \$6.6 million. For the year ended December 31, 2022, the amount of net reimbursement was \$46.4 million for zuranolone, \$15.8 million for SAGE-324 and \$11.0 million for costs that are reimbursable and included in unallocated expenses. For the year ended December 31, 2021, the amount of net reimbursement was \$61.1 million for zuranolone, \$9.4 million for SAGE-324 and \$9.3 million for costs that are reimbursable and included in unallocated expenses. The primary reason for the decrease in net reimbursement was the increase in spending by Biogen for zuranolone.

### ***Selling, General and Administrative Expenses***

The following table summarizes our selling, general and administrative expenses for the years ended December 31, 2022 and 2021:

	Year Ended December 31,		Increase (Decrease)
	2022	2021	
	(in thousands)		
Personnel-related	\$ 88,078	\$ 52,100	\$ 35,978
Stock-based compensation	35,714	54,883	(19,169)
Professional fees	56,833	43,428	13,405
Other	49,304	44,369	4,935
Net reimbursement from Biogen	(2,230)	(11,282)	9,052
	<u>\$ 227,699</u>	<u>\$ 183,498</u>	<u>\$ 44,201</u>

Selling, general and administrative expenses for the year ended December 31, 2022 were \$227.7 million, compared to \$183.5 million for the year ended December 31, 2021. The increase of \$44.2 million was primarily due to the following:

- an increase of \$36.0 million in personnel-related costs, primarily due to hiring employees to support ongoing permitted pre-launch and launch-readiness activities with respect to zuranolone and in anticipation of a potential commercialization of zuranolone, if approved;
- a decrease of \$19.2 million in non-cash stock-based compensation expense. The decrease was primarily due to grants of stock options with high exercise prices that became fully vested before or during the year ended December 31, 2022, resulting in less expense than in the year ended December 31, 2021. The decrease was also due to the recognition of \$6.7 million of expense related to performance-based vesting criteria during the year ended December 31, 2021. No expense was recognized related to the achievement of performance-based vesting criteria during the year ended December 31, 2022;
- an increase of \$13.4 million in professional fees, primarily due to permitted pre-launch and launch-readiness activities with respect to zuranolone;
- an increase in other expenses of \$4.9 million, primarily due to an increase in corporate infrastructure costs, such as information technology costs, to support the growth in our operations; and

- the net reimbursement from Biogen pursuant to the Biogen Collaboration Agreement decreased by \$9.1 million. For the year ended December 31, 2022, the amount of net reimbursement from Biogen to us was \$3.6 million for external costs and the amount of net reimbursement from us to Biogen for personnel-related costs was \$1.3 million. For the year ended December 31, 2021, the amount of net reimbursement from Biogen to us was \$9.3 million for external costs and \$2.0 million for personnel-related costs. The primary reason for the decrease in net reimbursement was an increase in the collaboration costs incurred by Biogen in anticipation of a potential commercialization of zuranolone, if approved.

### ***Interest Income, Net and Other income, Net***

Interest income, net, and other income, net, for the years ended December 31, 2022 and 2021 were \$14.2 million and \$3.0 million, respectively. The primary reason for the increase was the increase in interest rates.

### **Liquidity and Capital Resources**

We began to generate revenue from product sales in the second quarter of 2019 in conjunction with the launch of our first product, ZULRESSO, in June 2019. We have incurred net losses in each year since our inception, except for net income of \$606.1 million for the year ended December 31, 2020, reflecting revenue recognized under the Biogen Collaboration Agreement. As of December 31, 2022, we had an accumulated deficit of \$2.0 billion. On December 31, 2020, we completed the sale of 6,241,473 shares of our common stock in a private placement to BIMA at a price of approximately \$104.14 per share, resulting in aggregate gross proceeds of \$650.0 million. From our inception through December 31, 2022, we have received aggregate net proceeds of \$2.8 billion from the sales of redeemable convertible preferred stock prior to our initial public offering, the issuance of convertible notes, and the sales of common stock in our initial public offering in July 2014, follow-on offerings and in the sale of shares of our common stock to Biogen in connection with the Biogen Collaboration Agreement, which we refer to as the Biogen Equity Purchase. We also received \$1.0 billion in upfront payments under our collaborations with Biogen and Shionogi.

As of December 31, 2022, our primary sources of liquidity were our cash, cash equivalents and marketable securities, which totaled \$1.3 billion. We invest our cash in money market funds, U.S. government securities, corporate bonds, commercial paper, certificates of deposit and municipal securities, and our primary objectives are to preserve principal, provide liquidity and maximize income without significantly increasing risk.

The following table summarizes the primary sources and uses of cash for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Net cash provided by (used in):		
Operating activities	\$ (460,036)	\$ (378,182)
Investing activities	325,433	(1,002,448)
Financing activities	3,070	13,334
	<u>\$ (131,533)</u>	<u>\$ (1,367,296)</u>

### ***Operating Activities***

During the year ended December 31, 2022, net cash used in operating activities primarily resulted from our net loss of \$532.8 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, along with changes in our operating assets and liabilities of \$5.7 million, partially offset by \$67.1 million of non-cash items.

During the year ended December 31, 2021, net cash used in operating activities primarily resulted from our net loss of \$457.9 million, which was primarily attributable to our research and development activities and our selling, general and administrative expenses, along with changes in our operating assets and liabilities of \$18.5 million, partially offset by \$98.2 million of non-cash items.

### ***Investing Activities***

During the years ended December 31, 2022 and 2021, net cash provided by investing activities was \$325.4 million and net cash used by investing activities was \$1.0 billion, respectively. During the years ended December 31, 2022 and 2021, we purchased marketable securities and had sales and maturities of our marketable securities as part of managing our cash and investments portfolio. Additionally, during the year ended December 31, 2021, we invested the majority of the cash that we received from Biogen under the Biogen Collaboration Agreement and the Biogen Equity Purchase in marketable securities.

### ***Financing Activities***

During the years ended December 31, 2022 and 2021, net cash provided by financing activities was \$3.1 million and \$13.3 million, respectively. The decrease was mainly due to a decrease of proceeds from the exercises of stock options.

### ***Operating Capital Requirements***

We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of our current and future product candidates, and seek regulatory approvals for zuranolone and those other product candidates that are successfully developed; prepare for potential future commercialization of zuranolone and other product candidates beyond ZULRESSO that are successfully developed and approved, including engaging in pre-launch and launch-readiness activities; begin to commercialize any such products, if approved; and continue our efforts to identify and develop new product candidates beyond our current portfolio. We also expect to incur significant costs associated with general operations. In addition, we expect to incur significant commercialization expenses for product sales, marketing and outsourced manufacturing with respect to ZULRESSO, zuranolone, if approved and any other future products that are successfully developed and approved. Accordingly, we anticipate that we will need substantial additional funding in connection with our continuing operations.

We expect that our existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to anticipated funding from our ongoing collaborations, excluding revenues and milestones, will enable us to fund our operating expenses and capital expenditure requirements through 2024. During that time, we expect research and development and selling, general and administrative expenses to increase as we advance planned and ongoing clinical trials for SAGE-718 and SAGE-324; advance regulatory, engage in permitted pre-launch and launch-planning activities for zuranolone; prepare for the potential commercial launch of zuranolone; expand our research activities; and pursue our strategic plan.

Our current operating plan does not contemplate other activities that we may pursue or that all of our currently planned activities will proceed at the same pace, or that all of these activities will be fully initiated or completed during that time. We have based our estimates on assumptions that could change, and we may use our available capital resources sooner than we currently expect. We may also choose to change or increase our development, commercialization or other efforts. Because of the numerous risks and uncertainties associated with the development and commercialization of any product or product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete development of our current or future product candidates or to commercialize any approved product.

Our future capital requirements will depend on many factors, including:

- our ability to successfully receive FDA approval of our NDA to market zuranolone for the treatment of MDD and PPD, on the timelines we expect;
- the costs of regulatory, permitted pre-launch and launch-readiness activities associated with zuranolone;
- if zuranolone is approved for one or more indications, the costs associated with its commercial launch and the timing and amount of any revenues;

- the timing and amount of revenues from sales of ZULRESSO, which we expect will continue to be impacted by a number of factors, including: the rate, degree and level of market acceptance for ZULRESSO for the treatment of PPD in the U.S.; our decision to focus our efforts primarily on geographies that have existing, active ZULRESSO treating sites; the continued availability of healthcare settings in those geographies to administer ZULRESSO and the ability and willingness of such healthcare settings to make sufficient capacity available, particularly in light of the ongoing disruption to the U.S. healthcare system and related healthcare staffing shortages stemming from the downstream effects of the COVID-19 pandemic; the level of reimbursement for both ZULRESSO and the infusion in the healthcare setting both by commercial and government payors, and the nature of limitations on coverage and reimbursement; the number of healthcare professionals willing to prescribe ZULRESSO and women with PPD who agree to be treated with ZULRESSO; and the scope, duration and timing of the impact of the COVID-19 pandemic and its downstream effects;
- the timing and amount of costs associated with our commercialization of ZULRESSO;
- the initiation, progress, completion, timing, costs, and results of ongoing, planned and future non-clinical studies and clinical trials for our other existing and future product candidates; the number and length of clinical trials required by regulatory authorities to support regulatory approval; and the costs of preparing, submitting and supporting regulatory filings for our product candidates;
- the length, severity and costs of downstream disruptions and other changes to the macroeconomic environment as a result of the COVID-19 pandemic, including any capacity and resource constraints at our vendors and clinical trial sites on initiation and conduct of our clinical trials or on our supply chain;
- the ability of SAGE-324, SAGE-718 and our other clinical-stage product candidates to progress through clinical development successfully and on the timelines we expect; the outcome of discussions with regulatory authorities on regulatory pathways with respect to our product candidates; the timing, scope and outcome of regulatory filings and reviews and approvals of such product candidates, if we are successful in our development efforts; the scope and cost of any clinical trials or other commitments required post-approval for any approved products resulting from such development efforts, if successful; and the level, timing and amount of costs associated with permitted prelaunch activities and preparing for a potential future commercial launch of any such product candidate that is successfully developed and approved;
- the amounts we are entitled to receive, if any, from Biogen and Shionogi under our collaborations for profit-sharing, cost-sharing, development, regulatory, and sales milestones, and royalty payments;
- the size of the markets for which zuranolone and our other product candidates may be approved in the future, if successfully developed; the portion of the population in the approved indications for which zuranolone, if approved, and our future products are actually prescribed; and the rate and degree of market acceptance, pricing, and availability and level of reimbursement for zuranolone, if approved, and for our future products, if successfully developed and approved;
- the number and characteristics of the product candidates we pursue in development and the nature and scope of our discovery and development programs;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other products and technologies; and
- our ability to establish any future collaboration arrangements on favorable terms, if at all.

Until such time, if ever, as we can generate substantial product revenue and/or collaboration revenue and achieve sustained profitability, we expect to also finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or in light of other strategic considerations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt



financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends and may require the issuance of warrants, which could potentially dilute the ownership interest of our stockholders. If we raise additional funds through collaborations, strategic alliances, licensing arrangements or other agreements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. Raising funds may present challenges. Markets may experience volatility or become disrupted in the future for any number of reasons, including if the long-term negative effects of the COVID-19 pandemic, even after the pandemic has subsided, or other macroeconomic or geopolitical conditions, result in an economic recession, a decrease in corporate and consumer expenditures, prolonged unemployment, or other circumstances that could negatively impact general economic conditions. If we are unable to raise additional funds through equity or debt financings or other means when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

### Contractual Obligations and Commitments

The following table summarizes our contractual obligations at December 31, 2022 and the effect such obligations are expected to have on our liquidity and cash flow in future periods:

	Payments Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
	(in thousands)				
Operating lease commitments <sup>(1)</sup>	\$ 12,959	\$ 7,643	\$ 5,316	\$ —	\$ —
Total <sup>(1)(2)(3)</sup>	<u>\$ 12,959</u>	<u>\$ 7,643</u>	<u>\$ 5,316</u>	<u>\$ —</u>	<u>\$ —</u>

Amounts related to contingent milestone payments are not considered contractual obligations as they are contingent on the successful achievement of certain milestones. These contingent milestones may not be achieved. We have not included any of these amounts in the table as we cannot estimate or predict when, or if, these amounts will become due. We do not include amounts related to milestones for indications that we are no longer pursuing.

- (1) We lease office space in two multi-tenant buildings in Cambridge, Massachusetts, consisting, as of December 31, 2022, of 63,017 square feet in the first building under an operating lease, as amended, that will expire on August 31, 2024 and 40,419 square feet in the second building under an operating lease, as amended, that will expire on August 31, 2024. We lease office space in a multi-tenant building in Raleigh, North Carolina, consisting of 15,525 square feet under an operating lease that will expire on November 30, 2024. We may lease additional space prior to the expiration of our leases to meet the needs of the business. The minimum lease payments in the table do not include related common area maintenance costs or real estate taxes, because those costs are variable.

- (2) We have acquired exclusive and non-exclusive rights to use, research, develop and offer for sale certain products and patents under license agreements. The license agreements obligate us to make payments to the licensors for license fees, milestones, license maintenance fees and royalties. We are obligated to make future remaining milestone payments under these agreements of up to an aggregate of \$23.8 million upon achieving certain milestones, related to clinical development, regulatory approvals and sales. During the year ended December 31, 2022, we recorded no expense for milestones under these license agreements.
- (3) We enter into contracts in the normal course of business with CROs for clinical trials, non-clinical research studies and testing, manufacturing and other services and products as part of general operations. These contracts generally provide for termination upon notice, and we believe that our non-cancelable obligations under these agreements are not material.

#### **Item 7A. Quantitative and Qualitative Disclosures about Market Risk**

We had cash, cash equivalents and marketable securities of \$1.3 billion as of December 31, 2022. The primary objectives of our investment activities are to preserve principal, provide liquidity and maximize income without significantly increasing risk. Our primary exposure to market risk relates to fluctuations in interest rates, which are affected by changes in the general level of U.S. interest rates. Given the short-term nature of our cash, cash equivalents and marketable securities, we do not expect that a sudden change in market interest rates would have a material impact on our financial condition and/or results of operations. We do not own any derivative financial instruments.

We contract with vendors in foreign countries and have subsidiaries in Europe. As such, we have exposure to adverse changes in exchange rates of foreign currencies associated with our foreign transactions. We believe this exposure to be immaterial. We do not hedge against this exposure to fluctuations in exchange rates.

We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and marketable securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents and marketable securities that are in excess of federally insured limits at one or more financial institutions.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our results of operations during the year ended December 31, 2022.

#### **Item 8. Financial Statements and Supplementary Data**

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report. An index of those financial statements is found in Item 15.

#### **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

#### **Item 9A. Controls and Procedures**

##### **Evaluation of Disclosure Controls and Procedures**

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Securities Exchange Act of 1934) that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer, and our Chief Financial Officer, who is also our principal financial and accounting officer, as appropriate, to allow timely decisions regarding required disclosure.

As of December 31, 2022, our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures. Our management

recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our principal executive officer and principal financial and accounting officer have concluded, based upon the evaluation described above, that, as of December 31, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

### **Management’s Report on Internal Control over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) under the Securities Exchange Act of 1934). Our internal control over financial reporting is a process designed under the supervision of our principal executive officer and principal financial officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles. Management evaluated the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control—Integrated Framework* (the 2013 Framework). Management, under the supervision and with the participation of the principal executive officer and principal financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2022 and concluded that it was effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

### **Changes in Internal Control over Financial Reporting**

There were no changes to our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934) that occurred during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

### **Item 9B. Other Information**

Not applicable.

### **Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

**Item 10. Directors, Executive Officers and Corporate Governance**

The information required by this Item is incorporated herein by reference to the information that will be contained in “Election of Directors” and “Corporate Governance” in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

**Code of Business Conduct and Ethics.** We have adopted a Code of Business Conduct and Ethics, which we call our Values Code, that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. The current version of the Values Code, as may be amended from time to time, is available on our website at <http://investor.sagerx.com/corporate-governance>. A copy of the Values Code may also be obtained, free of charge, upon a request directed to: Sage Therapeutics, Inc., 215 First Street, Cambridge, Massachusetts 02142, Attention: SVP, General Counsel. We intend to disclose any amendment or waiver of a provision of the Values Code that applies to our principal executive officer, principal financial officer, or principal accounting officer, or persons performing similar functions, by posting such information on our website (available at [www.sagerx.com](http://www.sagerx.com)) and/or in our public filings with the Securities and Exchange Commission.

**Item 11. Executive Compensation**

The information required by this Item is incorporated herein by reference to the information that will be contained in “Executive Officer and Director Compensation,” “Compensation Committee Interlocks and Insider Participation” and “Compensation Committee Report,” but exclusive of any information contained under the heading “Pay Versus Performance” in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this Item is incorporated herein by reference to the information that will be contained in “Securities Authorized for Issuance Under Equity Compensation Plans” and “Security Ownership of Certain Beneficial Owners and Management” in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

**Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this Item is incorporated herein by reference to the information that will be contained in “Corporate Governance” and “Certain Relationships and Related Party Transactions” in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

**Item 14. Principal Accounting Fees and Services**

The information required by this Item is incorporated herein by reference to the information that will be contained in “Ratification of Appointment of Auditors” in our proxy statement related to the 2023 Annual Meeting of Stockholders, which we intend to file with the Securities and Exchange Commission within 120 days of the end of our fiscal year pursuant to General Instruction G(3) of Form 10-K.

**Item 15. Exhibits, Financial Statement Schedules**

(a) The following documents are filed as part of this report:

(1) Financial Statements:

[Report of Independent Registered Public Accounting Firm \(PCAOB ID 238\)](#)

F-1

[Consolidated Balance Sheets](#)

F-3

[Consolidated Statements of Operations and Comprehensive Income \(Loss\)](#)

F-4

[Consolidated Statements of Changes in Stockholders' Equity](#)

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[Consolidated Statements of Cash Flows](#)

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[Notes to Consolidated Financial Statements](#)

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(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits filed as part of this Annual Report are set forth on the Exhibit Index immediately following our consolidated financial statements. The Exhibit Index is incorporated herein by reference.

**Item 16. Form 10-K Summary**

Not applicable.

## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Sage Therapeutics, Inc.

### ***Opinions on the Financial Statements and Internal Control over Financial Reporting***

We have audited the accompanying consolidated balance sheets of Sage Therapeutics, Inc. and its subsidiaries (the “Company”) as of December 31, 2022 and 2021, and the related consolidated statements of operations and comprehensive income (loss), of changes in stockholders’ equity and of cash flows for each of the three years in the period ended December 31, 2022, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company’s internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control - Integrated Framework (2013)* issued by the COSO.

### ***Basis for Opinions***

The Company’s management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management’s Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company’s internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

### ***Definition and Limitations of Internal Control over Financial Reporting***

A company’s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company’s internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company’s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

### ***Critical Audit Matters***

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

#### *Accrued Research and Development Costs*

As described in Notes 2 and 4 to the consolidated financial statements, the Company has entered into various research and development contracts with research institutions and other companies. When billing terms under these contracts do not coincide with the timing of when the work is performed, management is required to make estimates of outstanding obligations to those third parties as of the end of the reporting period. Within accrued expenses, total accrued research and development costs amounted to \$32.6 million as of December 31, 2022, which include accruals for these estimated ongoing research and development costs. Any accrual estimates are based on a number of factors, including management's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period.

The principal considerations for our determination that performing procedures relating to accrued research and development costs is a critical audit matter are the significant judgment by management in determining the accrued costs which in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence for these accrued costs and the factors related to progress towards completion of the research and development activities, invoicing to date under the contracts, and communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to accrued research and development costs, including controls over the review of contracts, accumulating information on actual costs incurred during the period, and assessment of progress towards completion of the research and development activities. These procedures also included, among others, (i) testing management's process for estimating accrued research and development costs; (ii) evaluating the appropriateness of the method used by management to develop the estimates; (iii) evaluating the reasonableness of the factors used in determining the estimates related to progress towards completion of specific research and development activities and the associated cost incurred for services the Company has not yet been invoiced or otherwise notified of the actual cost at period end; and (iv) testing the completeness and accuracy of the underlying data including total costs included within executed contracts and actual billed expenses under these contracts.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
February 16, 2023

We have served as the Company's auditor since 2013.

**Sage Therapeutics, Inc. and Subsidiaries**  
**Consolidated Balance Sheets**  
(in thousands, except share and per share data)

	December 31, 2022	December 31, 2021
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 162,700	\$ 294,233
Marketable securities	1,109,794	1,448,063
Prepaid expenses and other current assets	50,826	39,841
Collaboration receivable - related party	13,660	18,506
Total current assets	1,336,980	1,800,643
Property and equipment, net	2,898	3,016
Restricted cash	1,269	1,269
Right-of-use operating asset	10,532	16,109
Other long-term assets	4,770	4,251
Total assets	<u>\$ 1,356,449</u>	<u>\$ 1,825,288</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 18,950	\$ 10,450
Accrued expenses	72,666	67,275
Operating lease liability, current portion	7,643	7,468
Total current liabilities	99,259	85,193
Operating lease liability, net of current portion	4,491	10,964
Other liabilities	100	100
Total liabilities	<u>103,850</u>	<u>96,257</u>
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value per share; 5,000,000 shares authorized at December 31, 2022 and December 31, 2021; no shares issued or outstanding at December 31, 2022 and December 31, 2021	—	—
Common stock, \$0.0001 par value per share; 120,000,000 shares authorized at December 31, 2022 and December 31, 2021; 59,512,158 and 58,940,083 shares issued at December 31, 2022 and December 31, 2021; 59,509,125 and 58,937,050 shares outstanding at December 31, 2022 and December 31, 2021	6	6
Treasury stock, at cost, 3,033 shares at December 31, 2022 and December 31, 2021	(400)	(400)
Additional paid-in capital	3,291,369	3,227,471
Accumulated deficit	(2,028,170)	(1,495,386)
Accumulated other comprehensive loss	(10,206)	(2,660)
Total stockholders' equity	1,252,599	1,729,031
Total liabilities and stockholders' equity	<u>\$ 1,356,449</u>	<u>\$ 1,825,288</u>

*The accompanying notes are an integral part of these consolidated financial statements.*



**Sage Therapeutics, Inc. and Subsidiaries**  
**Consolidated Statements of Operations and Comprehensive Income (Loss)**  
(in thousands, except share and per share data)

	Year Ended December 31,		
	2022	2021	2020
Product revenue, net	\$ 7,686	\$ 6,308	\$ 6,700
Collaboration revenue - related party	—	—	1,107,500
<b>Total revenue</b>	<b>7,686</b>	<b>6,308</b>	<b>1,114,200</b>
Operating costs and expenses:			
Cost of goods sold	813	553	565
Research and development	326,163	283,166	292,714
Selling, general and administrative	227,699	183,498	196,952
Restructuring	—	—	27,743
<b>Total operating costs and expenses</b>	<b>554,675</b>	<b>467,217</b>	<b>517,974</b>
Income (loss) from operations	(546,989)	(460,909)	596,226
Interest income, net	14,190	2,883	9,597
Other income, net	15	134	250
<b>Net income (loss)</b>	<b>\$ (532,784)</b>	<b>\$ (457,892)</b>	<b>\$ 606,073</b>
Net income (loss) per share—basic	\$ (8.98)	\$ (7.80)	\$ 11.66
Net income (loss) per share—diluted	\$ (8.98)	\$ (7.80)	\$ 11.43
Weighted average number of common shares outstanding—basic	59,306,094	58,670,230	51,983,188
Weighted average number of common shares outstanding—diluted	59,306,094	58,670,230	53,003,115
Comprehensive income (loss):			
Net income (loss)	\$ (532,784)	\$ (457,892)	\$ 606,073
Other comprehensive items:			
Unrealized loss on marketable securities	(7,546)	(3,075)	(880)
<b>Total other comprehensive loss</b>	<b>(7,546)</b>	<b>(3,075)</b>	<b>(880)</b>
<b>Total comprehensive income (loss)</b>	<b>\$ (540,330)</b>	<b>\$ (460,967)</b>	<b>\$ 605,193</b>

*The accompanying notes are an integral part of these consolidated financial statements.*

**Sage Therapeutics, Inc. and Subsidiaries**  
**Consolidated Statements of Changes in Stockholders' Equity**  
(in thousands, except share data)

	Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Other Comprehen- sive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
<b>Balances at December 31, 2019</b>	51,877,194	\$ 5	3,033	\$ (400)	\$ 2,587,322	\$ 1,295	\$ (1,643,567)	\$ 944,655
Issuance of common stock from exercises of stock options	117,025	—	—	—	5,082	—	—	5,082
Issuance of common stock under the employee stock purchase plan	72,719	—	—	—	4,936	—	—	4,936
Stock-based compensation expense	—	—	—	—	94,968	—	—	94,968
Issuance of common stock under the Stock Purchase Agreement - related party	6,241,473	1	—	—	417,499	—	—	417,500
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(880)	—	(880)
Net income	—	—	—	—	—	—	606,073	606,073
<b>Balances at December 31, 2020</b>	58,308,411	6	3,033	(400)	3,109,807	415	(1,037,494)	2,072,334
Issuance of common stock from exercises of stock options	307,378	—	—	—	12,397	—	—	12,397
Issuance of common stock under the employee stock purchase plan	46,759	—	—	—	2,761	—	—	2,761
Stock-based compensation expense	—	—	—	—	103,891	—	—	103,891
Vesting of restricted stock units, net of employee tax obligations	274,502	—	—	—	(1,385)	—	—	(1,385)
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(3,075)	—	(3,075)
Net loss	—	—	—	—	—	—	(457,892)	(457,892)
<b>Balances at December 31, 2021</b>	58,937,050	6	3,033	(400)	3,227,471	(2,660)	(1,495,386)	1,729,031
Issuance of common stock from exercises of stock options	150,045	—	—	—	1,037	—	—	1,037
Issuance of common stock under the employee stock purchase plan	57,239	—	—	—	2,346	—	—	2,346
Stock-based compensation expense	—	—	—	—	60,558	—	—	60,558
Vesting of restricted stock units, net of employee tax obligations	364,791	—	—	—	(43)	—	—	(43)
Change in unrealized loss on available-for-sale securities	—	—	—	—	—	(7,546)	—	(7,546)
Net loss	—	—	—	—	—	—	(532,784)	(532,784)
<b>Balances at December 31, 2022</b>	59,509,125	\$ 6	3,033	\$ (400)	\$ 3,291,369	\$ (10,206)	\$ (2,028,170)	\$ 1,252,599

*The accompanying notes are an integral part of these consolidated financial statements.*

**Sage Therapeutics, Inc. and Subsidiaries**  
**Consolidated Statements of Cash Flows**  
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
<b>Cash flows from operating activities</b>			
Net income (loss)	\$ (532,784)	\$ (457,892)	\$ 606,073
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Stock-based compensation expense	61,602	104,629	95,994
Premium on marketable securities	(1,500)	(23,641)	(1,736)
Amortization of premium on marketable securities	5,853	13,046	1,048
Depreciation expense	1,122	4,182	2,630
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(10,985)	(17,020)	3,879
Collaboration receivable - related party	4,846	(18,506)	—
Other long-term assets	(519)	(910)	452
Right-of-use operating asset	5,577	5,221	6,397
Operating lease liabilities, current	175	206	36
Operating lease liabilities, non-current	(6,473)	(5,944)	(6,825)
Accounts payable	8,433	6,689	(11,511)
Accrued expenses and other liabilities	4,617	11,758	(32,157)
Net cash provided by (used in) operating activities	<u>(460,036)</u>	<u>(378,182)</u>	<u>664,280</u>
<b>Cash flows from investing activities</b>			
Proceeds from sales and maturities of marketable securities	1,207,407	988,075	901,749
Purchases of marketable securities	(881,037)	(1,990,151)	(458,720)
Purchases of property and equipment	(937)	(372)	(345)
Net cash provided by (used in) investing activities	<u>325,433</u>	<u>(1,002,448)</u>	<u>442,684</u>
<b>Cash flows from financing activities</b>			
Proceeds from stock option exercises and employee stock purchase plan issuances	3,113	14,719	9,262
Payment of employee tax obligations related to vesting of restricted stock units	(43)	(1,385)	—
Proceeds from the sale of common stock under the Stock Purchase Agreement - related party	—	—	417,500
Net cash provided by financing activities	<u>3,070</u>	<u>13,334</u>	<u>426,762</u>
Net increase (decrease) in cash, cash equivalents and restricted cash	<u>(131,533)</u>	<u>(1,367,296)</u>	<u>1,533,726</u>
Cash, cash equivalents and restricted cash at beginning of period	295,502	1,662,798	129,072
Cash, cash equivalents and restricted cash at end of period	<u>\$ 163,969</u>	<u>\$ 295,502</u>	<u>\$ 1,662,798</u>
<b>Supplemental disclosure of non-cash operating and investing activities</b>			
Purchases of property and equipment included in accounts payable	\$ 137	\$ 70	\$ —
Lease asset de-recognized upon lease cancellation	\$ —	\$ 3,733	\$ 2,310

*The accompanying notes are an integral part of these consolidated financial statements.*

Notes to Consolidated Financial Statements

**1. Nature of the Business**

Sage Therapeutics, Inc. (“Sage” or the “Company”) is a biopharmaceutical company with a mission to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive.

The Company’s first product, ZULRESSO® (brexanolone) CIV injection, is approved in the U.S. as a treatment for postpartum depression (“PPD”) in adults. The Company launched ZULRESSO commercially in the U.S. in June 2019. The Company’s submission of a new drug application (an “NDA”) for its lead investigational product candidate, zuranolone, for the treatment of major depressive disorder (“MDD”) and PPD was accepted for filing and granted priority review by the U.S. Food and Drug Administration (“FDA”) in February 2023. The Company has a portfolio of other product candidates with a current focus on modulating two critical central nervous system (“CNS”) receptor systems, GABA and NMDA. The GABA receptor family, which is recognized as the major inhibitory neurotransmitter in the CNS, mediates downstream neurologic and bodily function via activation of GABA<sub>A</sub> receptors. The NMDA-type receptors of the glutamate receptor system are a major excitatory receptor system in the CNS. Dysfunction in these systems is implicated in a broad range of CNS disorders. The Company is currently targeting diseases and disorders of the brain with three key focus areas: depression, neurology and neuropsychiatry.

The Company was incorporated under the laws of the State of Delaware on April 16, 2010, and commenced operations on January 19, 2011 as Sterogen Biopharma, Inc. On September 13, 2011, the Company changed its name to Sage Therapeutics, Inc.

***Risks and Uncertainties***

The Company is subject to risks and uncertainties common to companies in the biotechnology and pharmaceutical industries, including, but not limited to, the risks associated with developing product candidates at each stage of non-clinical and clinical development; the challenges associated with gaining regulatory approval of such product candidates; the risks associated with the marketing and sale of pharmaceutical products; the potential for development by third parties of new technological innovations that may compete with the Company’s products and product candidates; the dependence on key personnel; the challenges of protecting proprietary technology; the need to comply with government regulations; the high costs of drug development; the uncertainty of being able to secure additional capital when needed to fund operations; and the direct or indirect impact of the COVID-19 pandemic on its development activities, operations and financial condition.

The product candidates developed by the Company require approvals from the FDA or foreign regulatory agencies prior to commercial sales. There can be no assurance that the current and future product candidates of the Company will receive, or that the Company’s current product, ZULRESSO, will maintain, the necessary approvals. If the Company fails to successfully complete clinical development and generate results sufficient to file for regulatory approval or is denied approval or approval is delayed for any of its product candidates, including zuranolone, such occurrences may have a material adverse impact on the Company’s business and its financial condition.

The Company is also subject to additional risks and uncertainties related to the ongoing COVID-19 pandemic and other macroeconomic and geopolitical events, which collectively have caused and may continue to cause major disruptions to businesses and economies worldwide.

The rapid spread of COVID-19 in the U.S. resulted in a significant reduction in patient demand for ZULRESSO and in the number of sites available to administer ZULRESSO at certain points during the pandemic. There have been and continue to be healthcare staffing shortages and other changes to the macroeconomic environment as downstream effects of the pandemic have continued. These factors have had a significant and sustained negative impact on the Company’s revenue from sales of ZULRESSO. While the Company has not experienced any other material disruptions to date as a result of the COVID-19 pandemic, any prolonged material disruptions to the work of the Company’s employees,

suppliers, contract manufacturers, or vendors could negatively impact the Company's activities, availability of supplies, or operating results. In addition, while the Company has seen slower patient recruitment in certain clinical trials due to the COVID-19 pandemic and its downstream effects, and has experienced some challenges in qualifying and activating clinical trial sites, including due to capacity and resource constraints and employee attrition at our vendors and at sites, the Company has not experienced other significant impacts to the Company's development activities as a result of the COVID-19 pandemic. Any material disruption to the Company's development activities may cause delays, increase the Company's costs and impact the Company's operating results. In addition, the COVID-19 pandemic initially caused major volatility in capital markets and a significant global economic downturn, and the Company's ability to access the capital markets in the future could be negatively impacted if there are long-term negative effects of the COVID-19 pandemic on the macroeconomic environment or capital markets.

Moreover, U.S. and global financial markets have experienced volatility and disruption due to other macroeconomic and geopolitical events such as rising inflation, the risk of a recession and the ongoing conflict between Russia and Ukraine. The Company cannot predict at this time to what extent it and its collaborators, employees, suppliers, contract manufacturers and/or vendors could potentially be negatively impacted by these events.

### ***Going Concern***

Under Accounting Standards Update ("ASU") No. 2014-15, *Presentation of Financial Statements—Going Concern* (Subtopic 205-40), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the financial statements are issued. The Company has incurred losses and negative cash flows from operations in each year since its inception, except for net income of \$606.1 million for the year ended December 31, 2020, reflecting revenue recognized under a collaboration and license agreement with Biogen MA Inc. ("BIMA") and Biogen International GmbH (collectively with BIMA, "Biogen") (the "Biogen Collaboration Agreement"). As of December 31, 2022, the Company had an accumulated deficit of \$2.0 billion. From its inception through December 31, 2022, the Company has received aggregate net proceeds of \$2.8 billion from the sales of redeemable convertible preferred stock prior to its initial public offering ("IPO"), the issuance of convertible notes, and the sales of common stock in its IPO in July 2014, in follow-on public offerings and to BIMA under a stock purchase agreement executed in connection with the Biogen Collaboration Agreement. The Company has also received \$1.0 billion in upfront payments under its collaborations with Biogen and Shionogi & Co., Ltd. ("Shionogi"). Until such time, if ever, as the Company can generate substantial product revenue and/or collaboration revenue and achieve sustained profitability, the Company expects to finance its cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances, licensing arrangements and other sources of funding. If the Company is unable to raise additional funds through equity or debt financings or other sources of funding when needed, the Company may be required to delay, limit, reduce or terminate product development or future commercialization efforts or grant rights to develop and market products or product candidates that the Company would otherwise prefer to develop and market itself.

The Company expects that, based on its current operating plans, the Company's existing cash, cash equivalents and marketable securities will be sufficient to fund its currently planned operations for at least the next 12 months from the filing date of this Annual Report. At some point after that time, the Company anticipates it will require additional financing to fund its future operations. Even if the Company believes it has sufficient funds for its current or future operating plans, the Company may seek to raise additional capital if market conditions are favorable or in light of other strategic considerations.

## **2. Summary of Significant Accounting Policies**

The following is a summary of significant accounting policies followed in the preparation of these consolidated financial statements.

### ***Basis of Presentation***

The accompanying consolidated financial statements include those of the Company and its subsidiaries after elimination of all intercompany accounts and transactions. The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S. (“GAAP”).

### ***Principles of Consolidation***

The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. Intercompany accounts and transactions have been eliminated.

### ***Use of Estimates***

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The full extent to which the COVID-19 pandemic and its downstream effects may directly or indirectly impact the Company’s business, results of operations and financial condition, including sales, expenses, reserves and allowances, manufacturing, clinical trials, research and development costs and employee-related amounts, will depend in large part on future developments, which cannot be predicted with confidence at this time, including: the scope, duration and severity of ongoing and future waves of the pandemic, including the impact of any variant strains of the COVID-19 virus; the extent of healthcare staffing shortages that have continued even as COVID-19 related restrictions have eased; the impact of the pandemic on the Company’s customers and vendors, including capacity and resource constraints; the impact of the downstream effects of the pandemic on business operations across the U.S.; and the scope and extent of any future actions or restrictive measures taken to contain or mitigate the impact of the pandemic. The Company has made estimates of the impact of the COVID-19 pandemic within its consolidated financial statements. Due to the evolving nature of the COVID-19 pandemic, its downstream effects, and their impacts, there may be changes to those estimates in future periods, and actual results could differ from those estimates.

### ***Cash Equivalents***

The Company considers all highly liquid investments with an original maturity of 90 days or less to be cash equivalents. As of December 31, 2022, cash equivalents were comprised of money market funds. As of December 31, 2021, cash equivalents were comprised of money market funds, U.S. commercial paper and international commercial paper.

### ***Marketable Securities***

Marketable securities consist of investments with original maturities greater than 90 days. The Company has classified its investments with maturities beyond one year as short-term, based on their highly liquid nature and because such marketable securities represent the investment of cash that is available for current operations. The Company considers its investment portfolio of marketable securities to be available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are reported as the accumulated other comprehensive items in stockholders’ equity. When the fair value is below the amortized cost of the asset, an estimate of expected credit losses is made. The credit-related impairment amount is recognized in net income (loss); the remaining impairment amount and unrealized gains are reported as a component of accumulated other comprehensive items in stockholders’ equity. Credit losses are recognized through the use of an allowance for credit losses account and subsequent improvements in expected credit losses are recognized as a reversal of an amount in the allowance for credit losses account. If the Company has the intent to sell the security or it is more likely than not that the Company will be required to sell the security prior to recovery of its amortized cost basis, then the allowance for the credit loss is written-off and the excess of the amortized cost basis of the asset over its fair value is recorded in the consolidated statements of operations and comprehensive income (loss). Regardless of the Company’s intent to sell a security, it performs additional analysis on all securities with unrealized losses to evaluate losses associated with the creditworthiness

of the security. Credit losses are identified where the Company does not expect to receive cash flows sufficient to recover the amortized cost basis of a security.

### ***Accounts Receivable***

The Company's trade accounts receivable consist of amounts due from specialty distributors, specialty pharmacies, and medically-supervised healthcare settings that have been certified under a Risk Evaluation and Mitigation Strategy ("REMS") program in the U.S. related to sales of ZULRESSO and have standard payment terms that generally require payment within 30 to 90 days from the invoice date. The Company monitors the financial performance and creditworthiness of customers so that it can properly assess and respond to changes in their credit profiles. The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for bad debts against the trade account receivables, when appropriate. As of December 31, 2022 and 2021, trade accounts receivable were \$1.5 million and \$1.1 million, respectively, and are included in prepaid expenses and other current assets on the consolidated balance sheets. As of December 31, 2022, the Company has not provided any allowance for bad debts against the trade accounts receivable.

### ***Inventory***

Prior to the initial date that regulatory approval is received for a product candidate of the Company, costs related to the production of inventory are recorded as research and development expense on the Company's consolidated statements of operations and comprehensive income (loss) in the period incurred. In connection with the FDA approval of ZULRESSO in March 2019, the Company subsequently began capitalizing inventory manufactured or purchased after this date.

Inventory is stated at the lower of cost or estimated net realizable value with cost determined on a first-in, first-out basis. Inventory costs include raw materials, third-party contract manufacturing, third-party packaging services, and freight. Raw and intermediate materials that may be utilized for either research and development or commercial purposes, after approval of the product by the FDA, are classified as inventory. Amounts in inventory that are used for research and development purposes are charged to research and development expense when the product enters the research and development process and can no longer be used for commercial purposes and, therefore, does not have an "alternative future use" as defined in authoritative guidance. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period and, if needed, writes down any excess and obsolete inventory to its estimated net realizable value in the period it is identified. If they occur, such impairment charges are recorded as a component of cost of goods sold in the consolidated statements of operations and comprehensive income (loss). As of December 31, 2022 and 2021, inventory was \$1.7 million and \$1.4 million, respectively, and are included in prepaid expenses and other current assets on the consolidated balance sheets.

### ***Property and Equipment***

Property and equipment are recorded at cost and depreciated over their estimated useful lives using the straight-line method. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to the Company's consolidated statements of operations and comprehensive income (loss). Repairs and maintenance costs are expensed as incurred.

### ***Leases***

The Company determines if an arrangement is a lease at contract inception. Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent the Company's obligation to make payments arising from the lease. Operating lease assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the Company will exercise those options. The Company uses the Company's incremental borrowing rate when the implicit interest rate is not readily determinable based upon the information available at the commencement date of the lease in determining the present value of the lease payments and the implicit interest rate when readily determinable.

The lease payments used to determine the Company's operating lease assets may include lease incentives, stated rent increases and escalation clauses linked to rates of inflation, when determinable, and are recognized in the Company's operating lease assets in the Company's consolidated balance sheets. In addition, the Company's contracts may contain lease and non-lease components. The Company combines lease and non-lease components, which are accounted for together as lease components.

The Company's operating leases are reflected in the right-of-use operating asset; operating lease liability, current portion; and operating lease liability, net of current portion in the Company's consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Short-term leases, defined as leases that have a lease term of 12 months or less at the commencement date, are not recorded on the Company's consolidated balance sheets and are recognized in the consolidated statements of operations and comprehensive income (loss) on a straight-line basis over the term of the lease.

Variable lease payments are the amounts owed by the Company to a lessor that are not fixed, such as reimbursement for common area maintenance and utilities costs for facility leases. Variable lease payments are expensed when incurred.

### ***Impairment of Long-Lived Assets***

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset group for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset group to its carrying value. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

### ***Cost of Goods Sold***

Cost of goods sold includes direct and indirect costs related to the manufacturing and distribution of ZULRESSO, including third-party manufacturing costs, packaging services, freight, third-party royalties payable on the Company's net product revenue and amortization of intangible assets associated with ZULRESSO. Cost of goods sold may also include period costs related to certain inventory manufacturing services, inventory adjustment charges, as well as manufacturing variances. In connection with the FDA approval of ZULRESSO in March 2019, the Company subsequently began capitalizing inventory manufactured or purchased after this date. As a result, certain manufacturing costs associated with product shipments of ZULRESSO were expensed prior to FDA approval and, therefore, are not included in cost of goods sold during the years ended December 31, 2022 and 2021.

### ***Research and Development Costs and Accruals***

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, overhead costs, depreciation, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

The Company has entered into various research and development contracts with research institutions and other companies both inside and outside of the U.S. These agreements are generally cancelable, and related costs are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research and development costs. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations to those third parties as of the end of the reporting period. Any accrual estimates are based on a number of factors, including the Company's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates are made in



determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs.

### ***Stock-Based Compensation***

The Company recognizes compensation expense for stock-based awards, including grants of stock options and restricted stock units, granted to employees, non-employee directors and non-employee consultants based on the estimated fair value on the date of grant, over the requisite service period. The Company recognizes stock-based compensation expense for only the portion of awards that are expected to vest.

For awards that vest upon achievement of a performance condition, the Company recognizes compensation expense when achievement of the performance condition is met or during the period from which meeting the condition is deemed probable until the expected date of meeting the performance condition, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

The fair value of each stock option grant is estimated using the Black-Scholes option-pricing model. Effective January 1, 2020, the Company began using the historical volatility of only its common stock, as there is adequate historical data for the duration of the expected term.

The expected term of the stock options granted to employees, non-employee directors and non-employee consultants by the Company has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" stock options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the date of grant for time periods approximately equal to the expected term of the award. The expected dividend yield is zero, based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

The Company also applies a forfeiture rate in order to calculate stock-based compensation expense. Expected forfeitures are based on the historical experience of the Company and management's expectations of future forfeitures. To the extent actual forfeitures differ from the estimates, the difference is recorded as a cumulative adjustment in the period in which the estimates are revised.

### ***Treasury Stock***

The Company records treasury stock at cost. Treasury stock consists of shares of the Company's common stock received from a then-employee as consideration for exercises of stock options.

### ***Basic and Diluted Net Income (Loss) Per Share***

Basic net income (loss) per share is computed by dividing the net income (loss) by the weighted average number of shares of common stock that were outstanding during the period. For computing diluted net income (loss) per share, the weighted average number of shares of common stock that were outstanding during the period is adjusted for the dilutive effect of common stock equivalents outstanding for the period by using the treasury stock method.

For periods in which the Company has reported net losses, diluted net loss per share is the same as basic net loss per share, because dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss for the years ended December 31, 2022 and 2021.

### ***Concentration of Credit Risk and of Significant Suppliers***

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company maintains accounts for all cash and cash equivalents at accredited financial institutions, in amounts that exceed federally insured limits. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is dependent on third-party manufacturers to supply products for research and development activities for its programs. The Company also relies on and expects to continue to rely on third-party manufacturers to supply it with active pharmaceutical ingredients (“API”) and formulated drugs; and to provide other services related to manufacturing activities for these programs. These programs could be adversely affected by a significant interruption in the supply of API and formulated drugs, or the interruption of manufacturing related services.

### ***Income Taxes***

The Company accounts for income taxes under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences attributable to differences between financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Valuation allowances are provided if, based on the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of Accounting Standards Codification (“ASC”) Topic 740, “*Income Taxes*” (“Topic 740”). When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company accrues for potential interest and penalties related to unrecognized tax benefits in income tax expense.

### ***Fair Value Measurements***

Fair value is the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Financial assets and liabilities carried at fair value are classified and disclosed in one of the following three categories:

- Level 1 — Quoted market prices in active markets for identical assets or liabilities.
- Level 2 — Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company’s cash equivalents and marketable securities at December 31, 2022 and 2021 were carried at fair value, determined according to the fair value hierarchy; see Note 3, Fair Value Measurements.

The carrying amounts reflected in the consolidated balance sheets for the collaboration receivable – related party, accounts payable and accrued expenses approximate their fair values due to their short-term maturities at December 31, 2022 and 2021, respectively.

### ***Segment Data***

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The singular focus of the Company is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive.

### ***Comprehensive Income (Loss)***

Comprehensive income (loss) includes net income (loss) and other changes in stockholders’ equity that result from transactions and economic events other than those with stockholders. The Company’s only element of other

comprehensive income (loss) is unrealized gains and losses on marketable securities that are considered to be available-for-sale.

### ***Revenue Recognition***

The Company generates revenue from the sale of ZULRESSO, which was approved by the FDA in March 2019 and the Company subsequently began selling in June 2019, and from collaboration and supply agreements with the Company's collaborators. To date, revenue from collaboration agreements has come from initial, upfront payments allocated to licenses of intellectual property delivered to the Company's collaborators and from the supply of material for clinical trials under a supply agreement.

Under ASC Topic 606, *Revenue from Contracts with Customers* ("Topic 606"), an entity recognizes revenue when or as performance obligations are satisfied by transferring control of promised goods or services to a customer, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations. The exercise of a material right may be accounted for as a contract modification or as a continuation of the contract for accounting purposes.

For contracts determined to be within the scope of Topic 606, the Company assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. Promised goods and services are considered distinct provided that: (i) the customer can benefit from the good or service either on its own or together with other resources that are readily available to the customer and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract.

The Company allocates the transaction price (the amount of consideration it expects to be entitled to from a customer in exchange for the promised goods or services) to each performance obligation and recognizes the associated revenue when (or as) each performance obligation is satisfied. The Company's estimate of the transaction price for each contract includes all variable consideration to which the Company expects to be entitled.

### ***Collaboration and License Revenue***

In assessing whether a promised good or service is distinct in the evaluation of a collaboration or license arrangement subject to Topic 606, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct.

The transaction price is then determined and allocated to the identified performance obligations in proportion to their standalone selling prices ("SSP") on a relative SSP basis. SSP is determined at contract inception and is not updated to reflect changes between contract inception and when the performance obligations are satisfied. Determining the SSP for performance obligations requires significant judgment. In developing the SSP for a performance obligation, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. In certain circumstances, the Company may apply the residual method to determine the SSP of a good or service if the standalone selling price is considered highly variable or uncertain. The Company validates the SSP for performance obligations by evaluating whether changes in the key

assumptions used to determine the SSP will have a significant effect on the allocation of arrangement consideration between multiple performance obligations.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

If an arrangement includes development and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

In determining the transaction price, the Company adjusts consideration for the effects of the time value of money if the timing of payments provides the Company with a significant benefit of financing. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less. The Company assessed its arrangements with Shionogi and Biogen and concluded that a significant financing component does not exist for either arrangement. For arrangements with licenses of intellectual property that include sales-based royalties or milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties or milestone payments relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty or milestone payment has been allocated has been satisfied.

The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time this is based on the use of an output or input method. Revenue from the Company's collaboration agreement with Shionogi has come from initial, upfront consideration upon execution of the agreement and for the supply of drug product for Shionogi's clinical trials. Revenue from the Company's collaboration agreement with Biogen has come from initial, upfront consideration related to the execution of the Biogen Collaboration Agreement. For additional information, refer to Note 6, *Collaboration Agreements*.

#### *Product Revenue, Net*

The Company recognizes product revenue, net of variable consideration related to certain allowances and accruals that are determined using the expected value method, in its consolidated financial statements at the point in time when control transfers to the customer, which is typically when the product has been delivered to the customer's location. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. The Company's only performance obligation identified for ZULRESSO is to deliver the product to the location specified by the customer's order. The Company records shipping and handling costs associated with delivery of product to its customers within selling, general and administrative expenses on its consolidated statements of operations and comprehensive income (loss). The Company expenses incremental costs of obtaining a contract as incurred if the expected amortization period of the asset would be less than one year. If the Company were to incur incremental costs with an amortization period greater than a year, such costs would be capitalized as contract assets, as they are expected to be recovered, and would be expensed by amortizing on a systematic basis that is consistent with the transfer to the customer of the goods or services to which the asset relates. The Company did not have any contract assets (unbilled receivables) at December 31, 2022, as customer invoicing

generally occurs before or at the time of revenue recognition. The Company did not have any contract liabilities at December 31, 2022, as the Company did not receive any payments in advance of satisfying its performance obligations to its customers. Amounts billed or invoiced that are considered trade accounts receivable are included in prepaid expenses and other current assets on the consolidated balance sheets.

As of December 31, 2022 and 2021, the Company had not provided any allowance for bad debts against the trade accounts receivable, and the amount of trade accounts receivable was not significant.

The Company records reserves, based on contractual terms, for the following components of variable consideration related to product sold during the reporting period, as well as its estimate of product that remains in the distribution channel inventory of its customers at the end of the reporting period. On a quarterly basis, the Company updates its estimates, if necessary, and records any material adjustments in the period they are identified.

*Chargebacks:* The Company estimates chargebacks from its customers who directly purchase the product from the Company for discounts resulting from contractual commitments to sell products to eligible healthcare settings at prices lower than the list prices charged to its customers. Customers charge the Company for the difference between what they pay to the Company for the product and the selling price to the eligible healthcare settings. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at the end of each reporting period that the Company expects will be sold to eligible healthcare settings, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

*Government Rebates:* The Company is subject to discount obligations under government programs, including Medicaid. The Company records reserves for rebates in the same period the related product revenue is recognized, resulting in a reduction of ZULRESSO product revenue and a current liability that is included in accrued expenses on its consolidated balance sheets. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimates of future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

*Trade Discounts and Allowances:* The Company generally provides customary invoice discounts on ZULRESSO sales to its customers for prompt payment and the Company pays fees for sales order management, data, and distribution services. The Company estimates its customers will earn these discounts and fees and deducts these discounts and fees in full from gross ZULRESSO revenue and accounts receivable at the time the Company recognizes the related revenue.

*Financial Assistance:* The Company provides voluntary financial assistance programs to patients with commercial insurance that have coverage and reside in states that allow financial assistance. The Company estimates the financial assistance amounts for ZULRESSO and records any such amounts within accrued expenses on its consolidated balance sheets. The calculation of the accrual for financial assistance is based on an estimate of claims and the cost per claim that the Company expects to receive using demographics for patients who have registered and been approved for assistance. Any adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability, which is included as a component of accrued expenses on the consolidated balance sheets.

*Product Returns:* Consistent with industry practice, the Company offers product return rights to customers for damaged, defective or expiring product, provided it is within a specified period around the product expiration date as set forth in the Company's return goods policy. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as a reserve within accrued expenses on the consolidated balance sheets. Product returns have been not significant to date and are not expected to be significant in the future.

### ***Collaborative Arrangements***

The Company analyzes its collaboration arrangements to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, *Collaborative Arrangements* (“Topic 808”). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For collaboration arrangements within the scope of Topic 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of Topic 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of Topic 606. For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election. For those elements of the arrangement that are accounted for pursuant to Topic 606, the Company applies the five-step model described above, and presents the arrangement as collaboration revenue in the consolidated statements of operations and comprehensive income (loss).

For collaboration arrangements that are within the scope of Topic 808, the Company evaluates the income statement classification for presentation of amounts due from or owed to other participants associated with multiple activities in a collaboration arrangement based on the nature of each separate activity. Payments or reimbursements that are the result of a collaborative relationship instead of a customer relationship, such as co-development and co-commercialization activities, are recorded as research and development expense or selling, general and administrative expense, in the event of a payment to the collaborative partner in a period, or a reduction to these expense line items in the event of a reimbursement from the collaboration partner in a period, as appropriate.

### ***Recently Issued Accounting Pronouncements***

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*. This standard enhances and simplifies various aspects of the income tax accounting guidance in ASC Topic 740, *Income Taxes*, including requirements related to hybrid tax regimes, the tax basis step-up in goodwill obtained in a transaction that is not a business combination, separate financial statements of entities not subject to tax, the intra-period tax allocation exception to the incremental approach, ownership changes in investments, changes from a subsidiary to an equity method investment, interim-period accounting for enacted changes in tax law, and the year-to-date loss limitation in interim-period tax accounting. The Company adopted the standard on the required effective date of January 1, 2021. This guidance did not have a significant impact on the Company’s consolidated financial statements and related disclosures.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company’s consolidated financial statements upon adoption.

### **3. Fair Value Measurements**

The Company’s cash equivalents are classified within Level 1 and Level 2 of the fair value hierarchy. The Company’s investments in marketable securities are classified within Level 2 of the fair value hierarchy.

The fair values of the Company’s marketable securities are based on prices obtained from independent pricing sources. Consistent with the fair value hierarchy described in Note 2, Summary of Significant Accounting Policies, marketable securities with validated quotes from pricing services are reflected within Level 2, as they are primarily based on observable pricing for similar assets or other market observable inputs. Typical inputs used by these pricing services include, but are not limited to, reported trades, benchmark yields, issuer spreads, bids, offers or estimates of cash flow, prepayment spreads and default rates. The Company performs validation procedures to ensure the reasonableness of this data. The Company performs its own review of prices received from the independent pricing services by comparing these

prices to other sources. After completing the validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of December 31, 2022 and 2021.

The following tables summarize the Company's cash equivalents and marketable securities as of December 31, 2022 and 2021:

	December 31, 2022			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
(in thousands)				
<b>Cash equivalents:</b>				
Money market funds	\$ 161,185	\$ 161,185	\$ —	\$ —
Total cash equivalents	161,185	161,185	—	—
<b>Marketable securities:</b>				
U.S. government securities	302,911	—	302,911	—
U.S. corporate bonds	354,495	—	354,495	—
International corporate bonds	127,248	—	127,248	—
U.S. commercial paper	63,114	—	63,114	—
International commercial paper	133,163	—	133,163	—
U.S. certificates of deposit	15,613	—	15,613	—
U.S. municipal securities	113,250	—	113,250	—
Total marketable securities	1,109,794	—	1,109,794	—
	<u>\$ 1,270,979</u>	<u>\$ 161,185</u>	<u>\$ 1,109,794</u>	<u>\$ —</u>

	December 31, 2021			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
(in thousands)				
<b>Cash equivalents:</b>				
Money market funds	\$ 289,440	\$ 289,440	\$ —	\$ —
U.S. commercial paper	2,000	—	2,000	—
International commercial paper	1,999	—	1,999	—
Total cash equivalents	293,439	289,440	3,999	—
<b>Marketable securities:</b>				
U.S. government securities	324,532	—	324,532	—
U.S. corporate bonds	627,780	—	627,780	—
International corporate bonds	236,812	—	236,812	—
U.S. commercial paper	80,176	—	80,176	—
International commercial paper	142,335	—	142,335	—
U.S. municipal securities	36,428	—	36,428	—
Total marketable securities	1,448,063	—	1,448,063	—
	<u>\$ 1,741,502</u>	<u>\$ 289,440</u>	<u>\$ 1,452,062</u>	<u>\$ —</u>

During the years ended December 31, 2022 and 2021, there were no transfers among the Level 1, Level 2 and Level 3 categories.

The following tables summarize the gross unrealized gains and losses of the Company's marketable securities as of December 31, 2022 and 2021:

	December 31, 2022				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses (in thousands)	Credit Losses	Fair Value
<b>Assets:</b>					
U.S. government securities	\$ 307,173	\$ —	\$ (4,262)	\$ —	\$ 302,911
U.S. corporate bonds	358,019	6	(3,530)	—	354,495
International corporate bonds	128,374	7	(1,133)	—	127,248
U.S. commercial paper	63,234	—	(120)	—	63,114
International commercial paper	133,338	—	(175)	—	133,163
U.S. certificates of deposit	15,613	—	—	—	15,613
U.S. municipal securities	114,249	31	(1,030)	—	113,250
	<u>\$ 1,120,000</u>	<u>\$ 44</u>	<u>\$ (10,250)</u>	<u>\$ —</u>	<u>\$ 1,109,794</u>

	December 31, 2021				
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses (in thousands)	Credit Losses	Fair Value
<b>Assets:</b>					
U.S. government securities	\$ 325,514	\$ —	\$ (982)	\$ —	\$ 324,532
U.S. corporate bonds	628,836	27	(1,083)	—	627,780
International corporate bonds	237,303	—	(491)	—	236,812
U.S. commercial paper	80,194	—	(18)	—	80,176
International commercial paper	142,358	—	(23)	—	142,335
U.S. municipal securities	36,518	—	(90)	—	36,428
	<u>\$ 1,450,723</u>	<u>\$ 27</u>	<u>\$ (2,687)</u>	<u>\$ —</u>	<u>\$ 1,448,063</u>

The following tables summarize the fair value and the unrealized losses of the Company's marketable securities that have been in a loss position for either less than twelve months or greater than twelve months as of December 31, 2022 and 2021:

	December 31, 2022					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
	(in thousands)					
U.S. government securities	\$ 112,243	\$ (1,517)	\$ 185,691	\$ (2,745)	297,934	\$ (4,262)
U.S. corporate bonds	208,507	(1,989)	130,633	(1,541)	339,140	(3,530)
International corporate bonds	50,982	(497)	68,993	(636)	119,975	(1,133)
U.S. commercial paper	24,768	(120)	—	—	24,768	(120)
International commercial paper	30,987	(175)	—	—	30,987	(175)
U.S. municipal securities	86,251	(497)	14,466	(533)	100,717	(1,030)
	<u>\$ 513,738</u>	<u>\$ (4,795)</u>	<u>\$ 399,783</u>	<u>\$ (5,455)</u>	<u>\$ 913,521</u>	<u>\$ (10,250)</u>



	December 31, 2021					
	Less than 12 months		Greater than 12 months		Total	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
	(in thousands)					
U.S. government securities	\$ 309,588	\$ (982)	\$ —	\$ —	\$ 309,588	\$ (982)
U.S. corporate bonds	601,475	(1,083)	—	—	601,475	(1,083)
International corporate bonds	231,672	(491)	—	—	231,672	(491)
U.S. commercial paper	21,968	(18)	—	—	21,968	(18)
International commercial paper	35,059	(23)	—	—	35,059	(23)
U.S. municipal securities	24,953	(90)	—	—	24,953	(90)
	<u>\$ 1,224,715</u>	<u>\$ (2,687)</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,224,715</u>	<u>\$ (2,687)</u>

As of December 31, 2022 and 2021, the unrealized losses on the Company's investments in U.S. government securities, U.S. corporate bonds, and international corporate bonds were caused by interest rate increases. The Company purchased those investments at a premium relative to their face amount. The current credit ratings are all within the guidelines of the investment policy of the Company and the Company does not expect the issuers to settle any security at a price less than the amortized cost basis of the investment. The Company does not intend to sell the investments and it is not probable that the Company will be required to sell the investments before recovery of their amortized cost basis.

As of December 31, 2022, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for U.S. government securities, U.S. corporate bonds, international corporate bonds and municipal securities with a fair value of \$211.2 million that had maturities of one to two years.

As of December 31, 2021, all marketable securities held by the Company had remaining contractual maturities of one year or less, except for U.S. government securities, U.S. corporate bonds, international corporate bonds and municipal securities with a fair value of \$436.1 million that had maturities of one to two years.

All marketable securities, including those with remaining contractual maturities of more than one year, are classified as current assets on the balance sheet because they are considered to be "available for sale" and the Company can convert them into cash to fund current operations.

There have been no impairments of the Company's assets measured and carried at fair value during the years ended December 31, 2022 and 2021.

#### 4. Balance Sheet Components

##### *Property and Equipment, net*

The following table summarizes property and equipment, net, as of December 31, 2022 and 2021:

	December 31, 2022	December 31, 2021
	(in thousands)	
Computer hardware and software	\$ 1,771	\$ 1,391
Furniture and equipment	1,714	1,208
Leasehold improvements	5,508	5,390
	8,993	7,989
Less: Accumulated depreciation	(6,095)	(4,973)
	<u>\$ 2,898</u>	<u>\$ 3,016</u>

Depreciation expense for the years ended December 31, 2022, 2021 and 2020 was \$1.1 million, \$4.2 million and \$2.6 million, respectively.

The useful life for computer hardware and software is three years, furniture and equipment is five years and leasehold improvements is the lesser of the useful life or the term of the respective lease.

### ***Accrued Expenses***

The following tables summarizes accrued expenses as of December 31, 2022 and 2021:

	December 31, 2022	December 31, 2021
	(in thousands)	
Accrued research and development costs	\$ 32,565	\$ 39,147
Employee-related	29,372	18,618
Professional services	10,172	8,893
Other	557	617
	<u>\$ 72,666</u>	<u>\$ 67,275</u>

## **5. Leases, Commitments and Contingencies**

### ***Operating Leases***

The Company leases office space and certain equipment. All of the leases recorded on the consolidated balance sheets are operating leases. The Company's leases have remaining lease terms ranging from less than one year to approximately two years. Some of the leases include options to extend the leases for up to five years. These options were not included for the purpose of determining the right-of-use assets and associated lease liabilities as the Company determined that the renewal of these leases is not reasonably certain so only the original lease term was taken into consideration. The leases do not include any restrictions or covenants that had to be accounted for under the lease guidance.

As of January 1, 2020, the Company leased office space in three multi-tenant buildings in Cambridge, Massachusetts, consisting of 63,017 square feet in the first building, under an operating lease that will expire on August 31, 2024; 40,419 square feet in the second building, under an operating lease that will expire on August 31, 2024 and 15,975 square feet in the third building, under an operating lease that began on March 1, 2019 and was initially scheduled to expire on February 29, 2024; and in a multi-tenant building in Raleigh, North Carolina, consisting of 15,525 square feet under an operating lease that will expire on November 30, 2024.

During the year ended December 31, 2021, the Company terminated the operating lease for office space in the third multi-tenant building in Cambridge, Massachusetts and the remaining right-of-use asset of \$3.7 million and the associated liabilities related to this lease were de-recognized upon termination of the lease. Additionally, during the year ended December 31, 2021, the Company entered into a sublease for a portion of the leased office space in the second multi-tenant building in Cambridge, Massachusetts.

From June 2018 to January 2019, the Company entered into leases for vehicles for field-based employees. These leases were determined to be operating leases and a right-of-use operating asset in the amount of \$5.3 million was recorded on the balance sheet upon implementation of the new lease standard on January 1, 2019. The leases were for a term of three years and were to expire on various dates through January 31, 2022. During the year ended December 31, 2020, these leases were terminated as part of the restructuring during April 2020, and the remaining right-of-use asset of \$2.3 million and the associated liabilities related to these leases were de-recognized upon termination of the leases. During the year ended December 31, 2020, the restricted cash of \$0.7 million related to these leases was returned to the Company by the lessor.

The following table shows the amounts of operating leases in the balance sheets as of December 31, 2022 and 2021:

Balance sheet location	Balance sheet caption	December 31,	
		2022	2021
(in thousands)			
<i>Assets</i>			
Right-of-use operating asset	Right-of-use operating asset	\$ 10,532	\$ 16,109
<i>Liabilities</i>			
Current operating lease liabilities	Operating lease liability, current portion	7,643	7,468
Long-term operating lease liabilities	Operating lease liability, net of current portion	4,491	10,964
		<u>\$ 12,134</u>	<u>\$ 18,432</u>

The following table shows the amounts of lease expense by lease type that was recognized during the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands)		
Operating lease cost	\$ 6,748	\$ 8,748	\$ 8,838
Variable lease cost	1,846	1,600	2,285
Short-term lease cost	206	101	74
Sublease income	(421)	(234)	-
	<u>\$ 8,379</u>	<u>\$ 10,215</u>	<u>\$ 11,197</u>

The Company made an accounting policy election not to apply the recognition requirements to short-term leases. The Company recognizes the lease payments for short-term leases as expense on a straight-line basis over the lease term, and variable lease payments in the period in which the obligation for those payments is incurred.

The minimum lease payments are expected to be as follows:

Years Ending December 31,	(In thousands)
2023	\$ 7,643
2024	5,316
Thereafter	-
Total lease payments	12,959
Less imputed interest	(825)
Present value of operating lease liabilities	<u>\$ 12,134</u>

The following table shows the weighted average remaining lease term and weighted average discount rate of the operating leases:

	Year ended December 31,	
	2022	2021
Weighted average remaining lease term in years	1.68	2.68
Weighted average discount rate	7.5%	7.5%

The interest rate implicit in lease contracts is typically not readily determinable and as such, the Company uses its incremental borrowing rate based on the information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

The following table shows the supplemental disclosure of cash flow information related to the operating leases included in cash flows used by operating activities in the consolidated statements of cash flows:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands)		
Cash paid for amounts included in the measurement of lease liabilities	\$ 7,468	\$ 9,264	\$ 9,231
Lease asset de-recognized upon lease cancellation			
Operating leases	\$ —	\$ 3,733	\$ 2,310

## License Agreements

### CyDex License Agreement

In September 2015, the Company amended and restated its existing commercial license agreement with CyDex Pharmaceuticals, Inc. (“CyDex”), a wholly owned subsidiary of Ligand Pharmaceuticals Incorporated.

Under the terms of the commercial license agreement as amended and restated, CyDex has granted to the Company an exclusive license to CyDex’s Captisol drug formulation technology and related intellectual property for the manufacture of pharmaceutical products incorporating brexanolone and the Company’s compound known as SAGE-689, and the development and commercialization of the resulting products for the treatment, prevention or diagnosis of any disease or symptom in humans or animals other than (i) the ocular treatment of any disease or condition with a formulation, including a hormone; (ii) topical ocular treatment of inflammatory conditions; (iii) treatment and prophylaxis of fungal infections in humans; and (iv) any ocular treatment for retinal degeneration. The Company is required to pay a royalty to CyDex on sales of brexanolone and will be required to pay a royalty on any sales of SAGE-689, if such product candidate is successfully developed in the future. Royalty rates are in the low single digits based on levels of net sales. From the effective date of the agreement to December 31, 2022, the Company has paid to CyDex \$1.0 million for licensing fees, which was recorded as research and development expense.

Under the amended and restated license agreement with CyDex, the Company agreed to make milestone payments on the achievement of clinical development and regulatory milestones in the amount of up to \$0.8 million in clinical milestones and up to \$3.8 million in regulatory milestones for each of the first two fields with respect to brexanolone; up to \$1.3 million in clinical milestones and up to \$8.5 million in regulatory milestones for each of the third and fourth fields with respect to brexanolone; and up to \$0.8 million in clinical milestones and up to \$1.8 million in regulatory milestones for one field with respect to SAGE-689. From the effective date of the agreement to December 31, 2022, the Company has recorded research and development expense and made cash payments of \$3.6 million related to these clinical development and regulatory milestones and has recorded an intangible asset and made a cash payment of \$3.0 million related to these regulatory milestones.

For the year ended December 31, 2020, additional clinical development milestones were met for the brexanolone program under the license agreement with CyDex, and accordingly, the Company recorded research and development expense and accrued expenses totaling \$1.3 million. The amount was paid in cash during the year ended December 31, 2021.

For the year ended December 31, 2021, an additional clinical development milestone was met under the license agreement with CyDex related to SAGE-689, and accordingly, the Company recorded research and development expense and made a cash payment of \$0.1 million. Additionally in the year ended December 31, 2021, the Company paid \$1.3 million for the additional clinical development milestones that were met for the brexanolone program under the license agreement with CyDex in the year ended December 31, 2020.

For the year ended December 31, 2022, the Company did not record any expense or intangible asset, or make any milestone payments related to clinical development or regulatory milestones for the brexanolone program or SAGE-689 under the license agreement with CyDex.

### ***University of California License Agreements***

In October 2013, the Company entered into a non-exclusive license agreement with the Regents of the University of California ("the Regents") under which the Company was granted a non-exclusive license to certain clinical data and clinical material related to brexanolone for use in the development and commercialization of biopharmaceutical products in the licensed field, including status epilepticus and postpartum depression. In May 2014, the license agreement was amended to add the treatment of essential tremor to the licensed field of use, materials and milestone fee provisions of the agreement. The Company paid to the Regents clinical development milestones of \$0.1 million, prior to December 31, 2015; no other milestones are outstanding under this non-exclusive license agreement. The Company is required to pay royalties of less than 1% on net sales for a period of fifteen years following the sale of the first product developed using the data and materials, and the Company began to pay these royalties in 2019. The license will terminate on the earlier to occur of (i) 27 years after the effective date or (ii) 15 years after the last-derived product is first commercially sold.

In June 2015, the Company entered into an exclusive license agreement with the Regents whereby the Company was granted an exclusive license to certain patent rights related to the use of allopregnanolone to treat various diseases. In exchange for such license, the Company paid an upfront payment of \$50,000 and was required to make payments of \$15,000 for annual maintenance fees until the calendar year following the first sale of ZULRESSO. The Company is obligated to make milestone payments following the achievement of specified regulatory and sales milestones of up to \$0.7 million and \$2.0 million in the aggregate, respectively. The Company pays royalties at a low single digit percentage of net sales of ZULRESSO, subject to specified minimum annual royalty amounts. Unless terminated by operation of law or by acts of the parties under the terms of the agreement, the license agreement will terminate when the last-to-expire patents or last-to-be abandoned patent applications expire, whichever is later. From the effective date of the agreement to December 31, 2022, the Company has recorded research and development expense and made cash payments of \$0.3 million related to these regulatory and sales milestones; and has recorded an intangible asset and made a cash payment of \$0.5 million related to these regulatory and sales milestones.

For the years ended December 31, 2022, 2021 and 2020, the Company did not record any expense or make any milestone payments under the license agreements with the Regents.

## **6. Collaboration Agreements**

### ***Shionogi***

In June 2018, the Company entered into a strategic collaboration with Shionogi for the clinical development and commercialization of zuranolone for the treatment of MDD and other potential indications in Japan, Taiwan and South Korea (the "Shionogi Territory"). In October 2018, the Company entered into a supply agreement with Shionogi for the Company to supply zuranolone clinical material to Shionogi.

Under the terms of the collaboration agreement, Shionogi is responsible for all clinical development and regulatory filings for zuranolone in MDD and other indications in the Shionogi Territory and would be responsible for commercialization of zuranolone in the Shionogi Territory, if zuranolone is successfully developed and obtains marketing approval in any of the countries within the Shionogi Territory. Shionogi was required to make an upfront payment to the Company of \$90.0 million, and the Company will be eligible to receive additional payments of up to \$485.0 million if certain regulatory and commercial milestones are achieved by Shionogi. The potential future milestone payments include up to \$70.0 million for the achievement of specified regulatory milestones, up to \$30.0 million for the achievement of specified commercialization milestones, and up to \$385.0 million for the achievement of specified net sales milestones. The Company is eligible to receive tiered royalties on sales of zuranolone in the Shionogi Territory, if development efforts are successful, with tiers averaging in the low to mid-twenty percent range, subject to other terms of the agreement. Shionogi has also granted to the Company certain rights to co-promote zuranolone in Japan. As between the Company and Shionogi, the Company maintains exclusive rights to develop and commercialize zuranolone outside of the Shionogi Territory. The upfront cash payment and any payments for milestones and royalties are non-refundable and non-creditable. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone payments or any royalty payments from Shionogi.

The Company concluded that Shionogi meets the definition of a customer because the Company is delivering intellectual property and know-how rights for the zuranolone program in support of territories in which the parties are not jointly sharing the risks and rewards. In addition, the Company determined that the Shionogi collaboration met the requirements to be accounted for as a contract, including that it was probable that the Company will collect the consideration to which the Company was entitled in exchange for the goods or services that will be delivered to Shionogi.

The Company determined that the performance obligations in the Shionogi collaboration agreement included the license to zuranolone and the supply of certain materials during the clinical development phase, which includes the supply of API. The performance obligation related to the license to zuranolone was determined to be distinct from other performance obligations and therefore was a separate performance obligation for which control was transferred upon signing. The obligation to provide certain clinical materials, including API for use during the development period, was determined to be a separate performance obligation. Given that Shionogi is not obligated to purchase any minimum amount or quantities of commercial API, the supply of API to Shionogi for commercial use was determined to be an option for Shionogi, rather than a performance obligation of the Company at contract inception and will be accounted for if and when exercised. The Company also determined that there was no separate material right in connection with the supply of API for commercial use as the expected pricing was not at a discount. Given this fact pattern, the Company has concluded the agreement has two performance obligations.

Under the clinical supply agreement, the Company is obligated to manufacture and supply to Shionogi (i) clinical quantities of API reasonably required by Shionogi for the development of licensed products in the Shionogi territory and (ii) quantities of drug product reasonably required for use by Shionogi in Phase 1 clinical trials of zuranolone in the Shionogi territory, in the quantities agreed to by the parties. Collaboration revenue from the clinical supply agreement pertains to the clinical material sold under the terms of the clinical supply agreement. The Company records the costs related to the clinical supply agreement in research and development expense on its consolidated statements of operations and comprehensive income (loss). During the years ended December 31, 2022, 2021 and 2020, no collaboration revenue was recognized related to the Company's agreement with Shionogi.

The Company completed the evaluation of the standalone selling prices of each of the performance obligations and determined that the standalone selling price of the license performance obligation was \$90.0 million. The Company recognized the transaction price allocated to the license performance obligation of \$90.0 million as revenue upon delivery of the license to Shionogi and resulting ability of Shionogi to use and benefit from the license, which was in the three months ended June 30, 2018. The remaining transaction price related to the performance obligation for the supply of certain clinical material is not significant. The potential milestone payments that the Company is eligible to receive were excluded from the transaction price, as all milestone amounts were fully constrained based on the probability of

achievement. The Company will re-evaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

### ***Biogen***

In November 2020, the Company entered into the Biogen Collaboration Agreement to jointly develop and commercialize SAGE-217 products for MDD, PPD and other disorders and SAGE-324 products for essential tremor and other disorders. Concurrently, the Company also entered into a stock purchase agreement with BIMA (the “Biogen Stock Purchase Agreement”) under which BIMA purchased shares of the Company’s common stock. The Biogen Collaboration Agreement became effective on December 28, 2020 (the “Effective Date”).

Under the terms of the Biogen Collaboration Agreement, the Company granted Biogen co-exclusive licenses to develop and commercialize SAGE-217 products and SAGE-324 products (each, a “Product Class” and together, the “Licensed Products”) in the U.S., an exclusive license to develop and commercialize SAGE-217 products in all countries of the world other than the U.S. and the Shionogi Territory, and an exclusive license to develop and commercialize SAGE-324 products in all countries of the world other than the U.S. The Company refers to the territories outside the U.S. to which Biogen has rights under the Biogen Collaboration Agreement with respect to the applicable Licensed Product as the “Biogen Territory”.

In connection with the effectiveness of the Biogen Collaboration Agreement and the closing of the sale of shares to BIMA in December 2020, the Company received \$1.5 billion in consideration, comprised of an upfront payment of \$875.0 million and the \$650.0 million purchase price for 6,241,473 newly issued shares of the Company’s common stock (the “Biogen Shares”). As a result of the purchase of the Biogen Shares, Biogen has become a related party of the Company.

The Company is eligible to receive additional payments of up to \$1.6 billion if certain regulatory and commercial milestones are achieved. The potential future milestone payments for SAGE-217 products include up to \$475.0 million for the achievement of specified regulatory and commercial milestones, including milestones totaling \$225.0 million for the first commercial sale of zuranolone in MDD and PPD, and up to \$300.0 million for the achievement of specified net sales milestones. The potential future milestone payments for SAGE-324 products include up to \$520.0 million for the achievement of specified regulatory and commercial milestones and up to \$300.0 million for the achievement of specified net sales milestones. The Company is also eligible to receive tiered royalties on net sales of SAGE-217 products and SAGE-324 products in the Biogen Territory at percentage rates ranging from the high teens to low twenties.

Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may never receive any milestone payments or any royalty payments under the Biogen Collaboration Agreement.

Development and commercialization activities in the U.S. are conducted pursuant to plans agreed to by the Company and Biogen and overseen by a joint steering committee that will consist at all times of an equal number of representatives of each party. The Company and Biogen will share equally in the costs for development and commercialization, as well as the profits and losses upon FDA approval and commencement of product sales, in the U.S., subject to the Company’s opt-out right described below. Biogen will be solely responsible for all development activities and costs related to any development and commercialization of SAGE-217 products and SAGE-324 products for the Biogen Territory, and the Company will receive royalties on any sales in the Biogen Territory, as mentioned above. Biogen will be the principal and record sales of SAGE-217 products globally. The Company will be the principal and record sales of SAGE-324 products in the U.S. and Biogen will record sales of SAGE-324 Products in the Biogen Territory.

The Company will supply API and bulk drug product for the Biogen Territory and API, bulk drug product and final drug product for the U.S. to support development and commercialization activities. Biogen has the right to assume manufacturing responsibilities for API for the Biogen Territory at any time during the term of the agreement and will, within a reasonable period of time after the Effective Date, assume manufacturing responsibility for bulk drug product for the Biogen Territory.

Unless terminated earlier, the Biogen Collaboration Agreement will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the date on which (a) in any country in the Biogen Territory, the royalty term has expired for all Licensed Products in a Product Class in such country, and (b) for the U.S., the parties agree to permanently cease to commercialize all Licensed Products in a Product Class. Biogen also has the right to terminate the Biogen Collaboration Agreement for convenience in its entirety, on a Product Class-by-Product Class basis or as to a particular region, upon advance written notice. The Company has an opt-out right to convert the co-exclusive licenses in the U.S. to an exclusive license to Biogen on a Product Class-by-Product Class basis. Following the exercise of the opt-out right, the Company would no longer share equally in the profits and losses in the U.S. and would be entitled to receive certain royalty payments at percentage rates ranging from the high teens to low twenties and additional sales milestones.

The Company concluded that the Biogen Collaboration Agreement and the Biogen Stock Purchase Agreement should be combined and treated as a single arrangement for accounting purposes as the agreements were entered into contemporaneously and in contemplation of one another. The Company determined that the combined agreements had elements that were within the scope of Topic 606 and Topic 808.

As of the Effective Date, the Company identified the following promises in the Biogen Collaboration Agreement that were evaluated under the scope of Topic 606: delivery of (i) a co-exclusive license for SAGE-217 products in the U.S.; (ii) an exclusive license for SAGE-217 products in the Biogen Territory; (iii) a co-exclusive license for SAGE-324 products in the U.S.; (iv) an exclusive license for SAGE-324 products in the Biogen Territory; (v) the clinical manufacturing supply of API and bulk drug product for SAGE-217 products in the Biogen Territory; and (vi) the clinical manufacturing supply of API and bulk drug product for SAGE-324 products in the Biogen Territory.

The Company also evaluated whether certain options outlined within the Biogen Collaboration Agreement represented material rights that would give rise to a performance obligation and concluded that none of the options convey a material right to Biogen and therefore are not considered separate performance obligations within the Biogen Collaboration Agreement.

The Company assessed the above promises and determined that the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. are reflective of a vendor-customer relationship and therefore represent performance obligations within the scope of Topic 606. The co-exclusive license for SAGE-217 products and SAGE-324 products in the U.S. are considered functional intellectual property and distinct from other promises under the contract. The exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory are considered functional licenses that are distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the licenses on its own or together with other readily available resources. As the co-exclusive licenses in the U.S. and the exclusive licenses in the Biogen Territory are delivered at the same time, they are considered one performance obligation at contract inception. The clinical manufacturing supply of API and bulk drug product for SAGE-217 products and SAGE-324 products for the Biogen Territory are considered distinct in the context of the Biogen Collaboration Agreement as Biogen can benefit from the manufacturing services together with the licenses transferred by the Company at the inception of the agreement. Therefore, each represents a separate performance obligation within a contract with a customer under the scope of Topic 606 at contract inception.

The Company considers the collaborative activities associated with the co-development, co-commercialization, and co-manufacturing of SAGE-217 products and SAGE-324 products in the U.S. to be separate units of account within the scope of Topic 808 as the Company and Biogen are both active participants in the development and commercialization activities and are exposed to significant risks and rewards that are dependent on the development and commercial success of the activities in the arrangement. The Company has determined that the supply of API and bulk drug product for the Biogen Territory and API, bulk drug product and final drug product for the U.S. to Biogen will be classified as collaboration revenue – related party in the consolidated statements of operations and comprehensive income (loss). During the years ended December 31, 2022 and 2021, no collaboration revenue – related party was recognized related to the Biogen Collaboration Agreement.

Payments to or reimbursements from Biogen related to the co-development, co-commercialization, and co-manufacturing activities and the agreement of the parties to share equally the cost of these activities will be accounted for



as an increase to or reduction of research and development expenses or selling, general and administrative expenses, depending on the nature of the activity.

During the year ended December 31, 2022, the Company recorded a net reimbursement of \$75.5 million for the amounts due from Biogen as a reduction of the related operating expense categories in the consolidated statement of operations and comprehensive income (loss). During the year ended December 31, 2021, the Company recorded a net reimbursement of \$91.1 million for the amounts due from Biogen as a reduction of the related operating expense categories in the consolidated statement of operations and comprehensive income (loss).

As of December 31, 2022, the Company recorded a Collaboration Receivable – Related Party of \$13.7 million in the consolidated balance sheet for the amounts due for the three months ended December 31, 2022. During the year ended December 31, 2022, no payments were made to Biogen and the Company received \$80.3 million from Biogen for the amounts due for the three months ended December 31, 2021 and the nine months ended September 30, 2022.

The following table summarizes expenses related to the Biogen Collaboration Agreement that were incurred by the Company and the related reimbursement from Biogen, reflected by category of operating expenses:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Expenses related to the Biogen Collaboration Agreement incurred by Sage	\$ 213,524	\$ 193,776
Net reimbursement from Biogen reflected in the consolidated statements of operations and comprehensive income (loss):		
Research and development expenses	(73,227)	(79,848)
Selling, general and administrative expenses	(2,230)	(11,282)
	<u>(75,457)</u>	<u>(91,130)</u>
Total net expenses related to the Biogen Collaboration Agreement in the consolidated statements of operations and comprehensive income (loss)	<u>\$ 138,067</u>	<u>\$ 102,646</u>

The Company determined the transaction price under Topic 606 at the inception of the Biogen Collaboration Agreement to be \$1.1 billion, consisting of the upfront payment of \$875.0 million plus \$232.5 million in excess proceeds from the equity investment under the Biogen Stock Purchase Agreement, when measured at fair value, plus future variable consideration for manufacturing supply of clinical API and bulk drug product for the Biogen Territory. The amount of variable consideration related to the future manufacturing services was not material. The Company determined that any variable consideration related to clinical development and regulatory milestones is deemed to be fully constrained and therefore excluded from the transaction price due to the high degree of uncertainty and risk associated with these potential payments, as the Company determined that it could not assert that it was probable that a significant reversal in the amount of cumulative revenue recognized will not occur. The Company also determined that royalties and sales milestones relate solely to the licenses of intellectual property and are therefore excluded from the transaction price under the sales- or usage-based royalty exception of Topic 606. Revenue related to these royalties and sales milestones will only be recognized when the associated sales occur, and relevant thresholds are met.

As noted above, the Company identified three performance obligations in the Biogen Collaboration Agreement: (i) the delivery of the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. and the exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory; (ii) the clinical manufacturing supply of API and bulk drug product for SAGE-217 products in the Biogen Territory; and (iii) the clinical manufacturing supply of the API and bulk drug product for SAGE-324 products in the Biogen Territory. The selling price of each performance obligation in the Biogen Collaboration Agreement was determined based on the Company's SSP with the objective of determining the price at which it would sell such an item if it were to be sold regularly on a standalone basis. The Company allocated the variable consideration related to the manufacturing obligations to the future clinical supply of SAGE-217 products and SAGE 324 products in the Biogen Territory and the remaining fixed consideration to the license

obligation. The variable consideration related to the manufacturing obligations was not material. As such, the entirety of the \$1.1 billion fixed consideration of the transaction price has been allocated to the transfer of the co-exclusive licenses for SAGE-217 products and SAGE-324 products in the U.S. and the exclusive licenses for SAGE-217 products and SAGE-324 products in the Biogen Territory. The Company recognizes revenue for the license performance obligations at a point in time, that is upon transfer of the licenses to Biogen. As control of these licenses was transferred on the Effective Date and Biogen could begin to use and benefit from the licenses, the Company recognized \$1.1 billion of license revenue during the year ended December 31, 2020 under the Biogen Collaboration Agreement. The Company will recognize revenue for the clinical manufacturing supply obligations at a point in time, that is upon the delivery of the supply to Biogen.

#### ***Accounting for the Biogen Stock Purchase Agreement***

In connection with the execution of the Biogen Collaboration Agreement, the Company and BIMA entered into the Biogen Stock Purchase Agreement. Pursuant to the Biogen Stock Purchase Agreement, the Company sold the Biogen Shares to BIMA at a price of approximately \$104.14 per share, which represented a 40 percent premium over the 30-day volume-weighted average share price as of the last trading day prior to the date the Biogen Collaboration Agreement and Biogen Stock Purchase Agreement were executed in November 2020, for aggregate consideration of \$650.0 million. The sale of the shares to BIMA closed on December 31, 2020.

The Biogen Stock Purchase Agreement includes certain standstill provisions, lock-up restrictions, and a voting agreement with respect to the Biogen Shares. Pursuant to the terms of the Biogen Stock Purchase Agreement, BIMA has agreed not to, and to cause its affiliates not to, directly or indirectly acquire the Company's securities, seek or propose a tender or exchange offer or merger between the Company and Biogen, solicit proxies or consents with respect to any matter, or undertake other specified actions, in each case subject to specified conditions. The standstill restrictions terminate on the earliest of (i) a specified regulatory milestone under the Biogen Collaboration Agreement, (ii) the date one year following the termination of the Biogen Collaboration Agreement and (iii) the seventh anniversary of the Effective Date. BIMA also agreed not to, and to cause its affiliates not to, sell or transfer any of the Biogen Shares for a period of eighteen months from the closing of the sale of the Biogen Shares, which period expired on June 30, 2022, and to limit sales and transfers of the Biogen Shares for an additional eighteen-month period, in each case subject to specified conditions and exceptions.

The Company determined the fair value of the common shares issued using an option pricing valuation model to take into consideration the holding period restrictions. The fair value of the Company's common stock was considered a Level 2 fair value measurement within the fair value hierarchy. The most significant assumptions within the model are the Company's stock price, the term of the restrictions and the stock price volatility, which is based upon a blend of historical and implied volatility of the Company's stock. Based on the fair value adjustments made by management, the fair value of the shares issued was determined to be \$417.5 million, which was \$232.5 million less than the proceeds received from BIMA for the issuance of the Company's common stock under the Biogen Stock Purchase Agreement. As such, the \$232.5 million in excess proceeds has been included in the \$1.1 billion transaction price of the Biogen Collaboration Agreement determined above.

## **7. Preferred Stock**

The Board of Directors of the Company (the "Board") is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. The Board can designate the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. The Board may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. As of December 31, 2022 and 2021, the Company had no shares of preferred stock issued or outstanding and preferred stock was classified as stockholders' equity.

## **8. Common Stock**

As of December 31, 2022 and 2021, the Company authorized 120,000,000 shares of common stock with a par value of \$0.0001 per share.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Board, if any. As of December 31, 2022 and 2021, no dividends have been declared.

On December 31, 2020, the Company completed the sale of 6,241,473 shares of its common stock in a private placement to BIMA at a price of approximately \$104.14 per share, resulting in aggregate gross proceeds to the Company of \$650.0 million. For additional information, refer to Note 6, *Collaboration Agreements*.

As of December 31, 2022, the Company had received 3,033 shares of the Company's common stock from a then-employee as consideration for exercises of stock options. The total cost of shares held in treasury at December 31, 2022 was \$0.4 million.

## **9. Stock-Based Compensation**

### ***Equity Plans***

On July 2, 2014, the stockholders of the Company approved the 2014 Stock Option and Incentive Plan (the "2014 Plan"), which became effective immediately prior to the completion of the Company's IPO. The 2014 Plan provides for the grant of restricted stock awards, restricted stock units, incentive stock options and non-statutory stock options. The 2014 Plan replaced the Company's 2011 Stock Option and Grant Plan (the "2011 Plan"). The Company no longer grants stock options or other awards under its 2011 Plan, but any stock options outstanding under the 2011 Plan remain outstanding and effective in accordance with their terms.

The 2014 Plan provides for an annual increase, to be added on the first day of each fiscal year, by up to 4% of the Company's outstanding shares of common stock as of the last day of the prior year. On January 1, 2022, 2,357,482 shares of common stock, representing 4% of the Company's outstanding shares of common stock as of December 31, 2021, were added to the 2014 Plan.

On December 15, 2016, the Board approved the 2016 Inducement Equity Plan (as amended and restated, the "2016 Plan"). The 2016 Plan provides for the grant of equity awards to individuals who have not previously been an employee or a non-employee director of the Company to induce them to accept employment and to provide them with a proprietary

interest in the Company. On September 20, 2018, the Board amended the 2016 Plan to increase the total number of shares reserved for issuance by 1,200,000 shares.

Terms of equity grants, including vesting requirements, are determined by the Board or the Compensation Committee of the Board, subject to the provisions of the applicable plan. Stock options granted by the Company that are not performance-based are considered time-based because they vest based on the continued service of the grantee with the Company during a specified period following grant. These awards, when granted to employees, generally vest ratably over four years, with 25% vesting at the one-year anniversary. All stock option awards expire 10 years after the date of grant.

As of December 31, 2022, the total number of shares underlying outstanding awards under all equity plans was 9,203,831 and the total number of shares available for future issuance under all equity plans was 7,086,615 shares.

### ***Restricted Stock Units***

The following table summarizes activity relating to time-based restricted stock units and performance restricted stock units:

	Shares	Weighted Average Grant Date Fair Value
Outstanding as of December 31, 2021	1,256,098	\$ 57.87
Granted	705,380	40.02
Vested	(366,014)	40.13
Forfeited	(179,983)	95.84
Outstanding as of December 31, 2022	<u>1,415,481</u>	<u>48.73</u>

#### *Time-based restricted stock units*

During the year ended December 31, 2020, the Company granted 550,890 time-based restricted stock units to certain employees of the Company. These time-based restricted stock units vested over two years, with 25% vesting at the one-year anniversary of the grant date and 75% vesting at the two-year anniversary of the grant date, which was in April 2021 and April 2022, respectively. During the year ended December 31, 2021, 113,941 of these time-based restricted stock units vested, with a fair value on the date of vesting equal to \$8.8 million. During the year ended December 31, 2022, 291,505 of these time-based restricted stock units vested, with a fair value on the date of vesting equal to \$9.5 million. During the year ended December 31, 2020, no time-based restricted stock units vested.

During the year ended December 31, 2021, the Company granted 268,119 time-based restricted stock units to certain employees of the Company. These time-based restricted stock units vest over four years, with 25% vesting at the one-year anniversary of the vesting start date, which was in September 2022; and the remaining 75% will vest ratably in quarterly increments over the remaining three years. During the year ended December 31, 2022, 74,509 of these time-based restricted stock units vested, with a fair value on the date of vesting equal to \$2.9 million.

During the year ended December 31, 2022, the Company granted no time-based restricted stock units.

At December 31, 2022, 160,403 time-based restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was \$5.0 million.

#### *Performance restricted stock units*

During the year ended December 31, 2020, the Company granted 471,386 performance restricted stock units to employees of the Company. These performance restricted stock units are related to the achievement of certain clinical and regulatory development milestones related to product candidates and commercial milestones.

During the year ended December 31, 2021, the Company granted 531,176 performance restricted stock units to employees of the Company. These performance restricted stock units are related to the achievement of certain clinical and regulatory development milestones related to product candidates and commercial milestones.

During the year ended December 31, 2022, the Company granted 705,380 performance restricted stock units to its employees and consultants. These performance restricted stock units are related to the achievement of certain clinical and regulatory development milestones related to product candidates and commercial milestones.

Recognition of stock-based compensation expense associated with performance restricted stock units commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

As of December 31, 2022, 2021 and 2020, for performance restricted stock units that were outstanding, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards in the years ended December 31, 2022, 2021 and 2020, respectively.

No performance restricted stock units vested during the years ended December 31, 2022 and 2020.

During the year ended December 31, 2021, two milestones for outstanding performance restricted stock units were achieved. For the first milestone that was met, the fair value of the performance restricted stock units that vested upon achievement was \$6.1 million and the Company recognized stock-based compensation expense related to this milestone of \$3.8 million. 39% of the performance restricted stock units that were granted during the year ended December 31, 2020 included this milestone as a vesting condition. For the second milestone that was met, the fair value of the performance restricted stock units that vested upon achievement was \$3.4 million and the Company recognized stock-based compensation expense related to this milestone of \$12.8 million. 38% of the performance restricted stock units that were granted during the year ended December 31, 2019 included this milestone as a vesting condition.

At December 31, 2022, 1,255,078 performance restricted stock units were both outstanding and unvested, and the total unrecognized stock-based compensation expense related to these awards was \$62.4 million.

### ***Stock Option Rollforward***

The following table summarizes activity related to time-based and performance-based stock options:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	7,283,439	\$ 84.17	6.74	\$ 16,590
Granted	1,181,487	\$ 39.45		
Exercised	(156,195)	\$ 7.84		
Forfeited	(520,381)	\$ 98.65		
Outstanding as of December 31, 2022	<u>7,788,350</u>	\$ 77.95	6.36	\$ 7,275
Vested and expected to vest as of December 31, 2022	<u>6,724,505</u>	\$ 78.86	6.05	\$ 6,917
Exercisable as of December 31, 2022	<u>5,109,027</u>	\$ 85.76	5.22	\$ 5,607

As of December 31, 2022, the Company had unrecognized stock-based compensation expense related to its outstanding and unvested time-based stock option awards of \$61.0 million, which is expected to be recognized over the remaining weighted average vesting period of 2.94 years.

The intrinsic value of stock options exercised during the years ended December 31, 2022, 2021 and 2020 was \$4.4 million, \$9.0 million and \$2.1 million, respectively.

### ***Performance-Based Stock Options***

Recognition of stock-based compensation expense associated with performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the milestones.

As of December 31, 2022, 2021 and 2020, for performance-based stock option grants that were outstanding, the achievement of the milestones that had not been met was considered not probable, and therefore no expense has been recognized related to these awards in the years ended December 31, 2022, 2021 and 2020, respectively.

During the year ended December 31, 2021, in connection with the hiring of its chief executive officer, the Company granted 650,000 stock options to its chief executive officer to purchase shares of common stock that contain performance-based vesting criteria, such that the shares underlying such stock options will vest upon the achievement of certain regulatory and commercial milestones. During the years ended December 31, 2022 and 2020, the Company granted no stock options to purchase shares of common stock that contain performance-based vesting criteria.

During the years ended December 31, 2022, 2021 and 2020, no milestones were achieved under performance-based stock options.

As of December 31, 2022, 650,000 performance-based stock options were both outstanding and unvested, the total unrecognized stock-based compensation expense related to these awards was \$8.2 million and the timing of recognition of this stock-based compensation expense is subject to judgment of the Company as to when the performance conditions are considered probable of being achieved.

### ***Stock-Based Compensation Expense***

The following table summarizes stock-based compensation expense recognized during the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands)		
Research and development	\$ 25,888	\$ 49,746	\$ 42,370
Selling, general and administrative	35,714	54,883	51,836
Restructuring	—	—	1,788
	<u>\$ 61,602</u>	<u>\$ 104,629</u>	<u>\$ 95,994</u>

The following table summarizes stock-based compensation expense by award type recognized during the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
	(in thousands)		
Stock options	\$ 54,971	\$ 78,516	\$ 90,064
Restricted stock units	5,587	25,375	4,904
Employee stock purchase plan	1,044	738	1,026
	<u>\$ 61,602</u>	<u>\$ 104,629</u>	<u>\$ 95,994</u>

The stock-based compensation expense recorded for the restructuring in the year ended December 31, 2020 is the incremental amount related to modifying the exercise period for outstanding, vested stock option grants that had been granted to employees whose employment was terminated in the restructuring.

For stock option awards, the fair value is estimated at the grant date using the Black-Scholes option-pricing model, taking into account the terms and conditions upon which stock options are granted. The fair value of the stock options is amortized on a straight-line basis for stock option awards to employees, non-employee directors and non-employee consultants over the requisite service period of the awards.

The weighted average grant date fair value per share of stock options granted under the Company's stock option plans during the years ended December 31, 2022, 2021 and 2020 was \$25.96, \$51.87 and \$37.53, respectively.

The fair value of each stock option granted under the Company's equity plans has been calculated on the date of grant using the following weighted average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected dividend yield	0%	0%	0%
Expected volatility	73%	76%	78%
Risk-free interest rate	2.49%	0.63%	0.97%
Expected term	6.03 years	5.92 years	5.98 years

*Expected dividend yield:* the Company has not paid, and does not anticipate paying, any dividends in the foreseeable future.

*Risk-free interest rate:* the Company determined the risk-free interest rate by using a weighted average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

*Expected volatility:* effective January 1, 2020, the Company began using the historical volatility of only its common stock, as there is adequate historical data for the duration of the expected term.

*Expected term (in years):* the expected term represents the period that the Company's stock option grants are expected to be outstanding. The expected term of the stock options granted to employees, non-employee directors and non-employee consultants by the Company has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" stock options. Under this approach, the weighted average expected life is presumed to be the average of the vesting term and the contractual term of the stock option. This approach is used because the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term due to the limited period of time that its stock has been publicly traded.

Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. The Company estimates forfeitures based on historical terminations. For the years ended December 31, 2022, 2021 and 2020, the weighted-average forfeiture rates were 19.2%, 16.7% and 20.6%, respectively.

### **2014 Employee Stock Purchase Plan**

On July 2, 2014, the Company's stockholders approved the 2014 Employee Stock Purchase Plan (the "ESPP"), which had been previously approved by the Board. The ESPP became effective upon the completion of the IPO. A total of 282,000 shares of common stock were authorized for issuance under the ESPP.

On June 16, 2022, the Company's stockholders approved an amendment to the ESPP to add 300,000 shares of common stock to the ESPP.

As of December 31, 2022, 281,877 shares have been issued and 300,123 shares are available for issuance under the ESPP. At December 31, 2022, accrued expenses includes \$0.8 million of stock-based compensation expense related to an enrollment period for which the related shares had not been issued as of December 31, 2022.

## 10. Net Income (Loss) Per Share

The following table shows the calculation of basic and diluted net income (loss) per share for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
Basic net income (loss) per share:			
Numerator:			
Net income (loss) (in thousands)	\$ (532,784)	\$ (457,892)	\$ 606,073
Denominator:			
Weighted average common stock outstanding—basic	59,306,094	58,670,230	51,983,188
Effect of dilutive securities:			
Stock options	—	—	721,791
Restricted stock units	—	—	292,241
Employee Stock Purchase Plan	—	—	5,895
Total dilutive securities	—	—	1,019,927
Weighted average common stock outstanding—diluted	59,306,094	58,670,230	53,003,115
Net income (loss) per share—basic	\$ (8.98)	\$ (7.80)	\$ 11.66
Net income (loss) per share—diluted	\$ (8.98)	\$ (7.80)	\$ 11.43

The following table summarizes common stock equivalents outstanding that were excluded from the calculation of diluted net loss per share because including them would have been anti-dilutive as of December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
	2022	2021	2020
Stock options	7,138,350	6,599,429	4,781,737
Restricted stock units	160,403	563,334	—
Employee stock purchase plan	76,105	23,625	—
	<u>7,374,858</u>	<u>7,186,388</u>	<u>4,781,737</u>

Stock options and restricted stock units that are outstanding and contain performance-based vesting criteria for which the performance conditions have not been met are excluded from the calculation of common stock equivalents outstanding.

## 11. Income Taxes

Income (loss) before income tax expense consists of the following:

	Year Ended December 31,		
	2022	2021	2020
		(in thousands)	
Domestic	\$ (532,539)	\$ (457,693)	\$ 639,986
Foreign	(245)	(199)	(33,913)
	<u>\$ (532,784)</u>	<u>\$ (457,892)</u>	<u>\$ 606,073</u>

There is no current or deferred provision for income taxes because the Company has historically incurred and utilized operating losses prior to the year ended December 31, 2022. As of December 31, 2022, the Company continues to maintain a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in the valuation allowance.



A reconciliation of the U.S. statutory rate to the Company's effective tax rate is as follows:

	Year Ended December 31,		
	2022	2021	2020
Tax due at statutory rate	21.0%	21.0%	21.0%
State taxes, net of federal	1.8	1.9	5.7
Biogen transaction-related items	—	—	(10.1)
Stock-based compensation	(1.9)	(5.2)	0.9
Foreign rate differential	—	—	1.2
Federal and state tax credits	2.1	3.5	(1.5)
Change in valuation allowance	(23.0)	(20.7)	(17.6)
Other	—	(0.5)	0.4
	0.0%	0.0%	0.0%

For the years ended December 31, 2022 and 2021, the impact from stock-based compensation on the Company's effective tax rate was primarily caused by shortfalls related to exercises and cancellations of non-qualified stock options.

For the year ended December 31, 2020, the Biogen transaction-related items consisted primarily of the excess proceeds from the equity investment under the Biogen Stock Purchase Agreement.

Significant components of the Company's net deferred tax assets at December 31, 2022 and 2021 are as follows:

	December 31,	
	2022	2021
	(in thousands)	
Net operating losses	\$ 347,880	\$ 305,824
Tax credits	118,393	106,176
Capitalized research and development expenses	66,849	—
Stock-based compensation	49,916	49,281
Accrued expenses	8,750	6,684
Depreciation and amortization	1,386	1,401
Right of use asset	(2,433)	(3,702)
Lease liability	2,803	4,236
Other	(258)	704
Total net deferred tax asset before valuation allowance	593,286	470,604
Valuation allowance	(593,286)	(470,604)
	\$ —	\$ —

On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into law. Under the TCJA provisions, effective with tax years beginning on or after January 1, 2022, taxpayers can no longer immediately expense qualified research and development expenditures. Taxpayers are now required to capitalize and amortize these costs over five years for research conducted within the United States or 15 years for research conducted abroad. As a result, the Company capitalized \$319.0 million of research and development expenses for the year ended December 31, 2022.

On August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. The IRA introduced new tax provisions, including a 15.0% corporate alternative minimum tax and a 1.0% excise tax on stock repurchases. The

provisions of the IRA will be effective for periods after December 31, 2022. The enactment of the IRA did not result in any material adjustments to our income tax provision or net deferred tax assets as of December 31, 2022.

As of December 31, 2022, the Company had federal net operating loss carryforwards of \$1.5 billion, of which \$30.2 million begin to expire in 2033 and the remainder do not expire but are subject to 80% limitation. As of December 31, 2022, the Company had state net operating loss carryforwards of \$669.5 million that begin to expire in 2031. As of December 31, 2022, the Company had federal and state research and development tax credits carryforwards of \$68.4 million and \$12.5 million, respectively, which begin to expire in 2031 and 2027, respectively. As of December 31, 2022, the Company had federal orphan drug tax credit carryforwards of \$40.1 million, which begin to expire in 2034.

As of December 31, 2022, net deferred tax assets before the valuation allowance increased \$122.7 million, primarily due to the capitalization of research and development expenses and the increase of federal and state net operating loss carryforwards due to the loss generated for the year ended December 31, 2022. This increase in net deferred tax assets was offset by a corresponding increase in the valuation allowance.

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of federal and state net operating loss and tax credit carryforwards. Under the applicable accounting standards, management has considered the Company's history of losses and concluded that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets. Accordingly, a full valuation allowance of \$593.3 million and \$470.6 million has been established at December 31, 2022 and 2021, respectively. The valuation allowance increased by \$122.7 million for the year ended December 31, 2022, primarily due to the capitalization of research and development expenses and generation of net operating losses. The valuation allowance increased by \$94.5 million and decreased by \$107.2 million for the years ended December 31, 2021 and 2020, respectively, primarily due to generation or utilization of net operating losses.

Pursuant to Section 382 of the Internal Revenue Code, and similar state tax law, certain substantial changes in the Company's ownership may result in a limitation on the amount of net operating loss and tax credit carryforwards that may be used in future years. Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. The Company completed a Section 382 study through December 31, 2020. Based on the study, the Company underwent two ownership changes for Section 382 purposes which occurred on March 11, 2014 and December 31, 2015. As a result of the ownership changes, the Company's net operating loss and tax credit carryforwards as of the ownership change dates are subject to limitation under Section 382; however, these limitations are not expected to cause any of the impacted net operating loss and tax credit carryforwards to expire unused. Any net operating losses or tax credits generated after the December 2015 change are not subject to this annual limitation. However, subsequent ownership changes, as defined by Section 382, may potentially further limit the amount of net operating loss and tax credit carryforwards that could be utilized to offset future taxable income and tax.

The Company applies the authoritative guidance on accounting for and disclosure of uncertainty in tax positions, which requires the Company to determine whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals or litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority.

The following table reconciles the beginning and ending amounts of gross unrecognized tax benefits, excluding interest and penalties, if any, for the years ended December 31, 2022 and 2021:

	2022	2021
	(in thousands)	
Balance as of January 1	\$ 6,084	\$ -
Increases related to current year tax positions	697	396
Increases related to prior year tax positions	65	5,688
Balance as of December 31	\$ 6,846	\$ 6,084

For the years ended December 31, 2022 and 2021, the increases in unrecognized tax benefits related to current year and prior year tax positions primarily related to the Company's federal and state tax credits.

The Company's policy is to record interest and penalties related to income taxes as part of the tax provision. As of December 31, 2022 and 2021, the Company had no accrued interest or penalties related to income taxes and no amounts have been recognized in the Company's statements of operations and comprehensive income (loss) for the years ended December 31, 2022, 2021 and 2020.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal, state and foreign jurisdictions, where applicable. There are currently no pending tax examinations, and the Company's tax returns are generally open under statute from 2019 to the present. Tax attributes such as net operating losses and tax credits generated prior to 2019 and utilized in open years may still be adjusted upon examination.

## 12. Employee Benefit Plan

The Company maintains a 401(k) profit sharing plan (the "401(k) Plan") for its employees. Each employee may elect to contribute a portion of his or her compensation to the 401(k) Plan, subject to annual limits established by the Internal Revenue Service. For the years ended December 31, 2022, 2021 and 2020, the Company matched 50% of eligible contributions to the 401(k) Plan up to 6% of employee contributions. For the years ended December 31, 2022, 2021 and 2020 the Company contributed \$3.0 million, \$1.8 million and \$2.2 million, respectively, to the 401(k) Plan.

## Exhibit Index

Exhibit No.	Description
3.1	<a href="#"><u>Fifth Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 000-36544) filed on July 25, 2014)</u></a>
3.2	<a href="#"><u>Amended and Restated Bylaws of the Registrant, as amended on August 6, 2020 (incorporated by reference to Exhibit 3.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 10, 2020)</u></a>
4.1	<a href="#"><u>Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
4.2	<a href="#"><u>Description of Securities (incorporated by reference to Exhibit 4.2 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 27, 2020)</u></a>
10.1+	<a href="#"><u>2014 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.2**	<a href="#"><u>Amended and Restated Commercial License by and between the Registrant and CyDex Pharmaceuticals, Inc., dated September 25, 2015 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2015)</u></a>
10.3**	<a href="#"><u>Non-Exclusive License Agreement by and between the Registrant and the Regents of University of California, dated October 23, 2013, as amended May 14, 2014 (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.4	<a href="#"><u>Lease Agreement, by and between the Registrant and ARE-MA Region No. 38, LLC, dated December 11, 2011, as amended by First Amendment to Lease, by and between ARE-MA Region No. 38, LLC, dated October 26, 2012, and Second Amendment to Lease, by and between ARE-MA Region No. 38, LLC, dated May 9, 2013 (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.5+	<a href="#"><u>Offer letter by and between the Registrant and Jeffrey M. Jonas, dated July 18, 2013 (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.6+	<a href="#"><u>Offer letter by and between the Registrant and Albert J. Robichaud, dated September 25, 2011 (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.7+	<a href="#"><u>Offer letter by and between the Registrant and Kimi Iguchi, dated February 7, 2013 (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.8+	<a href="#"><u>Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Jeffrey M. Jonas, dated August 19, 2013 (incorporated by reference to Exhibit 10.11 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.9+	<a href="#"><u>Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Albert J. Robichaud, dated November 7, 2011 (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>

Exhibit No.	Description
10.10+	<a href="#"><u>Non-Solicitation, Confidentiality and Assignment Agreement by and between the Registrant and Kimi Iguchi, dated March 8, 2013 (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.11	<a href="#"><u>Form of Indemnification Agreement to be entered into between the Registrant and its directors (incorporated by reference to Exhibit 10.16 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.12	<a href="#"><u>Form of Indemnification Agreement to be entered into between the Registrant and its officers (incorporated by reference to Exhibit 10.17 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.13**	<a href="#"><u>Supply Agreement by and between the Registrant and CyDex Pharmaceuticals, Inc., dated December 13, 2012, as amended August 21, 2013 and April 30, 2014 (incorporated by reference to Exhibit 10.18 of the Registrant's Registration Statement on Form S-1 (File No. 333-196849) filed on July 8, 2014)</u></a>
10.14+	<a href="#"><u>Severance and Change In Control Agreement between the Registrant and Jeffrey M. Jonas, dated September 25, 2014 (incorporated by reference to Exhibit 10.20 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on March 6, 2015)</u></a>
10.15+*	<a href="#"><u>Severance and Change In Control Agreement between the Registrant and Kimi Iguchi, dated September 30, 2014, as amended</u></a>
10.16+*	<a href="#"><u>Severance and Change In Control Agreement between the Registrant and Albert J. Robichaud, dated September 25, 2014, as amended</u></a>
10.17**	<a href="#"><u>Exclusive License Agreement by and between the Registrant and the Regents of the University of California, dated June 6, 2015 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q/A (File No. 001-36544) filed on October 31, 2015)</u></a>
10.18	<a href="#"><u>Third Amendment to Lease, by and between Registrant and ARE-MA Region No. 38, LLC, dated September 9, 2015 (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2015)</u></a>
10.19	<a href="#"><u>Fourth Amendment to Lease, by and between the Registrant and ARE-MA Region No. 38, LLC, dated October 27, 2015 (incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2015)</u></a>
10.20	<a href="#"><u>Amendment No. 3 to Supply Agreement, by and between the Registrant and CyDex Pharmaceuticals, Inc., dated September 25, 2015 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2015)</u></a>
10.21	<a href="#"><u>Fifth Amendment to Lease, by and between the Registrant and ARE-MA Region No. 38, LLC, dated December 9, 2015 (incorporated by reference to Exhibit 10.29 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 29, 2016)</u></a>
10.22	<a href="#"><u>Lease Agreement, by and between the Registrant and Jamestown Premier 245 First, LLC, dated May 24, 2016 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 9, 2016)</u></a>
10.23+	<a href="#"><u>2016 Annual Bonus Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Current Report on Form 8-K (File No. 001-36544) filed on May 3, 2016)</u></a>

Exhibit No.	Description
10.24	<a href="#">Sixth Amendment to Lease by and between ARE-MA Region No. 38, LLC and the Registrant, dated May 8, 2017 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 3, 2017)</a>
10.25	<a href="#">First Amendment to Lease by and between CLPF-Cambridge Science Center LLC and the Registrant dated April 4, 2018 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on May 5, 2018)</a>
10.26+	<a href="#">Amended and Restated 2016 Inducement Equity Plan and forms of agreements thereunder, as amended and restated on September 20, 2018 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2018)</a>
10.27	<a href="#">Seventh Amendment to Lease by and between ARE-MA Region No. 38, LLC and the Registrant, dated October 23, 2018 (incorporated by reference to Exhibit 10.3 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 6, 2018)</a>
10.28	<a href="#">Eighth Amendment to Lease by and between ARE-MA Region No. 38, LLC and the Registrant, dated March 29, 2019 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 6, 2019)</a>
10.29+	<a href="#">Form of Performance-Based Restricted Stock Unit Award Agreement Under the Sage Therapeutics, Inc. 2014 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 10, 2020)</a>
10.30*†	<a href="#">Biogen Collaboration and License Agreement by and among the Registrant, Biogen MA Inc. and Biogen International GmbH, dated November 27, 2020</a>
10.31†	<a href="#">Stock Purchase Agreement by and between the Registrant and Biogen MA Inc., dated November 27, 2020 (incorporated by reference to Exhibit 10.39 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)</a>
10.32+	<a href="#">Offer Letter by and between the Registrant and Barry Greene, dated December 15, 2020 (incorporated by reference to Exhibit 10.40 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)</a>
10.33+	<a href="#">Severance and Change In Control Agreement between the Registrant and Barry Greene, dated December 15, 2020 (incorporated by reference to Exhibit 10.41 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)</a>
10.34+	<a href="#">Letter Agreement between the Registrant and Jeffrey Jonas, dated December 15, 2020 (incorporated by reference to Exhibit 10.42 of the Registrant's Annual Report on Form 10-K (File No. 001-36544) filed on February 24, 2021)</a>
10.35+	<a href="#">Offer Letter by and between the Registrant and Christopher Benecchi, dated September 13, 2021 (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 2, 2021)</a>
10.36+*	<a href="#">Severance and Change In Control Agreement between the Registrant and Christopher Benecchi, dated September 13, 2021, as amended</a>
10.37	<a href="#">Side Letter to Biogen Collaboration and License Agreement, by and among the Registrant, Biogen MA Inc. and Biogen International GmbH, dated October 21, 2021 (incorporated by reference to Exhibit 10.4 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on November 2, 2021)</a>
10.38+	<a href="#">2014 Employee Stock Purchase Plan, as amended, dated June 16, 2022 (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 2, 2022)</a>
10.39+*	<a href="#">Offer Letter by and between the Registrant and Laura Gault, dated October 18, 2022</a>
10.40+*	<a href="#">Severance and Change in Control Agreement between the Registrant and Laura Gault, dated October 18, 2022, as amended</a>
10.41+*	<a href="#">CNS Innovation Advisory Board Consulting Agreement between the Registrant and Jeff Jonas, dated November 8, 2022</a>
10.42+*	<a href="#">Amended and Restated Non-Employee Director Compensation Policy, dated December 16, 2022</a>

Exhibit No.	Description
21.1*	<a href="#">Subsidiaries of the Registrant</a>
23.1*	<a href="#">Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm</a>
24.1*	<a href="#">Power of Attorney (see signature page of this Annual Report on Form 10-K)</a>
31.1*	<a href="#">Certification of Principal Executive Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</a>
31.2*	<a href="#">Certification of Principal Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</a>
32.1***	<a href="#">Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002</a>
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as inline XBRL and contained in Exhibit 101.*)

(+) Management contract or compensatory plan or arrangement.

(\*) Filed herewith.

(\*\*) Confidential treatment has been granted by the Securities and Exchange Commission as to certain portions.

(\*\*\*) The certifications furnished in Exhibit 32.1 hereto are deemed to accompany this Annual Report on Form 10-K and will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certifications will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

(†) Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K.

## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

### SAGE THERAPEUTICS, INC.

Date: February 16, 2023

By: /s/ Barry E. Greene

Barry E. Greene  
Chief Executive Officer, President and Director  
(Principal Executive Officer)

We, the undersigned directors and officers of Sage Therapeutics, Inc., hereby severally constitute and appoint Barry E. Greene and Kimi Iguchi, and each of them singly, our true and lawful attorneys-in-fact, with full power to them, and to each of them singly, to sign for us and in our names in the capacities indicated below, any and all amendments to this Annual Report on Form 10-K, and to file or cause to be filed the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of us might or could do in person, and hereby ratifying and confirming all that said attorneys-in-fact, and each of them, or their substitute or substitutes, shall do or cause to be done by virtue of this power of attorney.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities indicated below and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Barry E. Greene</u> Barry E. Greene	Chief Executive Officer, President and Director (Principal Executive Officer)	February 16, 2023
<u>/s/ Kimi Iguchi</u> Kimi Iguchi	Chief Financial Officer (Principal Financial and Accounting Officer)	February 16, 2023
<u>/s/ Jeffrey M. Jonas</u> Jeffrey M. Jonas, M.D.	Director	February 16, 2023
<u>/s/ Michael F. Cola</u> Michael F. Cola	Director	February 16, 2023
<u>/s/ Steven Paul</u> Steven Paul, M.D.	Director	February 16, 2023
<u>/s/ Kevin P. Starr</u> Kevin P. Starr	Director	February 16, 2023
<u>/s/ James Frates</u> James Frates	Director	February 16, 2023
<u>/s/ Geno Germano</u> Geno Germano	Director	February 16, 2023
<u>/s/ Elizabeth Barrett</u> Elizabeth Barrett	Director	February 16, 2023
<u>/s/ George Golumbeski</u> George Golumbeski, Ph.D.	Director	February 16, 2023



## SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Severance and Change in Control Agreement (this “Agreement”) is made as of September 30, 2014 by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Kimi Iguchi (the “Executive”) and shall become effective on the date of the effectiveness of the Company’s registration statement on Form S-1 under the Securities Exchange Act of 1933, as amended.

**1. Purpose.** The Company considers it essential to the best interests of its stockholders to promote and preserve the continuous employment of key management personnel. The Board of Directors of the Company (the “Board”) recognizes that, as is the case with many corporations, the possibility of a Change in Control (as defined in Section 2 hereof) exists and that such possibility, and the uncertainty and questions that it may raise among management, may result in the departure or distraction of key management personnel to the detriment of the Company and its stockholders. Therefore, the Board has determined that appropriate steps should be taken to reinforce and encourage the continued attention and dedication of members of the Company’s key management, including the Executive, to their assigned duties without distraction, including in the face of potentially disturbing circumstances arising from the possibility of a Change in Control. Nothing in this Agreement shall be construed to affect the at-will nature of the employment relationship, the Executive shall not have any right to be retained in the employ of the Company.

**2. Change in Control.** A “Change in Control” shall be deemed to have occurred upon the occurrence of any one of the following events: (a) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (b) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (c) the sale of all of the stock of the Company to an unrelated person, entity or group thereof acting in concert, or (d) any other transaction in which the owners of the Company’s outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

### **3. Terminating Event.**

A “Terminating Event” shall mean any of the events provided in this Section 3:

(a) Termination by the Company. Termination by the Company of the employment of the Executive with the Company for any reason other than for Cause, death or Disability. For purposes of this Agreement, “Cause” shall mean, as determined by the Company in good faith:

(i) the indictment the Executive of any felony, any crime involving the Company, or any crime involving fraud, moral turpitude or dishonesty;

(ii) any unauthorized use or disclosure of the Company’s proprietary information which has an adverse effect on the Company’s business or reputation. As used in this paragraph, “Proprietary Information” means any information in whatever form, tangible or intangible, related to the business of the Company unless the information is publicly available in hard copy or electronic format, through lawful means;

(iii) any intentional misconduct or gross negligence on the Executive’s part which has a materially adverse effect on the Company’s business or reputation; or

(iv) the Executive’s repeated and willful failure to perform the duties, functions and responsibilities of the Executive’s position after a written warning from the Company.

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A Terminating Event shall not be deemed to have occurred pursuant to this Section 3(a) solely as a result of the Executive becoming an employee of any direct or indirect successor to the business or assets of the Company, rather than continuing as an employee of the Company following a Change in Control. For purposes hereof, the Executive will be considered "Disabled" if, as a result of the Executive's incapacity due to physical or mental illness, the Executive shall have been absent from his duties to the Company on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

(b) Termination by the Executive for Good Reason. Termination by the Executive of the Executive's employment with the Company for Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following, the occurrence of any of the following events:

- (i) a material diminution in the Executive's responsibilities, authority or duties;
- (ii) a material diminution in the Executive's base salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all senior management employees of the Company;
- (iii) a material change, defined as miles or more, in the geographic location at which the Executive is required to provide services to the Company, not including business travel and short-term assignments; or
- (iv) a material breach of this Agreement by the Company.

"Good Reason Process" shall mean that (i) the Executive reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive provides a Notice of Termination to the Company within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

**4. Change in Control Payment.** In the event a Terminating Event occurs on or within the 12 months immediately after a Change in Control (such 12-month period, the "Change in Control Period"), subject to the Executive signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property and non-disparagement, in the form attached hereto as Attachment A (the "Separation Agreement and Release") and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination or end of the Cure Period, the following shall occur

(a) the Company shall pay to the Executive an amount equal to the sum of (i) 9 months of the Executive's annual base salary in effect immediately prior to the Terminating Event (or the Executive's annual base salary in effect immediately prior to the Change in Control, if higher), and (ii) a pro rata portion of the Executive's target bonus for the fiscal year in which the termination of employment occurs, determined by multiplying the target bonus by a fraction, the numerator of which shall be the number of days during the fiscal year in which the Executive was employed by the Company and the denominator of which shall be 365;

(b) if the Executive was participating in the Company's group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a lump sum payment, in an amount equal to 12 times the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company;

(c) notwithstanding anything to the contrary in any applicable option agreement or stock-based award agreement, all stock options and other stock-based awards with time-based vesting held by the Executive shall immediately accelerate and become fully exercisable and nonforfeitable as of the Executive's Date of Termination conditioned upon the Separation Agreement and Release becoming irrevocable; and

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(d) the amounts payable under this Section 4 shall be paid out in a lump sum commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the amounts shall be paid in the second calendar year by the last day of such 60-day period. All other wages earned, including, but not limited to, accrued vacation, to the Date of Termination shall be paid on the Date of Termination.

**5. Severance Outside the Change in Control Period.** In the event a Terminating Event occurs at any time other than during the Change in Control Period, subject to the Executive signing the Separation Agreement and Release and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination, the following shall occur:

(a) the Company shall pay to the Executive an amount equal to 12 months times the Executive's annual base salary in effect immediately prior to the Terminating Event;

(b) if the Executive was participating in the Company's group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a monthly cash payment for 12 months in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company; and

(c) the amounts payable under this Section 5 shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Amount shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

**6. Additional Limitation.**

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the "Compensatory Payments"), would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), (or any successor provision), then the Compensatory Payments shall be reduced so that the sum of all of the Compensatory Payments shall be \$1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code (or any successor provision); provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Compensatory Payments were not subject to such reduction. In such event, the Compensatory Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Compensatory Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (i) cash payments not subject to Section 409A of the Code; (ii) cash payments subject to Section 409A of the Code; (iii) equity-based payments and acceleration; and (iv) non-cash forms of benefits; provided that in the case of all the foregoing Compensatory Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 6, the "After Tax Amount" means the amount of the Compensatory Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive's receipt of the Compensatory Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

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(c) The determination as to whether a reduction in the Compensatory Payments shall be made pursuant to Section 6(a) shall be made by an accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

#### **7. Section 409A.**

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's "separation from service" within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death.

(b) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(c) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(d) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

**8. Term.** This Agreement shall take effect on the date first set forth above and shall terminate upon the earlier of (a) the termination of the Executive's employment with the Company for any reason other than the occurrence of a Terminating Event, or (b) the date all amounts have been paid to the Executive upon a Terminating Event pursuant to Section 4 or Section 5 hereof.

**9. Withholding.** All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

#### **10. Notice and Date of Termination.**

(a) Notice of Termination. After a Change in Control and during the term of this Agreement, any purported termination of the Executive's employment (other than by reason of death) shall be communicated

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by written Notice of Termination from one party hereto to the other party hereto in accordance with this Section 10. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) **Date of Termination.** "Date of Termination" shall mean: (i) if the Executive's employment is terminated by his death, the date of his death; (ii) if the Executive's employment is terminated on account of Executive's Disability or by the Company for Cause, the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause the date on which a Notice of Termination is given; (iv) if the Executive's employment is terminated by the Executive without Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

**11. No Mitigation.** The Company agrees that, if the Executive's employment by the Company is terminated during the term of this Agreement, the Executive is not required to seek other employment or to attempt in any way to reduce any amounts payable to the Executive by the Company pursuant to Section 4 or Section 5 hereof. Further, the amount of any payment provided for in this Agreement shall not be reduced by any compensation earned by the Executive as the result of employment by another employer.

**12. Consent to Jurisdiction.** The parties hereby consent to the jurisdiction of the Superior Court or the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

**13. Integration.** This Agreement constitutes the entire agreement between the parties with respect to severance pay, benefits and accelerated vesting in connection with any termination of employment, to the extent inconsistent with any prior agreements supersedes the inconsistent provisions of such prior agreements between the parties concerning such subject matter, including without limitation any provisions of any offer letter or employment agreement relating to severance pay or benefits in connection with the ending of Executive's employment relationship with the Company. In the interest of clarity, any agreement relating to confidentiality, noncompetition, nonsolicitation or assignment of inventions shall not be affected by the Agreement.

**14. Successor to the Executive.** This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after a Terminating Event but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

**15. Enforceability.** If any portion or provision of this Agreement (including, without limitation, any portion or provision of any Section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

**16. Waiver.** No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

**17. Notices.** Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service of by

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registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company, or to the Company at its main office, attention of the Board of Directors.

**18. Amendment.** This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

**19. Effect on Other Plans and Agreements.** An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 6 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such agreement and this Agreement, the terms of this Agreement shall govern and Executive may receive payment under this Agreement only and not both. Further, Section 4 and Section 5 of this Agreement are mutually exclusive and in no event shall Executive be entitled to payments or benefits pursuant to Section 4 and Section 5 of this Agreement.

**20. Governing Law.** This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

**21. Successor to Company.** The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

**22. Gender Neutral.** Wherever used herein, a pronoun in the masculine gender shall be considered as including the feminine gender unless the context clearly indicates otherwise.

**23. Counterparts.** This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

*[Remainder of Page Intentionally Left Blank]*

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IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

**SAGE THERAPEUTICS, INC.**

By:           /s/ Jeffrey M. Jonas          

Name: Jeffrey M. Jonas

Title: Chief Executive Officer

          /s/ Kimi Iguchi          

Kimi Iguchi

[Signature Page to Severance and Change in Control Agreement]

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**AMENDMENT TO SEVERANCE AND CHANGE IN CONTROL AGREEMENT**

This Amendment to Severance and Change in Control Agreement (this “Amendment”) is made as of February 15, 2023 (the “Amendment Effective Date”) by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Kimi Iguchi (the “Executive”).

**WHEREAS**, the Company and the Executive previously entered into a certain Severance and Change in Control Agreement dated as of September 30, 2014 (the “Agreement”); and

**WHEREAS**, the Agreement contains a scrivener’s error and the parties desire to amend the terms of the Agreement to clarify the intent of the parties.

**NOW THEREFORE**, for good and valuable mutual consideration, including, but not limited to, your continued employment and access to Company confidential information, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree to amend the Agreement as follows:

1. Section 5(a) of the Agreement is hereby deleted in its entirety and replaced with the following:

“(a) the Company shall pay to the Executive an amount equal to 12 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event;”

2. All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. Except as set forth in this Amendment the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this Amendment, the terms of this Amendment will prevail.
3. This Amendment may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original, but such counterparts shall together constitute one and the same document.

**IN WITNESS WHEREOF**, the parties have executed this Amendment as of the Amendment Effective Date.

**KIMI IGUCHI**

**By:** /s/ Kimi Iguchi  
duly authorized

**Print Name:**

**Title:** Chief Financial Officer

**SAGE THERAPEUTICS, INC.**

**By:** /s/ Barry Greene  
duly authorized

**Print Name:** Barry Greene

**Title:** Chief Executive Officer

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## SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Severance and Change in Control Agreement (this “Agreement”) is made as of September 25, 2014 by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Albert Robichaud (the “Executive”) and shall become effective on the date of the effectiveness of the Company’s registration statement on Form S-1 under the Securities Exchange Act of 1933, as amended.

**1. Purpose.** The Company considers it essential to the best interests of its stockholders to promote and preserve the continuous employment of key management personnel. The Board of Directors of the Company (the “Board”) recognizes that, as is the case with many corporations, the possibility of a Change in Control (as defined in Section 2 hereof) exists and that such possibility, and the uncertainty and questions that it may raise among management, may result in the departure or distraction of key management personnel to the detriment of the Company and its stockholders. Therefore, the Board has determined that appropriate steps should be taken to reinforce and encourage the continued attention and dedication of members of the Company’s key management, including the Executive, to their assigned duties without distraction, including in the face of potentially disturbing circumstances arising from the possibility of a Change in Control. Nothing in this Agreement shall be construed to affect the at-will nature of the employment relationship, the Executive shall not have any right to be retained in the employ of the Company.

**2. Change in Control.** A “Change in Control” shall be deemed to have occurred upon the occurrence of any one of the following events: (a) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (b) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (c) the sale of all of the stock of the Company to an unrelated person, entity or group thereof acting in concert, or (d) any other transaction in which the owners of the Company’s outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

### **3. Terminating Event.**

A “Terminating Event” shall mean any of the events provided in this Section 3:

(a) Termination by the Company. Termination by the Company of the employment of the Executive with the Company for any reason other than for Cause, death or Disability. For purposes of this Agreement, “Cause” shall mean, as determined by the Company in good faith:

(i) the indictment the Executive of any felony, any crime involving the Company, or any crime involving fraud, moral turpitude or dishonesty;

(ii) any unauthorized use or disclosure of the Company’s proprietary information which has an adverse effect on the Company’s business or reputation. As used in this paragraph, “Proprietary Information” means any information in whatever form, tangible or intangible, related to the business of the Company unless the information is publicly available in hard copy or electronic format, through lawful means;

(iii) any intentional misconduct or gross negligence on the Executive’s part which has a materially adverse effect on the Company’s business or reputation; or

(iv) the Executive’s repeated and willful failure to perform the duties, functions and responsibilities of the Executive’s position after a written warning from the Company.

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A Terminating Event shall not be deemed to have occurred pursuant to this Section 3(a) solely as a result of the Executive becoming an employee of any direct or indirect successor to the business or assets of the Company, rather than continuing as an employee of the Company following a Change in Control. For purposes hereof, the Executive will be considered “Disabled” if, as a result of the Executive’s incapacity due to physical or mental illness, the Executive shall have been absent from his duties to the Company on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

(b) Termination by the Executive for Good Reason. Termination by the Executive of the Executive’s employment with the Company for Good Reason. For purposes of this Agreement, “Good Reason” shall mean that the Executive has complied with the “Good Reason Process” (hereinafter defined) following, the occurrence of any of the following events:

- (i) a material diminution in the Executive’s responsibilities, authority or duties;
- (ii) a material diminution in the Executive’s base salary except for across-the-board salary reductions based on the Company’s financial performance similarly affecting all or substantially all senior management employees of the Company;
- (iii) a material change, defined as miles or more, in the geographic location at which the Executive is required to provide services to the Company, not including business travel and short-term assignments; or
- (iv) a material breach of this Agreement by the Company.

“Good Reason Process” shall mean that (i) the Executive reasonably determines in good faith that a “Good Reason” condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the Executive cooperates in good faith with the Company’s efforts, for a period not less than 30 days following such notice (the “Cure Period”), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive provides a Notice of Termination to the Company within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

**4. Change in Control Payment.** In the event a Terminating Event occurs on or within the 12 months immediately after a Change in Control (such 12-month period, the “Change in Control Period”), subject to the Executive signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property and non-disparagement, in the form attached hereto as Attachment A (the “Separation Agreement and Release”) and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination or end of the Cure Period, the following shall occur

(a) the Company shall pay to the Executive an amount equal to the sum of (i) 9 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event (or the Executive’s annual base salary in effect immediately prior to the Change in Control, if higher), and (ii) a pro rata portion of the Executive’s target bonus for the fiscal year in which the termination of employment occurs, determined by multiplying the target bonus by a fraction, the numerator of which shall be the number of days during the fiscal year in which the Executive was employed by the Company and the denominator of which shall be 365;

(b) if the Executive was participating in the Company’s group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a lump sum payment, in an amount equal to 12 times the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company;

(c) notwithstanding anything to the contrary in any applicable option agreement or stock-based award agreement, all stock options and other stock-based awards with time-based vesting held by the Executive shall immediately accelerate and become fully exercisable and nonforfeitable as of the Executive’s Date of Termination conditioned upon the Separation Agreement and Release becoming irrevocable; and

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(d) the amounts payable under this Section 4 shall be paid out in a lump sum commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the amounts shall be paid in the second calendar year by the last day of such 60-day period. All other wages earned, including, but not limited to, accrued vacation, to the Date of Termination shall be paid on the Date of Termination.

**5. Severance Outside the Change in Control Period.** In the event a Terminating Event occurs at any time other than during the Change in Control Period, subject to the Executive signing the Separation Agreement and Release and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination, the following shall occur:

(a) the Company shall pay to the Executive an amount equal to 12 months times the Executive's annual base salary in effect immediately prior to the Terminating Event;

(b) if the Executive was participating in the Company's group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a monthly cash payment for 12 months in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company; and

(c) the amounts payable under this Section 5 shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Amount shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

**6. Additional Limitation.**

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the "Compensatory Payments"), would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), (or any successor provision), then the Compensatory Payments shall be reduced so that the sum of all of the Compensatory Payments shall be \$1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code (or any successor provision); provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Compensatory Payments were not subject to such reduction. In such event, the Compensatory Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Compensatory Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (i) cash payments not subject to Section 409A of the Code; (ii) cash payments subject to Section 409A of the Code; (iii) equity-based payments and acceleration; and (iv) non-cash forms of benefits; provided that in the case of all the foregoing Compensatory Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 6, the "After Tax Amount" means the amount of the Compensatory Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive's receipt of the Compensatory Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

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(c) The determination as to whether a reduction in the Compensatory Payments shall be made pursuant to Section 6(a) shall be made by an accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

#### **7. Section 409A.**

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's "separation from service" within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death.

(b) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(c) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(d) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

**8. Term.** This Agreement shall take effect on the date first set forth above and shall terminate upon the earlier of (a) the termination of the Executive's employment with the Company for any reason other than the occurrence of a Terminating Event, or (b) the date all amounts have been paid to the Executive upon a Terminating Event pursuant to Section 4 or Section 5 hereof.

**9. Withholding.** All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

#### **10. Notice and Date of Termination.**

(a) Notice of Termination. After a Change in Control and during the term of this Agreement, any purported termination of the Executive's employment (other than by reason of death) shall be communicated

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by written Notice of Termination from one party hereto to the other party hereto in accordance with this Section 10. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) **Date of Termination.** "Date of Termination" shall mean: (i) if the Executive's employment is terminated by his death, the date of his death; (ii) if the Executive's employment is terminated on account of Executive's Disability or by the Company for Cause, the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause the date on which a Notice of Termination is given; (iv) if the Executive's employment is terminated by the Executive without Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

**11. No Mitigation.** The Company agrees that, if the Executive's employment by the Company is terminated during the term of this Agreement, the Executive is not required to seek other employment or to attempt in any way to reduce any amounts payable to the Executive by the Company pursuant to Section 4 or Section 5 hereof. Further, the amount of any payment provided for in this Agreement shall not be reduced by any compensation earned by the Executive as the result of employment by another employer.

**12. Consent to Jurisdiction.** The parties hereby consent to the jurisdiction of the Superior Court or the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

**13. Integration.** This Agreement constitutes the entire agreement between the parties with respect to severance pay, benefits and accelerated vesting in connection with any termination of employment, to the extent inconsistent with any prior agreements supersedes the inconsistent provisions of such prior agreements between the parties concerning such subject matter, including without limitation any provisions of any offer letter or employment agreement relating to severance pay or benefits in connection with the ending of Executive's employment relationship with the Company. In the interest of clarity, any agreement relating to confidentiality, noncompetition, nonsolicitation or assignment of inventions shall not be affected by the Agreement.

**14. Successor to the Executive.** This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after a Terminating Event but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

**15. Enforceability.** If any portion or provision of this Agreement (including, without limitation, any portion or provision of any Section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

**16. Waiver.** No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

**17. Notices.** Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service of by

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registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company, or to the Company at its main office, attention of the Board of Directors.

**18. Amendment.** This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

**19. Effect on Other Plans and Agreements.** An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 6 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such agreement and this Agreement, the terms of this Agreement shall govern and Executive may receive payment under this Agreement only and not both. Further, Section 4 and Section 5 of this Agreement are mutually exclusive and in no event shall Executive be entitled to payments or benefits pursuant to Section 4 and Section 5 of this Agreement.

**20. Governing Law.** This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

**21. Successor to Company.** The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

**22. Gender Neutral.** Wherever used herein, a pronoun in the masculine gender shall be considered as including the feminine gender unless the context clearly indicates otherwise.

**23. Counterparts.** This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

*[Remainder of Page Intentionally Left Blank]*

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IN WITNESS WHEREOF, the parties have executed this Agreement effective on the date and year first above written.

**SAGE THERAPEUTICS, INC.**

By: /s/ Jeffrey M. Jonas

Name: Jeffrey M. Jonas

Title: Chief Executive Officer

/s/ Albert Robichaud

Albert Robichaud

[Signature Page to Severance and Change in Control Agreement]

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**AMENDMENT TO SEVERANCE AND CHANGE IN CONTROL AGREEMENT**

This Amendment to Severance and Change in Control Agreement (this “Amendment”) is made as of February 15, 2023 (the “Amendment Effective Date”) by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Albert Robichaud (the “Executive”).

**WHEREAS**, the Company and the Executive previously entered into a certain Severance and Change in Control Agreement dated as of September 25, 2014 (the “Agreement”); and

**WHEREAS**, the Agreement contains a scrivener’s error and the parties desire to amend the terms of the Agreement to clarify the intent of the parties.

**NOW THEREFORE**, for good and valuable mutual consideration, including, but not limited to, your continued employment and access to Company confidential information, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree to amend the Agreement as follows:

1. Section 5(a) of the Agreement is hereby deleted in its entirety and replaced with the following:  
  
“(a) the Company shall pay to the Executive an amount equal to 12 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event;”
2. All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. Except as set forth in this Amendment the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this Amendment, the terms of this Amendment will prevail.
3. This Amendment may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original, but such counterparts shall together constitute one and the same document.

**IN WITNESS WHEREOF**, the parties have executed this Amendment as of the Amendment Effective Date.

**ALBERT ROBICHAUD**

**By:** /s/ Albert Robichaud  
duly authorized

**Print Name:** Albert Robichaud

**Title:** Chief Scientific Officer

**SAGE THERAPEUTICS, INC.**

**By:** /s/ Barry Greene  
duly authorized

**Print Name:** Barry Greene

**Title:** Chief Executive Officer

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Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

**COLLABORATION AND LICENSE AGREEMENT**

**BETWEEN**

**SAGE THERAPEUTICS, INC.,**

**BIOGEN MA INC.**

**AND**

**BIOGEN INTERNATIONAL GMBH**

**Dated November 27, 2020**

IF " DOCVARIABLE "SWDocIDLocation" 4096" = "1" " DOCPROPERTY "SWDocID" ActiveUS 185387629v.1" ""

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## COLLABORATION AND LICENSE AGREEMENT

This COLLABORATION AND LICENSE AGREEMENT (this “**Agreement**”), dated as of November 27, 2020 (the “**Execution Date**”), is entered into by and between Sage Therapeutics, Inc., a Delaware corporation having its principal place of business at 215 First Street, Cambridge, Massachusetts 02142, U.S.A., (“**Sage**”), and Biogen MA Inc., a corporation organized under the laws of the Commonwealth of Massachusetts having an office at 225 Binney Street, Cambridge, MA 02142 (“**BIMA**”), and Biogen International GmbH, a Gesellschaft mit beschränkter Haftung organized under the laws of Switzerland, whose registered office is at Neuhofstrasse 30, 6340 Baar, Switzerland (“**BIG**”, together with BIMA, collectively, “**Biogen**”). Sage and Biogen are referred to in this Agreement individually as a “**Party**” and collectively as the “**Parties**.”

### RECITALS:

**WHEREAS**, Sage is a commercial-stage biopharmaceutical company committed to discovering, developing and commercializing novel medicines to treat central nervous system (CNS) disorders;

**WHEREAS**, Biogen is a global pharmaceutical company engaged in the research, development and commercialization of products useful in the treatment and prevention of human diseases and conditions; and

**WHEREAS**, Sage and Biogen desire to collaborate to Develop, Manufacture, perform Medical Affairs Activities with respect to and Commercialize the Licensed 217 Products and the Licensed 324 Products in the Profit-Share Territory (all as defined below), and Biogen desires to obtain, and Sage desires to grant to Biogen, an exclusive license in the Biogen Territory and a co-exclusive license in the Profit-Share Territory, in each case, to Develop, Manufacture, perform Medical Affairs Activities with respect to and Commercialize the Licensed 217 Products and the Licensed 324 Products, all in accordance with the terms and conditions set forth herein; and

**WHEREAS**, Biogen desires to have an exclusive option under certain circumstances to be granted an exclusive license in the Biogen Territory and a co-exclusive license in the Profit-Share Territory, in each case, to Develop, Manufacture, perform Medical Affairs Activities with respect to and Commercialize the Licensed [\*\*] Products, all in accordance with the terms and conditions set forth herein.

**NOW, THEREFORE**, in consideration of the foregoing premises and the mutual covenants herein contained, the Parties hereby agree as follows:

### 1. DEFINITIONS

#### 1.1 Definitions.

Unless specifically set forth to the contrary herein, the following terms, whether used in the singular or plural, will have the respective meanings set forth below:

**1.1.1** “[\*\*] **Competing Product**” shall have the same definition as the Licensed Product that it replaces as set forth in Section 3.10.2 (Further Development of Licensed [\*\*] Products), if the replacement mechanism of such Section 3.10.2 (Further Development of Licensed [\*\*] Products) is implemented.

**1.1.2** “[\*\*] **Substitution**” has the meaning set forth in Section 3.10.2 (Further Development of Licensed [\*\*] Products).



**1.1.3** “**217 Competing Product**” means any product (other than a Licensed 217 Product and, in the case of Sage, ZULRESSO® (brexanolone) in PPD), the Principal Mode of Action of which is positive allosteric modulation of the GABA<sub>A</sub> Receptor intended for the treatment of MDD, PPD, TRD, GAD or BPD. Notwithstanding any provision to the contrary set forth in this Agreement, a 217 Competing Product will include any product (other than a Licensed 217 Product and, in the case of Sage, ZULRESSO® (brexanolone) in PPD) intended for the treatment of MDD, PPD, TRD, GAD or BPD, the Principal Mode of Action of which is positive allosteric modulation of the GABA<sub>A</sub> Receptor alone or combined with any other therapeutic agent.

**1.1.4** “**217 Regulatory/Commercial Milestone Event**” has the meaning set forth in Section 9.6.1 (Licensed 217 Products Regulatory/Commercial Milestones).

**1.1.5** “**217 Regulatory/Commercial Milestone Payment**” has the meaning set forth in Section 9.6.1 (Licensed 217 Products Regulatory/Commercial Milestones).

**1.1.6** “**217 Sales Milestone Event**” has the meaning set forth in Section 9.7.1.1 (Licensed 217 Products Sales Milestones).

**1.1.7** “**217 Sales Milestone Payment**” has the meaning set forth in Section 9.7.1.1 (Licensed 217 Products Sales Milestones).

**1.1.8** “**324 Competing Product**” means any product (other than a Licensed 324 Product), the Principal Mode of Action of which is positive allosteric modulation of the GABA<sub>A</sub> Receptor intended for the treatment of ET, Epilepsy or any symptomatic treatment of Parkinson’s Disease. Notwithstanding any provision to the contrary set forth in this Agreement a 324 Competing Product will include any product (other than a Licensed 324 Product) intended for the treatment of ET, Epilepsy or any symptomatic treatment of Parkinson’s Disease, the Principal Mode of Action of which is positive allosteric modulation of the GABA<sub>A</sub> Receptor alone or combined with any other therapeutic agent.

**1.1.9** “**324 Regulatory/Commercial Milestone Event**” has the meaning set forth in Section 9.6.2 (Licensed 324 Products Regulatory/Commercial Milestones).

**1.1.10** “**324 Regulatory/Commercial Milestone Payment**” has the meaning set forth in Section 9.6.2 (Licensed 324 Products Regulatory/Commercial Milestones).

**1.1.11** “**324 Sales Milestone Event**” has the meaning set forth in Section 9.7.2.1 (Licensed 324 Products Sales Milestones).

**1.1.12** “**324 Sales Milestone Payment**” has the meaning set forth in Section 9.7.2.1 (Licensed 324 Products Sales Milestones).

**1.1.13** “**Abbreviated New Drug Application**” or “**ANDA**” has the meaning set forth in the FD&C Act (21 U.S.C. § 355(b)(2), 21 U.S.C. § 355(j) and 21 C.F.R. § 314.3), as amended.

**1.1.14** “**Acquired Business**” has the meaning set forth in Section 11.7.2 (Acquired Business Exception).

**1.1.15** “**Acquirer**” means, collectively, with respect to a Change of Control of a Party, the Third Party referenced in the definition of Change of Control and such Third Party’s Affiliates, as determined immediately prior to the closing of such Change of Control.

- 1.1.16** “**Additional Development Proposal**” has the meaning set forth in Section 3.3.2 (Additional Indications Development).
- 1.1.17** “**Additional Indications Development**” has the meaning set forth in Section 3.3.2 (Additional Indications Development)
- 1.1.18** “**Affiliate**” means, with respect to a Person, any other Person that (directly or indirectly) controls, is controlled by, or is under common control with, such Person, whether now or in the future. For purposes of this Agreement, a Person will be deemed to control another Person if it owns or controls, directly or indirectly, fifty percent (50%) or more of the equity securities of such other Person entitled to vote in the election of directors (or, in the case that such other Person is not a corporation, for the election of the corresponding managing authority), or otherwise has the power to direct, or cause the direction of, the management and policies of such other Person, whether through ownership of voting securities, by contract, or otherwise. The Parties acknowledge that in the case of certain entities organized under the Laws of certain countries outside the United States, the maximum percentage ownership permitted by Law for a foreign investor may be less than fifty percent (50%), and that in such case such lower percentage will be substituted in the preceding sentence; *provided* that such foreign investor has the power to direct the management and policies of such entity. For clarity, a Person may be or become an Affiliate of another Person and may cease to be an Affiliate of such Person, in each case, during the Term of this Agreement.
- 1.1.19** “**Agreement**” has the meaning set forth in the preamble.
- 1.1.20** “**Alliance Manager**” has the meaning set forth in Section 2.1 (Alliance Manager)
- 1.1.21** “**Allowable Overruns**” means, on a plan-by-plan basis, any amount incurred by a Party in the performance of the activities taken as a whole under a Joint Development Plan, Joint Medical Affairs Plan or Joint Commercialization Plan or with respect to CMC Activities under a Manufacturing Plan, in each case, that is (a) above the applicable amounts budgeted for the performance of such activities taken as a whole under the corresponding Joint Development Budget, Joint Medical Affairs Budget, Joint Commercialization Budget or Manufacturing Budget, as applicable, in each case, by **[\*\*]** percent (**[\*\*]**%) or less for such Calendar Year, *provided* that such amounts were not attributable to a breach of this Agreement by the performing Party; or (b) otherwise approved by the JSC.
- 1.1.22** “**Antitrust Law**” means any federal, state or foreign law, regulation or decree, including the HSR Act, designed to prohibit, restrict or regulate actions for the purpose or effect of monopolization or restraint of trade.
- 1.1.23** “**Audited Party**” has the meaning set forth in Section 9.11.3.1 (Record Retention; Audits).
- 1.1.24** “**Auditing Party**” has the meaning set forth in Section 9.11.3.1 (Record Retention; Audits).
- 1.1.25** “**Auditor**” has the meaning set forth in Section 9.11.3.1 (Record Retention; Audits).
- 1.1.26** “**Bankruptcy Code**” has the meaning set forth in Section 14.5.1 (Termination for Insolvency).

**1.1.27** “**Biogen**” has the meaning set forth in the preamble.

**1.1.28** “**Biogen Background Know-How**” means any and all Know-How (a) Controlled by Biogen or any of its Affiliates (solely or jointly with any Third Party) as of the Execution Date, or (b) that during the Term arises and is Controlled by Biogen or its Affiliates, or otherwise comes into the Control of, Biogen or its Affiliates, in each case ((a) and (b)), independently from the performance of activities under this Agreement and that is used and incorporated into the Development, Manufacture or Commercialization of any Licensed Product by or on behalf of Biogen or its Affiliates in the performance of activities under any Joint Development Plan, Joint Commercialization Plan, Joint Medical Affairs Plan or Manufacturing Plan.

**1.1.29** “**Biogen Background Patents**” means any and all Patents (a) Controlled by Biogen or any of its Affiliates (solely or jointly with any Third Party) as of the Execution Date, or (b) that during the Term arise and are Controlled by Biogen or its Affiliates, or otherwise come into the Control of, Biogen or its Affiliates, in each case ((a) and (b)), independently from the performance of activities under this Agreement and that claim any Biogen Background Know-How.

**1.1.30** “**Biogen Background Technology**” means the Biogen Background Know-How and Biogen Background Patents.

**1.1.31** “**Biogen Collaboration Know-How**” has the meaning set forth in Section 13.2.1 (Ownership).

**1.1.32** “**Biogen Collaboration Patents**” means all Collaboration Patents that claim any Biogen Collaboration Know-How, but expressly excluding all Biogen Background Patents and Biogen’s interest in the Joint Collaboration Patents.

**1.1.33** “**Biogen Collaboration Technology**” means the Biogen Collaboration Know-How and the Biogen Collaboration Patents.

**1.1.34** “**Biogen Indemnitees**” has the meaning set forth in Section 12.2 (General Indemnification by Sage).

**1.1.35** “**Biogen Licensed Technology**” means the Biogen Background Technology and Biogen Collaboration Technology.

**1.1.36** “**Biogen Prosecuted Patents**” has the meaning set forth in Section 13.2.1 (General).

**1.1.37** “**Biogen Publications**” has the meaning set forth in Section 10.2.1 (Publication).

**1.1.38** “**Biogen Territory**” means (a) with respect to all Licensed 217 Products: (i) unless and until Sage exercises an Opt-Out Right in accordance with Section 9.5 (Sage Opt-Out) for such Licensed 217 Products, all countries of the world other than the Profit-Share Territory and the Existing Partner Territory, and (ii) if Sage has exercised an Opt-Out Right in accordance with Section 9.5 (Sage Opt-Out) for such Licensed 217 Products, then from and after the Opt-Out Date, all countries of the world other than the Existing Partner Territory, and (b) with respect to all Licensed 324 Products: (i) unless and until Sage exercises an Opt-Out Right in accordance with Section 9.5 (Sage Opt-Out) for such Licensed 324 Products, all countries of the world other than the Profit-Share Territory, and (ii) if Sage has exercised an

Opt-Out Right in accordance with Section 9.5 (Sage Opt-Out) for such Licensed 324 Products then from and after the Opt-Out Date, all countries of the world.

**1.1.39** “**Biogen Territory Royalties**” has the meaning set forth in Section 9.8.1 (Biogen Territory Royalties).

**1.1.40** “**Blocking New Technology**” has the meaning set forth in Section 8.3.2.2 (Inclusion Process).

**1.1.41** “**BPD**” means bipolar depression.

**1.1.42** “**Branding Strategy**” has the meaning set forth in Section 5.11.1 (Branding).

**1.1.43** “**Business Day**” means a day other than a Saturday, Sunday or a bank or other public holiday in Massachusetts, United States.

**1.1.44** “**Calendar Quarter**” means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31 of each Calendar Year.

**1.1.45** “**Calendar Year**” means each successive period of twelve (12) months commencing on January 1 and ending on December 31.

**1.1.46** “**Change of Control**” means, with respect to a Party, (a) a merger or consolidation of such Party with a Third Party that results in the voting securities of such Party outstanding immediately prior thereto, or any securities into which such voting securities have been converted or exchanged, ceasing to represent more than fifty percent (50%) of the combined voting power of the surviving entity or the parent of the surviving entity immediately after such merger or consolidation, (b) a transaction or series of related transactions in which a Third Party, together with its Affiliates, becomes the direct or indirect beneficial owner of more than fifty percent (50%) of the combined voting power of the outstanding securities of such Party, or (c) the sale or other transfer to a Third Party of all or substantially all of such Party’s and its controlled Affiliates’ assets in the aggregate. Notwithstanding the foregoing, any transaction or series of transactions effected for the bona fide primary purpose of financing the operations of the applicable Party or changing the form or jurisdiction of organization of such Party will not be deemed a “Change of Control” for purposes of this Agreement.

**1.1.47** “**Clinical Data**” means the original source patient data and case report forms (CRFs) collected or generated by, on behalf of, or under the authority of a Party with respect to Clinical Studies conducted for any Licensed Product, together with all analysis, reports and results with respect thereto.

**1.1.48** “**Clinical Study**” means, with respect to any product, a Phase 1 Study, Phase 2 Study, Phase 3 Study, Phase 4 Study or other voluntary or required study (including a non-interventional study) in humans to obtain information regarding such product, including information relating to the safety, tolerability, pharmacological activity, pharmacokinetics, dose ranging or efficacy of such product.

**1.1.49** “**CMC**” means, chemistry, manufacturing and controls with respect to a product, which includes (a) manufacturing and process development records for such product and (b) all chemistry, manufacturing and control procedures necessary or reasonably useful for the manufacture of such product.

**1.1.50** “**CMC Activities**” means those formulation development, process development and other CMC-related activities, including sourcing and testing of all raw materials and components used in the manufacture of a product, and activities designed to support preparation of the Chemistry, Manufacturing and Controls sections of any Regulatory Materials or Regulatory Approval.

**1.1.51** “**Collaboration Know-How**” has the meaning set forth in [Section 13.2.1](#) (Ownership).

**1.1.52** “**Collaboration Patents**” means all Patents with a priority date after the Effective Date that claim any Collaboration Know-How.

**1.1.53** “**Collaboration Technology**” means the Collaboration Know-How and Collaboration Patents.

**1.1.54** “**Combination Product**” means any Licensed Product containing (a) a Sage Molecule and (b) one or more Other Components sold for a fixed price.

**1.1.55** “**Commercialization**” or “**Commercialize**” means, with respect to any product, any and all activities directed to marketing, advertising, promoting, distributing, importing, exporting, using, offering to sell, and selling or otherwise commercializing such product, including: pre-launch activities to prepare a market for potential sales, modeling and pharmaco-economic studies, epidemiological studies; government affairs, and public policy activities; patient services, patient advocacy engagement; and activities related to pricing and reimbursement, including seeking and maintaining any required Pricing and Reimbursement Approvals; but excluding, in each case, any activities directed to Manufacturing, Development or Medical Affairs Activities. “**Commercialize**” and “**Commercialized**” will be construed accordingly.

**1.1.56** “**Commercialization Lead Party**” for a given Commercialization activity has the meaning set forth in [Section 5.2.1.1](#) (General).

**1.1.57** “**Commercialization Wind-Down Period**” has the meaning set forth in [Section 14.6.5](#) (Sell-Off and Appointment as Distributor).

**1.1.58** “**Commercially Reasonable Efforts**” means with respect to the efforts to be expended by a Party or its Affiliate with respect to any objective related to the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of a product, [\*\*].

**1.1.59** “**Committee**” means the Joint Steering Committee, the Joint Development Committee, the Joint Commercialization Committee or any committees formed by the Joint Steering Committee pursuant to [Section 2.2.2.25](#) (Specific Responsibilities of the JSC) as applicable.

**1.1.60** “**Competing Product**” means the 217 Competing Products and the 324 Competing Products, in each case, individually or collectively as the context requires.

**1.1.61** “**Competitive Infringement**” means, on a Licensed Product-by-Licensed Product basis, where the making, using, selling, offering for sale, or importing, by any Third Party (other than any Sublicensee or authorized purchaser or other authorized transferee of a Party with respect to such Licensed Product), Acquirer or Acquired Business, in each case, of any pharmaceutical product in the Territory is Covered by any Sage Licensed Patent or any Collaboration Patent, including the filing of an Abbreviated New Drug Application with any applicable Regulatory Authority with respect to a Licensed Product as the reference product by any such Third Party.

**1.1.62** “**Confidential Information**” means (a) the terms of this Agreement and (b) any and all Know-How and other confidential or proprietary information, whether communicated in writing or orally or by any other method, that is or has been provided by or on behalf of one Party or any of its Affiliates to the other Party or any of its Affiliates in connection with the performance of activities under this Agreement, whether prior to, on or after the Execution Date, including information pertaining to the terms of this Agreement.

**1.1.63** “**Control**” or “**Controlled**” means the possession (whether by ownership, license, sublicense or otherwise, other than by a license, sublicense or other right granted pursuant to this Agreement) by a Party or its Affiliates (a) with respect to any Materials or other tangible Know-How, of the legal authority or right to physical possession of such Materials or tangible Know-How, with the right to provide such Materials or tangible Know-How to the other Party on the terms set forth herein, (b) with respect to Patents, Regulatory Approvals, Regulatory Materials, intangible Know-How or other intellectual property or subject matter, of the legal authority or right to grant a license, sublicense, access or right to use or right to reference (as applicable) to the other Party under such Patents, Regulatory Approvals, Regulatory Materials, intangible Know-How or other intellectual property or subject matter on the terms set forth herein, or (c) with respect to a product or component thereof, the legal authority or right to grant a license, sublicense, access or right to use (as applicable) to the other Party under Patents that Cover or Know-How that is incorporated in or embodies, such product or component on the terms set forth herein, in each case ((a), (b) and (c)), (i) without breaching or otherwise violating the terms or conditions of any agreement or other arrangement with any Third Party in existence as of the time such Party or its Affiliates would first be required hereunder to grant such license, sublicense, rights of access or right of use to or (ii) with respect to Materials, Know-How or Patents developed, acquired or licensed by a Party after the Execution Date, without incurring any additional payment obligations to a Third Party that are not subject to an allocation agreed between the Parties pursuant to this Agreement or otherwise in writing.

Notwithstanding any provision in this Agreement to the contrary, if there is a Change of Control of a Party during the Term, such Party will be deemed not to Control any Patents, Regulatory Approvals, Regulatory Materials, Know-How or other intellectual property rights, subject matter or product or component thereof that are owned or in-licensed immediately prior to such Change of Control by such Acquirer of such acquired Party, except if (A) such Patents, Regulatory Approvals, Regulatory Materials, Know-How or other intellectual property rights, subject matter or product or component thereof owned or in-licensed by the Acquirer were generated from participation by employees or consultants of such Acquirer in furtherance of Development, Manufacturing, Medical Affairs Activities or Commercialization activities with respect to Licensed Products under this Agreement after such Change of Control, (B) any Patents, Regulatory Approvals, Regulatory Materials, Know-How or other intellectual property, subject matter or product or component thereof owned or in-licensed by such Third Party were not used in the performance of Development, Manufacturing, Medical Affairs Activities or Commercialization activities with respect to Licensed Products under this Agreement prior to the consummation of such Change of Control, but after the consummation of such Change of Control, such acquired Party or any of its Affiliates uses any such Patents, Regulatory Approvals, Regulatory Materials, Know-How or other intellectual property or proprietary subject matter in the performance of Development, Manufacturing, Medical Affairs Activities or Commercialization activities with respect to Licensed Products under this Agreement, or (C) prior to the consummation of such Change of Control, such acquired Party or any of its Affiliates also Controlled such Patents, Regulatory Approvals, Regulatory Submissions, Know-How or other intellectual property rights, subject matter or product or component thereof owned or in-licensed by such Acquirer, in each of which cases ((A)–(C)), such Patents, Regulatory Approvals, Regulatory Materials, Know-How or other intellectual property rights, subject matter or product or component thereof owned or in-licensed by such Acquirer will be deemed Controlled by the acquired Party for purposes of this Agreement.

**1.1.64** “Cover,” “Covering” or “Covered” means that, with respect to any Patent and product (including a Licensed Product) in the Territory, but for a license granted to any Person under any claim included in such Patent, the manufacture, use, sale, offer for sale or importation of such product (including a Licensed Product) in the Field in the applicable Territory by such Person would infringe such claim, or in the case of a claim that has not yet issued, would infringe such claim if it were to issue.

**1.1.65** “Defending Party” has the meaning set forth in Section 13.5.4 (Cooperation Regarding Enforcement, Defense or Post-Grant Proceedings).

**1.1.66** “Detail” or “Detailing” means, with respect to a Licensed Product in the Profit-Share Territory, the communication by a Sales Representative to a health care provider during a sales call in accordance with the approved Joint Commercialization Plan (a) involving face-to-face contact or contact by means of an e-detail or video, (b) describing in a manner consistent with applicable Law and industry standards and the quality of similar presentations made by a Party’s Sales Representatives for such Party’s other products (if applicable) the FDA-approved indicated uses and other relevant characteristics of such Licensed Product, (c) using the Promotional Materials in an effort to increase the prescribing or hospital ordering preferences of such Licensed Product for its FDA-approved indicated uses and (d) made at such health care provider’s office, in a hospital, at another appropriate alternate care setting, or in any other venue approved by the JCC. A Detail does not include a Sample drop made by a Sales Representative. For the avoidance of doubt, discussions at conventions or other scientific meetings will not constitute “Details” or “Detailing.”

**1.1.67** “Detail Cost” means with respect to a Detail provided by either Party in the Profit-Share Territory, the cost-per-Detail as set forth in the Joint Commercialization Budget.

**1.1.68** “Develop” and “Development” means, with respect to any product, any and all activities that relate to obtaining, maintaining or expanding Regulatory Approval of such product, including any and all activities related to the design, research, discovery, generation, identification, profiling, characterization, pre-clinical development, or Nonclinical Studies of such product, CMC Activities, clinical drug development activities conducted before or after obtaining Regulatory Approval for such product that are reasonably related to or leading to the development, preparation, or submission of data and information to a Regulatory Authority for the purpose of obtaining, supporting, expanding or maintaining Regulatory Approval of such product, together with all activities related to pharmacokinetic profiling, design and conduct of Clinical Studies [\*\*] of such product, pharmacovigilance activities, adverse event reporting, and regulatory affairs, statistical analysis, report writing and the creation and submission of Regulatory Materials related to the foregoing (including the services of outside advisors and consultants in connection therewith); but excluding, in each case, any activities directed to Medical Affairs Activities, Commercialization or Manufacturing.

**1.1.69** “Development Expense Report” has the meaning set forth in Section 9.3.1 (Joint Development Costs Reconciliation).

**1.1.70** “Development Lead Party” for a given Development activity has the meaning set forth in Section 3.2.1 (General).

**1.1.71** “Disclosing Party” has the meaning set forth in Section 10.1.1 (Nondisclosure and Non-Use Obligations).

**1.1.72** “Disputes” has the meaning set forth in Section 15.3.1 (Disputes).

**1.1.73** “**Distribution Costs**” means the FTE Costs and Out-of-Pocket Costs, incurred by a Party or its Affiliate or for such Party’s or its Affiliate’s account during the Term and pursuant to the Agreement that are directly or reasonably allocable to the distribution of a Licensed Product in the Profit-Share Territory, including: [\*\*].

**1.1.74** “**Distribution Matters**” means all issues and decisions regarding the distribution of the Licensed Products in the Profit-Share Territory, including decisions as to whether and with which wholesalers, specialty pharmacies and distributors to contract, and the terms of contracts with such wholesalers and distributors.

**1.1.75** “**Distribution Plan**” has the meaning set forth in Section 5.7.3 (Distribution in the Profit-Share Territory).

**1.1.76** “**DOJ**” means the U.S. Department of Justice.

**1.1.77** “**Dollars**” or “**\$**” means the legal tender of the United States of America.

**1.1.78** “**Effective Date**” means the date on which all of the HSR Conditions (as defined in the SPA) have been met, unless either Party terminates this Agreement or the SPA at any time prior to the Closing Date (as defined in the SPA) in accordance with the terms hereof or thereof, in which case the Effective Date will be deemed not to have occurred.

**1.1.79** “**EMA**” means the European Medicines Agency.

**1.1.80** “**EP Background Patent**” has the meaning set forth in Section 8.3.1.3(a) (Third Party Payments owed to Existing Partner).

**1.1.81** “**EP CMC Patent**” has the meaning set forth in Section 8.3.1.3(a) (Third Party Payments owed to Existing Partner).

**1.1.82** “**EP-Enhanced 217 Product**” has the meaning set forth in Section 8.3.1.3(a) (Third Party payments owed to Existing Partner).

**1.1.83** “**Execution Date**” has the meaning set forth in the preamble.

**1.1.84** “**ET**” means the Indication that is Essential Tremor.

**1.1.85** “**Executive Officer**” means, for Sage, its Chief Executive Officer or another senior executive designee with decision-making authority, responsibilities and seniority comparable thereto, and for Biogen, its Chief Executive Officer or another senior executive designee with decision-making authority, responsibilities and seniority comparable thereto. In the event that the position of any of the Executive Officers identified in this Section 1.1.85 (Executive Officer) no longer exists due to a Change of Control, corporate reorganization, corporate restructuring or the like, then the applicable Executive Officer will be replaced with another executive officer with responsibilities and seniority comparable to the eliminated Executive Officer.

**1.1.86** “**Existing Partner**” means Shionogi & Co., Ltd and any successor in interest thereto.



- 1.1.87** “**Existing Partner Agreement**” means that certain Collaboration and License Agreement between Sage and the Existing Partner, dated as of June 12, 2018, as may be amended or restated from time to time.
- 1.1.88** “**Existing Partner Territory**” means Japan, the Republic of Korea (South Korea) and Taiwan.
- 1.1.89** “**Existing Sage Agreement**” has the meaning set forth in Section 1.1.110 (In-License Agreement).
- 1.1.90** “**Exploit**” means to make, have made, use, import, export, offer to sell, sell, Develop, Manufacture, perform Medical Affairs Activities, Commercialize or otherwise exploit. “**Exploitation**” will be construed accordingly.
- 1.1.91** “**FD&C Act**” means the United States Federal Food, Drug and Cosmetic Act, as amended.
- 1.1.92** “**FDA**” means the United States Food and Drug Administration or any successor agency thereto.
- 1.1.93** “**Field**” means any and all uses in humans.
- 1.1.94** “**Finance Expert**” has the meaning set forth in Section 2.7.3.6 (Final Decision-Making Authority).
- 1.1.95** “**Finance Officers**” has the meaning set forth in Section 9.3.1 (Development Costs Reconciliation).
- 1.1.96** “**Finance Working Group**” has the meaning set forth in Section 9.4 (Finance Working Group).
- 1.1.97** “**First Commercial Sale**” means, on a Licensed Product-by-Licensed Product and country-by-country basis, the first commercial sale in such country of such Licensed Product by Biogen or any of its Related Parties to a Third Party for end use consumption in such country following receipt of Regulatory Approval and, if applicable, Pricing and Reimbursement Approval, in each case, for such Licensed Product in such country. First Commercial Sale excludes transfers of a Licensed Product to Third Parties as *bona fide* Samples, as donations, for Clinical Study purposes or for any expanded access program, compassionate sales or use program (including named patient program or single patient program), indigent program, or for other charitable or promotional purposes or similar limited purposes.
- 1.1.98** “**Force Majeure**” has the meaning set forth in Section 15.12 (Force Majeure).
- 1.1.99** “**FTE**” means a full time person, or in the case of less than a full time person, a full time equivalent person year, carried out by an appropriately qualified employee of a Party or its Affiliates, based on [\*\*] person hours per year. Overtime, and work on weekends, holidays, and the like will not be counted with any multiplier (*e.g.*, time and a half or double time) toward the number of hours that are used to calculate the FTE contribution. Each employee utilized by a Party in connection with its performance under this Agreement may be less than or greater than one FTE based on the hours actually worked by such employee and will be treated as an FTE on a *pro rata* basis based upon the actual number of such hours worked divided by [\*\*].

**1.1.100** “**FTE Costs**” means, for any period, the FTE Rate multiplied by the number of FTEs in such period. FTEs will be pro-rated on a daily basis if necessary.

**1.1.101** “**FTE Rate**” means (a) for scientific, research and development, regulatory or other technical personnel, [\*\*] Dollars (\$[\*\*]) per one (1) full scientific, clinical, medical, regulatory or technical FTE per a full Calendar Year, which rate includes all direct and indirect costs of a Party’s FTE, including personnel and travel expenses, and (b) for all distribution, sales and marketing, field-facing medical personnel and medical science liaisons, and other non-scientific, non-clinical, non-research or development, non-regulatory and non-technical personnel, the rates to be determined by the Finance Working Group and approved by the JSC and set forth in the applicable initial Joint Commercialization Plan and Joint Commercialization Budget or the Joint Medical Affairs Plan and Joint Medical Affairs Budget. Starting [\*\*], (i) the foregoing rate in clause (a) will adjust on [\*\*] of each Calendar Year by an amount equal to the change, if any, in the Consumer Price Index for All Urban Consumers (CPI U) for the U.S. City Average, calculated by the Bureau of Labor Statistics during the immediately preceding Calendar Year, and (ii) the rates in clause (b) will be adjusted by [\*\*] of each Calendar Year for the next Calendar Year (concurrently with the JCC’s preparation of annual amendments to each then-current Joint Commercialization Plan and the corresponding Joint Commercialization Budget) based on the reassessments and recommendations of the Finance Working Group and as approved by the JSC. Notwithstanding the foregoing, for any Calendar Year during the Term that is less than a full year, the referenced rate in clause (a) and the rates determined by the Finance Working Group and approved by the JSC under clause (b) will be proportionately reduced to reflect such portion of FTEs for such full Calendar Year.

**1.1.102** “**GAAP**” means generally accepted accounting principles as practiced in the United States, as consistently applied.

**1.1.103** “**GABA<sub>A</sub> Receptor**” means the ionotropic receptor for the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).

**1.1.104** “**GAD**” means Generalized Anxiety Disorder.

**1.1.105** “**Generic Competition**” in a country means (a) a Generic Product with respect to a Licensed Product is being marketed and sold by a Third Party (without a license, authorization or other grant of rights by Biogen or Sage) in such country in the Biogen Territory in a Calendar Quarter and (b) [\*\*].

**1.1.106** “**Generic Product**” means (a) (i) a Third Party product containing the same active ingredient as that contained in a Licensed Product (whether approved under an ANDA, or other applicable abbreviated or expedited approval process), and (ii) [\*\*], or (b) [\*\*].

**1.1.107** “**Governmental Authority**” means any applicable government authority, court, tribunal, arbitrator, agency, department, legislative body, commission or other instrumentality of (a) any government of any country or territory, (b) any nation, state, province, county, city or other political subdivision thereof or (c) any multinational or supranational body.

**1.1.108** “**Guaranteed Obligations**” has the meaning set forth in Section 15.14 (Performance by BIMA and BIG).

**1.1.109** “**HSR Act**” means the Hart Scott Rodino Antitrust Improvements Act of 1976, as amended, and the rules promulgated thereunder.

**1.1.110** “**In-License Agreement**” means any agreement between a Party and a Third Party pursuant to which such Party obtains rights to any Third Party intellectual property rights (including Know-How and Patents) or materials that are necessary or reasonably useful for the Development, Manufacture, performance of Medical Affairs with respect to or Commercialization of any Licensed Product pursuant to this Agreement. In-License Agreements existing as of the Execution Date with respect to Sage are those certain agreements between Sage and a Third Party listed on Schedule 1.1.110 (Existing Sage Agreements and Provisions) (each, an “**Existing Sage Agreement**”).

**1.1.111** “**Incremental Taxes**” has the meaning set forth in Section 9.11.5.3 (Tax Actions).

**1.1.112** “**IND**” means any Investigational New Drug Application, as defined in 21 C.F.R. § 312, or any corresponding application in any country or jurisdiction other than the United States.

**1.1.113** “**Indemnified Party**” has the meaning set forth in Section 12.3 (Indemnification Procedure).

**1.1.114** “**Indemnified Persons**” means the Sage Indemnitees or the Biogen Indemnitees, as applicable.

**1.1.115** “**Indemnifying Party**” has the meaning set forth in Section 12.3 (Indemnification Procedure).

**1.1.116** “**Indication**” means any separate and distinct human disease, syndrome, disorder, illness or condition intended to be treated by any therapeutic product, excluding different lines of treatment or patient populations (*e.g.*, pediatric) for the same disease, disorder, illness or condition.

**1.1.117** “**Initiation**” means, with respect to a Clinical Study of a product, [\*\*] pursuant to the applicable protocol for such Clinical Study.

**1.1.118** “**Inventory Build Costs**” means the Manufacturing Costs incurred in connection with the production or acquisition of supplies of a Licensed Product prior to First Commercial Sale of such Licensed Product, to the extent that such costs and expenses are not incurred in connection with the performance of a Clinical Study and would ordinarily be included as a cost of Development under GAAP.

**1.1.119** “**IP Committee**” means the intellectual property committee as more fully described in Section 13.4.1 (IP Committee).

**1.1.120** “**IP Counsels**” has the meaning set forth in Section 8.3.2.4 (New Technology Disputes).

**1.1.121** “**IP Expert**” has the meaning set forth in Section 8.3.2.4 (New Technology Disputes).

**1.1.122** “**IP Head**” means (a) with respect to Biogen, the representative designated by Biogen via the IP Committee and (b) with respect to Sage, the representative designated by Sage via the IP Committee, in each case, as confirmed by the Parties to the JSC.

**1.1.123** “**JCC Communication Plan**” has the meaning set forth in Section 2.4.3 (Meetings).

- 1.1.124** “**JDC Communication Plan**” has the meaning set forth in Section 2.3.3 (Meetings).
- 1.1.125** “**JMC Communication Plan**” has the meaning set forth in Section 2.6.3 (Meetings).
- 1.1.126** “**Joint Collaboration Know-How**” has the meaning set forth in Section 13.2.1 (Ownership).
- Know-How.  
**1.1.127** “**Joint Collaboration Patents**” means all Collaboration Patents that claim any Joint Collaboration Patents.
- 1.1.128** “**Joint Collaboration Technology**” means the Joint Collaboration Know-How and Joint Collaboration Patents.
- 1.1.129** “**Joint Commercialization Budget**” has the meaning set forth in Section 5.2.1 (General).
- 1.1.130** “**Joint Commercialization Committee**” or “**JCC**” has the meaning set forth in Section 2.4.1 (Formation; Composition; Dissolution).
- 1.1.131** “**Joint Commercialization Costs**” means:
- (a) the FTE Costs and Out-of-Pocket Costs that are directly or reasonably allocable to the performance of Commercialization activities by or on behalf of a Party or any of its Affiliates for the Licensed Products in the Profit-Share Territory in accordance with the applicable Joint Commercialization Plan and the amounts budgeted for the performance of such activities in the applicable Joint Commercialization Budget, whether prior to or after receipt of Regulatory Approvals, including [\*\*], in all cases, *plus* applicable Allowable Overruns;
  - (b) [\*\*];
  - (c) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*] and in accordance with the applicable Joint Commercialization Plan and Joint Commercialization Budget [\*\*];
  - (d) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*];
  - (e) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*];
  - (f) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*];
  - (g) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*]; and
  - (h) [\*\*] to be treated as Joint Commercialization Costs pursuant to Section [\*\*].

Joint Commercialization Costs specifically exclude any FTE Costs, Out-of-Pocket Costs and other costs and expenses: [\*\*].

If any cost or expense is directly or reasonably allocable to more than one Commercialization cost category set forth above, then such cost or expense will only be counted

once (*i.e.*, as a Joint Commercialization Cost with respect to only one such category). No cost or expense included as a Joint Commercialization Cost will (A) also be included as a Joint Development Cost or a Joint Medical Affairs Cost, (B) be (or have been) included in the calculation of Net Sales as a deduction from the total amount billed or invoiced on sales of the applicable Licensed Product in the Profit-Share Territory, or (C) be an amount for which one Party or the other is solely responsible under this Agreement. Joint Commercialization Costs will be recognized and calculated in accordance with GAAP.

**1.1.132** “**Joint Commercialization Plan**” has the meaning set forth in Section 5.2.1 (General).

**1.1.133** “**Joint Development Budget**” has the meaning set forth in Section 3.2.1 (General).

**1.1.134** “**Joint Development Committee**” or “**JDC**” has the meaning set forth in Section 2.3.1 (Formation; Composition; Dissolution).

**1.1.135** “**Joint Development Costs**” means:

- (a) the FTE Costs and Out-of-Pocket Costs that are directly or reasonably allocable to the performance of Development activities by or on behalf of a Party or any of its Affiliates for the Licensed Products for the Profit-Share Territory and incurred by or on behalf of a Party or any of its Affiliates in accordance with the applicable Joint Development Plan and the amounts budgeted for the performance of such activities in the applicable Joint Development Budget *plus* applicable Allowable Overruns, including: [\*\*];
- (b) [\*\*] to be treated as Joint Development Costs pursuant to Section [\*\*];
- (c) [\*\*] treated as Joint Development Costs pursuant to Section [\*\*] and in accordance with the applicable Joint Development Plan and Joint Development Budget, including [\*\*];
- (d) [\*\*] to be treated as Joint Development Costs pursuant to Section [\*\*];
- (e) [\*\*] to be treated as Joint Development Costs pursuant to Section [\*\*]; and
- (f) [\*\*] to be treated as Joint Development Costs pursuant to Section [\*\*].

Joint Development Costs specifically exclude any FTE Costs, Out-of-Pocket Costs and other costs and expenses [\*\*].

If any cost or expense is directly or reasonably allocable to more than one Joint Development Cost category above, then such cost or expense will only be counted once (*i.e.*, as a Joint Development Cost with respect to only one such category). No cost or expense included as a Joint Development Cost will: (1) also be included as a Joint Commercialization Cost or a Joint Medical Affairs Cost; or (2) be an amount for which one Party or the other is solely responsible under this Agreement. Joint Development Costs will be recognized and calculated in accordance with GAAP.

**1.1.136** “**Joint Development Plan**” has the meaning set forth in Section 3.2.1 (General).

**1.1.137** “**Joint Manufacturing Committee**” or “**JMC**” has the meaning set forth in Section 2.6.1 (Joint Manufacturing Committee; Formation; Composition; Dissolution).

**1.1.138** “**Joint Medical Affairs Budget**” has the meaning set forth in Section 4.2 (Joint Medical Affairs Plans).

**1.1.139** “**Joint Medical Affairs Costs**” means the FTE Costs and Out-of-Pocket Costs that are directly or reasonably allocable to the performance of Medical Affairs activities by or on behalf of a Party or any of its Affiliates for the Licensed Products in the Profit-Share Territory and incurred by or on behalf of a Party or any of its Affiliates in accordance with the applicable Joint Medical Affairs Plan and the amounts budgeted for the performance of such activities in the applicable Joint Medical Affairs Budget plus applicable Allowable Overruns.

Joint Medical Affairs Costs specifically exclude any FTE Costs, Out-of-Pocket Costs and other costs and expenses [\*\*].

If any cost or expense is directly or reasonably allocable to more than one Joint Medical Affairs Cost category above, then such cost or expense will only be counted once (i.e., as a Joint Medical Affairs Cost with respect to only one such category). No cost or expense included as a Joint Medical Affairs Cost will: (i) also be included as a Joint Development Cost or a Joint Commercialization Cost; or (ii) be an amount for which one Party or the other is solely responsible under this Agreement. Joint Medical Affairs Costs will be recognized and calculated in accordance with GAAP.

**1.1.140** “**Joint Medical Affairs Plan**” has the meaning set forth in Section 4.2 (Joint Medical Affairs Plans).

**1.1.141** “**Joint Medical Affairs Subcommittee Communication Plan**” has the meaning set forth in Section 2.5.3 (Joint Medical Affairs Subcommittee; Meetings).

**1.1.142** “**Joint Program Activities**” means any activities with respect to a Licensed Product conducted by either Party or any of its Affiliates, Sublicensees or Subcontractors during the Term consisting of (a) Development for the purpose of, or in support of, (i) obtaining, maintaining or expanding Regulatory Approval in the Profit-Share Territory of such Licensed Product, or (ii) Commercializing such Licensed Product in the Profit-Share Territory, in each case ((i) and (ii)), in accordance with the corresponding Joint Development Plan for such Licensed Product, (b) Commercialization of such Licensed Product in the Profit-Share Territory in accordance with the corresponding Joint Commercialization Plan for such Licensed Product, (c) Medical Affairs Activities with respect to such Licensed Product in the Profit-Share Territory in accordance with the corresponding Joint Medical Affairs Plan for such Licensed Product or (d) the Manufacture of such Licensed Product for use in any of the activities set forth under clause (a), (b) or (c).

**1.1.143** “**Joint Program Damages**” means any Losses incurred in connection with any Third Party Claim, as well as any reasonable attorneys’ fees and costs of litigation incurred by either Party (or any of its Indemnified Persons) from Third Party Claims that arise from or are related to the performance of Joint Program Activities, *other than* Losses arising out of (a) any breach of, or inaccuracy in, any representation or warranty made by a Party in this Agreement, or any breach or violation of any covenant or agreement of a Party in this Agreement, or (b) the gross negligence, willful misconduct by or of a Party or any of its respective Affiliates or Sublicensees or any of their respective directors, officers, employees or agents in the performance of such Party’s obligations or exercise of its rights under this Agreement.

**1.1.144** “**Joint Publications**” has the meaning set forth in Section 10.2.1 (Publication).

- 1.1.145** “**Joint Publications Working Group**” has the meaning set forth in [Section 10.2.1](#) (Publication).
- 1.1.146** “**Joint Steering Committee**” or “**JSC**” has the meaning set forth in [Section 2.2.1](#) (Formation; Composition; Dissolution).
- 1.1.147** “**JRA Exception**” has the meaning set forth in [Section 13.1.2](#) (JRA Exception).
- 1.1.148** “**KINETIC Study**” means the double-blind, placebo-controlled Phase 2 Study to evaluate the safety and efficacy of the Licensed 324 Product compared to placebo on upper limb tremor reduction in individuals with Essential Tremor (ET) entitled “A Study to Evaluate the Efficacy, Safety, and Tolerability of SAGE-324 in Participants With Essential Tremor” and identified as NCT04305275 and SAGE324-ETD-201, ongoing as of the Execution Date.
- 1.1.149** “**Know-How**” means any proprietary data, results and information of any type whatsoever, in any tangible or intangible form, including know-how, trade secrets, knowledge, practices, techniques, methods, processes, inventions, developments, specifications, formulations, formulae, instructions, skills, materials or compositions of matter of any type or kind (patentable or otherwise), experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, software, algorithms, specifications, marketing reports, study designs, protocols, Materials, clinical and non-clinical study reports, clinical and non-clinical information or data, regulatory submission documents and summaries, expertise, stability, technology, test data including pharmacological, biological, chemical, biochemical, toxicological, and clinical test data, analytical and quality control data, stability data and other data, studies and procedures.
- 1.1.150** “**Launch Window**” means, for a Licensed Product in the Profit-Share Territory, the time period beginning [\*\*] before the anticipated date of the First Commercial Sale for such Licensed Product in the Profit-Share Territory (as determined by the JCC and for which Sage has received written notice) and ending on [\*\*].
- 1.1.151** “**Laws**” means all applicable laws, statutes, rules, regulations, orders, judgments, injunctions, ordinances or other pronouncements having the binding effect of law of any Governmental Authority, including if either Party is or becomes subject to a legal obligation to a Regulatory Authority or other Governmental Authority (such as a corporate integrity agreement or settlement agreement with a Governmental Authority).
- 1.1.152** “**Lead Publishing Party**” for a given publication has the meaning set forth in [Section 10.2.1](#) (Publication).
- 1.1.153** “**Licensed [\*\*] Product Substitution Date**” has the meaning set forth in [Section 3.10.3](#) (Effects of [\*\*] Substitution).
- 1.1.154** “**Licensed [\*\*] Products**” means (a) the product containing SAGE-[\*\*], for which data from Nonclinical Studies exists as of the Execution Date, in any dosage strength, and (b) any and all other products containing SAGE-[\*\*], in any dosage strength, formulation or method of delivery, whether as the sole active ingredient or in combination with one or more Other Components.
- 1.1.155** “**Licensed 217 Products**” means (a) the product containing SAGE-217 or “zuranolone” (as its International Nonproprietary Name (INN) and United States Adopted Name (USAN)), which is the subject of Clinical Studies as of the Execution Date, in any dosage strength, and (b) any and

all other products containing SAGE-217, in any dosage strength, formulation or method of delivery, whether as the sole active ingredient or in combination with one or more Other Components.

**1.1.156** “**Licensed 324 Products**” means (a) the product containing SAGE-324, which is the subject of Clinical Studies as of the Execution Date, in any dosage strength, and (b) any and all other products containing SAGE-324, in any dosage strength, formulation or method of delivery, whether as the sole active ingredient or in combination with one or more Other Components.

**1.1.157** “**Licensed Products**” means the Licensed 217 Products and the Licensed 324 Products, in each case, individually or collectively as the context requires.

**1.1.158** “**Long Term Joint Commercialization Budget**” has the meaning set forth in Section 5.2.1.1 (General).

**1.1.159** “**Long Term Joint Development Budget**” has the meaning set forth in Section 3.2.1 (General).

**1.1.160** “**Long Term Joint Medical Affairs Budget**” has the meaning set forth in Section 4.2.1 (General).

**1.1.161** “**Losses**” has the meaning set forth in Section 12.1 (General Indemnification by Biogen).

**1.1.162** “**LP U.S. TM Strategy**” has the meaning set forth in Section 5.11.4.1 (Profit-Share Territory).

**1.1.163** “**LP U.S. Trademark**” means those Trademarks to be used in connection with the Commercialization of each Licensed Product in the Profit-Share Territory, as selected jointly by the Parties through the JCC pursuant to Section 5.11.4.1 (Profit-Share Territory).

**1.1.164** “**Major Commercialization Activity**” means any of the following matters with respect to a Licensed Product in the Profit-Share Territory: [\*\*].

**1.1.165** “**Major Development Activity**” means the Development activities set forth on Schedule 1.1.165 (Major Development Activities).

**1.1.166** “**Major European Countries**” means [\*\*].

**1.1.167** “**Major Medical Affairs Activity**” means the Medical Affairs activities set forth on Schedule 1.1.167 (Major Medical Affairs Activities).

**1.1.168** “**Manufacturing**” or “**Manufacture**” means, with respect to any product (including active pharmaceutical ingredient and other material contained therein), any and all activities related to the manufacture of such product, including qualification, validation and scale-up, pre-clinical, clinical and commercial manufacture, packaging, labeling, filling, finishing, assembly, processing, in-process and finished product testing, release of such product or any component or ingredient thereof, quality assurance, quality control and audit activities related to manufacturing, testing and release of such product, ongoing stability tests, storage, shipping, supply or storage of such product (or any components or process steps involving such product or any companion diagnostic), placebo or comparator agent, as the case may be, product characterization, technical support activities, and regulatory activities related to any of the



foregoing, but excluding any activities directed to Development, Medical Affairs Activities or Commercialization of such product.

**1.1.169** “**Manufacturing Budget**” has the meaning set forth in Section 7.2 (Manufacturing Plans).

**1.1.170** “**Manufacturing Costs**” means the consolidated fully burdened manufacturing cost incurred by a Party or its Affiliate for a Sage Molecule or Licensed Product and in accordance with GAAP (consistently applied by such Party and its Affiliates with respect to all small molecule compounds and products), which will be the sum of:

for Manufacturing activities with respect to a Sage Molecule or Licensed Product performed by or on behalf of a Party or its Affiliates, [\*\*]%) of the actual costs of materials consumed or incorporated into, and direct labor and other actual costs incurred in the performance of such Manufacturing activities specifically related or reasonably allocable to the relevant Sage Molecule or Licensed Product, as applicable, including: ordinary course quality assurance costs, stability testing cost, characterization testing, quality control, release testing of drug substance and drug product, reasonably allocable equipment maintenance costs, customs and duty and charges levied by governmental authorities, labelling and packaging, failed lot charges, excess and obsolete inventory write-off, and manufacturing scrap incurred in the ordinary course of production (and not attributable to the gross negligence of such Party or its Affiliates), reasonably allocable cost of freight into or between Manufacturing sites, technology transfer costs related to new processes or facilities, any actual amounts paid by a Party or its Affiliate to a contract manufacturing organization Subcontractor that are solely and specifically related to the Manufacture of such Licensed Product (or Sage Molecules included therein or any components of the foregoing), including capacity reservation or cancellation fees paid to a Third Party, and costs to manage arrangements with contract manufacturing organizations that are specifically related or reasonably allocable the Manufacture of a Sage Molecule or Licensed Product (including to qualify or audit Manufacturing sites of such contract manufacturing organizations utilized in the Manufacture of a Sage Molecule or Licensed Product), *plus* a reasonable allocation of the Manufacturing site’s fixed and direct overhead consistent with the applicable Party’s costing methodology, including leasing costs and depreciation for capital expenditures for equipment (but not other capital expenses) and facilities costs, in each case, to the extent specifically related or reasonably allocable to the relevant Sage Molecule or Licensed Product (or components of the foregoing), which will be calculated in accordance with GAAP; *provided* that any such allocation of overhead will be made on the basis of normal capacity operation of the relevant facility and in any event will exclude (a) except as otherwise set forth in this definition, any costs and charges related to excess, idle or unused manufacturing capacity and (b) allocation of general corporate overhead; *provided, further* that such allocation of overhead may take into account idle capacity at a Party or its Affiliate’s own Manufacturing sites that was originally reserved under the Manufacturing Plan in good faith and not more than [\*\*] in advance for Manufacture of the relevant Sage Molecule or Licensed Product and such idle capacity if not otherwise able to be filled by such Party or its applicable Affiliates despite reasonable efforts to do so.

**1.1.171** “**Manufacturing Lead Party**” for a given Manufacturing activity means the Party with day-to-day operational responsibility with respect to the Manufacture of the applicable Licensed Products as set forth under the applicable Manufacturing Plan.

**1.1.172** “**Manufacturing Plan**” has the meaning set forth in Section 7.2 (Manufacturing Plans).

**1.1.173** “**Manufacturing Technology Transfer**” has the meaning set forth in Section 7.8.1 (Manufacturing Technology Transfer).

**1.1.174** “**Material Adverse Product Effect**” means (a) [\*\*], or (b) [\*\*].

**1.1.175** “**Material Communications**” means written, telephonic or in person communications from or with any Regulatory Authority concerning any of the following: product quality attributes (*e.g.*, purity, toxicity, drug/drug interactions); significant or new safety findings (*e.g.*, Serious Adverse Events, emerging safety signals); clinical or non-clinical findings affecting patient safety; lack of efficacy; potential pathways to Regulatory Approval; receipt or denial of Regulatory Approval; the design of Clinical Studies, or the need for additional Clinical Studies or Nonclinical Studies (*e.g.*, additional toxicology or carcinogenicity studies).

**1.1.176** “**Material Commercialization Subcontractor**” has the meaning set forth in Section 5.14 (Commercialization Subcontract).

**1.1.177** “**Material Development Subcontractor**” has the meaning set forth in Section 3.9 (Development Subcontract).

**1.1.178** “**Materials**” means all tangible compositions of matter, devices, articles of manufacture, assays, biological, chemical or physical materials and other similar materials.

**1.1.179** “**MDD**” means the Indication that is Major Depressive Disorder.

**1.1.180** “**Medical Affairs Activities**” means, with respect to a Licensed Product, any and all activities performed by or on behalf of a Party’s or its Affiliates’ medical affairs departments interacting with physicians or other healthcare professionals who may utilize or conduct research related to a drug or biological product, including: supporting continuing medical education and other medical programs and communications; development, publication, and dissemination of publications; development and fulfillment of medical information responses; development and execution of disease awareness education including symposia and digital education initiatives; sponsorship and booth exhibition at key congresses; conducting health economic, burden of illness/disease, natural history and real world evidence studies;; supporting educational fellowships and research grants, supporting external research efforts such as scientific research agreements and investigator initiated trials (following Regulatory Approval); medical resourcing, training and allocation; medical and scientific platform and content development; conducting appropriate activities involving opinion leaders, including communications and engagement; conducting medical science liaison activities; advisory boards or other consulting programs (to the extent related to medical affairs or clinical guidance) ; establishing patient registries and expanded access programs; post-approval investigator initiated trials or scientific research agreements; life cycle management activities and clinical research (including Phase 4 Optional Studies and investigator initiated research (IIR)).

**1.1.181** “**Medical Affairs Lead Party**” for a given Medical Affairs Activity has the meaning set forth in Section 4.2 (Joint Medical Affairs Plans).

**1.1.182** “**NDA**” means any New Drug Application as described in 21 C.F.R. § 314, or any corresponding application for Regulatory Approval in any country or jurisdiction other than the United States.

**1.1.183** “**Net Revenues**” means, to the extent allocable to a Licensed Product in the Profit-Share Territory, and, if applicable, for one or more such Licensed Products: (a) the total Net Sales of all such Licensed Products in the Profit-Share Territory; *plus* (b) Other Income received in connection with such Licensed Products in the Profit-Share Territory. Net Revenues will be accounted for in accordance with GAAP, as consistently applied by such Party in the Profit-Share Territory.

**1.1.184** “**Net Sales**” means with respect to a Licensed Product, the gross amount invoiced in a country by or on behalf of [\*\*], (each of the foregoing Persons, a “**Selling Party**”) for the sale or other disposition of such Licensed Product in such country to Third Parties [\*\*] in *bona fide* arms’ length transactions in the Territory, less the following deductions:

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Such amounts will be determined consistent with a Selling Party’s customary practices and in accordance with GAAP. It is understood that any accruals for individual items reflected in Net Sales are periodically (at least [\*\*]) tried up and adjusted by each Selling Party consistent with its customary practices and in accordance with GAAP.

Notwithstanding anything to the contrary set forth in this Agreement, [\*\*].

In the case of any Combination Product sold in a given country and reporting period, Net Sales for the purpose of determining royalties and Sales Milestone Events of the Combination Product in such country will be calculated by multiplying actual Net Sales of such Combination Product by the fraction  $A/(A+B)$ , where A is the invoice price of the applicable Sage Molecule if sold separately in the same indication in such country, and B is the total invoice price of the Other Components in the Combination Product, if sold separately in the same indication in such country.

If, on a country-by-country basis in a particular reporting period, the Licensed Product is sold separately in the same indication in a country, but the Other Components in the Combination Product are not sold separately in the same indication in such country, then Net Sales for the purpose of determining royalties and Sales Milestone Events of the Combination Product for such country will be calculated by multiplying actual Net Sales of the Combination Product by the fraction  $A/C$ , where A is the invoice price of the Sage Molecule if sold separately in the same indication in such country, and C is the invoice price of the Combination Product in such country.

If, on a country-by-country basis in a particular reporting period, the Licensed Product in the Combination Product is not sold separately in the same indication in such country, but the Other Components included in the Licensed Product are sold separately in the same indication in such country, then Net Sales for the purpose of determining royalties and Sales Milestone Events of the Combination Product for such country will be calculated by multiplying actual Net Sales of the Combination Product by the fraction  $(C-B)/C$ , where B is the invoice price of the Other Components included in such Combination Product if sold separately in the same indication in such country, and C is the invoice price of the Combination Product in such country.

If neither the Licensed Product nor the Other Components are sold separately in the same indication in a given country during a particular reporting period, then Net Sales will be calculated based on [\*\*].

Any disputes between the Parties relating to the calculation of Net Sales under this Section 1.1.184 (Net Sales) based on non-cash consideration or allocation of Net Sales for a Combination Product will be resolved pursuant to the dispute resolution procedures in Section 15.3.5 (Expert Arbitration).

**1.1.185** “**New License Agreement**” has the meaning set forth in Section 14.6.8 (Sublicense Survival).

- 1.1.186** “**New Technology**” has the meaning set forth in [Section 8.3.2.1](#) (New Technology).
- 1.1.187** “**New Technology Terms**” has the meaning set forth in [Section 8.3.2.2](#) (Inclusion Process).
- 1.1.188** “**Non-Defending Party**” has the meaning set forth in [Section 13.5.4](#) (Cooperation Regarding Enforcement, Defense or Post-Grant Proceedings).
- 1.1.189** “**Non-Major Commercialization Activities**” means the day-to-day, operational Commercialization activities performed for a Licensed Product in the Profit-Share Territory under a Joint Commercialization Plan, including any Commercialization matter within a Joint Commercialization Plan that is not a Major Commercialization Activity.
- 1.1.190** “**Non-Major Development Activities**” means the day-to-day, operational Development activities performed for a Licensed Product in the Profit-Share Territory under a Joint Development Plan.
- 1.1.191** “**Non-Major Medical Affairs Activities**” means the day-to-day, operational Medical Affairs Activities performed for a Licensed Product in the Profit-Share Territory under a Joint Medical Affairs Plan.
- 1.1.192** “**Non-Major Regulatory Activities**” means the day-to-day, operational regulatory matters within the scope of a Party’s responsibility under [Section 6.1](#) (Regulatory Lead Responsibilities).
- 1.1.193** “**Non-Proposing Party**” has the meaning set forth in [Section 3.3.2](#) (Additional Indications Development).
- 1.1.194** “**Nonclinical Studies**” means all non-human animal studies for any Licensed Product, including preclinical studies, non-clinical and toxicology studies.
- 1.1.195** “**Ongoing 217 Studies**” means the Clinical Studies and Nonclinical Studies for the Licensed 217 Product ongoing, paused or planned as of the Execution Date, as identified on [Schedule 1.1.195](#) (Ongoing 217 Studies).
- 1.1.196** “**OP&L Share**” means the Parties’ equal sharing of the Operating Profits or the Operating Losses for the Licensed Products pursuant to [Section 9.3.3](#) (Profit Sharing Following First Commercial Sale).
- 1.1.197** “**Operating Profit (or Loss)**” means, for a given period of time, Net Revenue of a Licensed Product for the Profit-Share Territory during such period, less the sum of: (a) Joint Development Costs for such Licensed Product *plus* (b) Joint Medical Affairs Costs for such Licensed Product *plus* (c) Joint Commercialization Costs for such Licensed Product, in each case ((a), (b) and (c)) incurred during such time period. For clarity, Operating Profit (or Loss) will be determined prior to application of any income taxes, and if such terms are used individually, “Operating Profit” will mean a positive Operating Profit (or Loss), and “Operating Loss” will mean a negative Operating Profit (or Loss). Operating Profit (or Loss) will be recognized and calculated in accordance with GAAP.
- 1.1.198** “**Opt-Out Date**” has the meaning set forth in [Section 9.5.1](#) (Exercise of Opt-Out).

- 1.1.199 “**Opt-Out Products**” has the meaning set forth in Section 9.5.1 (Exercise of Opt-Out).
- 1.1.200 “**Opt-Out Right**” has the meaning set forth in Section 9.5.1 (Exercise of Opt-Out).
- 1.1.201 “**Opt-Out Wind-Down Activities**” has the meaning set forth in Section 9.5.2 (Effect of Opt-Out).
- 1.1.202 “**Opt-Out Wind-Down Costs**” has the meaning set forth in Section 9.5.2 (Effect of Opt-Out).
- 1.1.203 “**Opt-Out Wind-Down Period**” has the meaning set forth in Section 9.5.2 (Effect of Opt-Out).
- 1.1.204 “**Other Component**” means one or more additional therapeutic agents (other than any Sage Molecule)

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1.1.205 “**Other Income**” means with respect to a Product Class (a) any payment received by a Party or its Affiliate from a Sublicensee prior to Sage’s exercise of its Opt-Out Right with respect to the Product Class of such Licensed Product in consideration for the grant of rights (including an option to obtain rights) to Develop, Manufacture, perform Medical Affairs Activities for or Commercialize a Licensed Product in the Profit-Share Territory, and (b) to the extent not already described in clause (a), other payments when recognized as income or an offset to an expense in accordance with GAAP by a Party or its Affiliate that is attributable to such Licensed Product described in the foregoing clause (a) in the Profit-Share Territory; *provided, however*, that Other Income will not include any such payments received by such Party or its Affiliate from a Sublicensee [\*\*].

1.1.206 “**Out-of-Pocket Costs**” means, with respect to certain activities for a Licensed Product hereunder, specifically identifiable expenses paid or payable by either Party or its Affiliates to Third Parties in consideration for the conduct of such activities, including payments to contract personnel (including contractors, consultants and Subcontractors).

1.1.207 “**Panel**” has the meaning set forth in Section 15.3.5.1 (Expert Arbitration).

1.1.208 “**Parties**” has the meaning set forth in the preamble.

1.1.209 “**Party**” has the meaning set forth in the preamble.

1.1.210 “**Patents**” means all (a) patents, (b) patent applications, including all provisional and non-provisional applications, patent cooperation treaty (PCT) applications, substitutions, divisions and renewals, continuations, continuations-in-part, any patent issued with respect to any such patent applications, (c) all patents-of-addition, reissues, reexaminations, renewals, extensions or restorations by existing or future extension or restoration mechanisms (including any supplementary protection certificate or equivalents thereof), (d) inventor’s certificates or letters patent, and (e) and all other counterparts and substantially equivalent form of government issued right substantially similar to any of the foregoing described in clauses (a) through (d) above, in any country or jurisdiction.

1.1.211 “**Patent Costs**” means the Out-of-Pocket Costs paid to outside legal counsel or other Third Parties, and filing and maintenance expenses, incurred in Prosecuting and Maintaining Patents

and enforcing and defending them, but excluding any Third Party Payments described in [Section 8.3](#) (Third Party In-Licenses Payments).

**1.1.212** “**Paying Party**” has the meaning set forth in [Section 9.11.1](#) (Manner of Payment).

**1.1.213** “**Payments**” has the meaning set forth in [Section 9.11.5.1](#) (General).

**1.1.214** “**Person**” means any natural person, corporation, unincorporated organization, partnership, association, sole proprietorship, joint stock company, joint venture, limited liability company, trust or government, or Governmental Authority, or any other similar entity.

**1.1.215** “**Pharmacovigilance Agreement**” has the meaning set forth in [Section 6.10](#) (Reporting Adverse Events).

**1.1.216** “**Phase 1 Study**” means a clinical study of an investigational product in human subjects with the primary objective of characterizing its safety, metabolism, tolerability, pharmacokinetics and clinical pharmacology and identifying a recommended dose and regimen for future studies and that satisfies the requirements of 21 C.F.R. § 312.21(a), as amended (or its successor regulation), or, with respect to any other country or region, the equivalent of such a clinical trial in such other country or region.

**1.1.217** “**Phase 2 Study**” means a clinical study of an investigational product in human subjects with the objective of exploring the feasibility, safety, dose ranging, or efficacy of a pharmaceutical or biologic product that satisfies the requirements of 21 C.F.R. § 312.21(b), as amended (or its successor regulation), or, with respect to any other country or region, the equivalent of such a clinical trial in such other country or region. Notwithstanding the foregoing, solely for purposes of [Section 9.6.1](#) (Licensed 217 Products Regulatory/Commercial Milestones) and [Section 9.6.2](#) (Licensed 324 Products Regulatory/Commercial Milestones), the Phase 2 Study must be prospectively designed to generate sufficient data (if successful) to commence a Phase 3 Study for such product.

**1.1.218** “**Phase 3 Study**” means a clinical study of an investigational product in human subjects that the FDA permits to be conducted under an open IND and that is performed to gain evidence with statistical significance of the efficacy of such product in a target population, and to obtain expanded evidence of safety for such product that is needed to evaluate the overall benefit-risk relationship of such product, to form the basis for approval of an NDA by a Regulatory Authority and to provide an adequate basis for physician labeling, in a manner that meets the requirements of 21 C.F.R. § 312.21(c), as amended (or its successor regulation), or, with respect to any other country, the equivalent of such a clinical study in such other country. Notwithstanding any provision to the contrary set forth in this Agreement, treatment of patients as part of an expanded access program, compassionate sales or use program (including named patient program or single patient program), or an indigent program, in each case, will not be included in determining whether or not a clinical trial is a Phase 3 Study or whether a patient has been dosed thereunder.

**1.1.219** “**Phase 4 Optional Study**” any post-approval clinical study for a product in a country with respect to any Indication for which Regulatory Approval has been received in a particular country, including investigator-initiated clinical studies initiated after Regulatory Approval of a product or post-marketing surveillance studies of a product, in each case, that is not a Phase 4 Required Study.

**1.1.220** “**Phase 4 Required Study**” means any post-approval clinical study initiated following receipt of Regulatory Approval for a product in a country in an Indication or to be conducted after receipt of Regulatory Approval of a product in an Indication, in each case, that was required by the applicable Regulatory Authority in any country in the Territory as a condition of receiving or maintaining

a Regulatory Approval for such product with respect to such Indication in such country (such as post-marketing approval studies and observational studies, if required by any Regulatory Authority in any country in the Territory to support or maintain Regulatory Approval for such product in such Indication in such country) or that is required for a label extension for a product in such country.

**1.1.221** “**Phase 4 Study**” means any Phase 4 Required Study or any Phase 4 Optional Study.

**1.1.222** “**PhRMA Code**” means the Code of the Pharmaceutical Research and Manufacturers of America.

**1.1.223** “**PM Strategy**” has the meaning set forth in Section 13.4.1.3(a) (IP Committee Responsibilities).

**1.1.224** “**Post-Grant Proceedings**” means, with respect to a particular Patent, [\*\*] and other similar proceedings by or against a Third Party with respect to such Patent.

**1.1.225** “**PPD**” means the Indication that is Postpartum Depression.

**1.1.226** “**Pre-Commercialization Expense Report**” has the meaning set forth in Section 9.3.2 (Reconciliation/Reimbursement Prior to First Commercial Sale).

**1.1.227** “**Preapproved Subcontractor**” means any of the Subcontractors set forth on Schedule 1.1.227 (Preapproved Subcontractors) as such list may be updated from time-to-time as set forth in Section 3.9 (Development Subcontracts) or Section 5.14 (Commercialization Subcontracts), as applicable.

**1.1.228** “**Pricing and Reimbursement Approval**” means an approval, agreement, determination or other decision by the applicable Governmental Authority of a country or jurisdiction that establishes prices charged to end-users for pharmaceutical or biologic products at which a particular pharmaceutical or biologic product will be reimbursed by the Regulatory Authority or other applicable Governmental Authority in such country or jurisdiction.

**1.1.229** “**Pricing Matters**” means, with respect to a Licensed Product in the Profit-Share Territory, [\*\*].

**1.1.230** “**Principal Mode of Action**” means, for an individual molecule, [\*\*].

**1.1.231** “**Prior Confidentiality Agreement**” has the meaning set forth in Section 15.4 (Entire Agreement; Amendments).

**1.1.232** “**Proceeding**” means any action, suit, claim, investigation or other proceeding.

**1.1.233** “**Product Class**” means collectively, either (a) all Licensed 217 Products, or (b) all Licensed 324 Products.

**1.1.234** “**Profit-Share Regulatory Strategy**” has the meaning set forth in Section 6.1 (Regulatory Lead Responsibilities).

**1.1.235** “**Profit-Share Territory**” means the United States.

**1.1.236** “**Promotional Materials**” means (a) all written, printed, graphic, digital, electronic, audio or video matter, including journal advertisements, sales visual aids, leave-behind items, formulary binders, reprints, direct mail, direct-to-consumer advertising, internet postings and sites and broadcast advertisements intended for use or used by or on behalf of either Party or their respective Affiliates in connection with any promotion of a Licensed Product, or in connection with market access, pricing, contracting or patient support activities related to a Licensed Product, and (b) all field and patient support training materials.

**1.1.237** “**Promotional Materials Rules**” has the meaning set forth in Section 2.2.2.13 (Specific Responsibilities of the JSC).

**1.1.238** “**Proposing Party**” has the meaning set forth in Section 3.3.2 (Additional Indications Development).

**1.1.239** “**Prosecution and Maintenance**” means, with respect to a particular Patent, the preparation, filing, prosecution and maintenance of such Patent (and the foreign equivalents of any of the foregoing), [\*\*]. “Prosecute and Maintain” and “Prosecuting and Maintaining” have corresponding meanings.

**1.1.240** “**Post-Commercialization Expense Report**” has the meaning set forth in Section 9.3.3.2 (Calculation and Payment).

**1.1.241** “**Publications**” means any and all publications, abstracts, posters and other presentations in scientific or medical journals or forums of data and results generated from activities in furtherance of this Agreement.

**1.1.242** “**Publications Plan**” has the meaning set forth in Section 10.2.1 (Publication).

**1.1.243** “**Receiving Party**” has the meaning set forth in Section 10.1.1 (Nondisclosure and Non-Use Obligations).

**1.1.244** “**Region**” means any of [\*\*].

**1.1.245** “**Regulatory Approval**” means, with respect to a particular country or other regulatory jurisdiction, any approvals, licenses, registrations, or authorizations of any Regulatory Authority necessary for the Manufacture, Development, marketing, importation or sale of a product for one or more indications in such country or regulatory jurisdiction, excluding, if applicable, Pricing and Reimbursement Approvals in such country or regulatory jurisdiction.

**1.1.246** “**Regulatory Authority**” means any Governmental Authority involved in granting approvals for the Development, Manufacturing or Commercialization of pharmaceutical products, including the FDA, the EMA, the European Commission, the Japanese Ministry of Health, Labour and Welfare, Japan’s Pharmaceuticals and Medical Devices Agency and the People’s Republic of China’s National Medical Products Administration.

**1.1.247** “**Regulatory Exclusivity**” means any exclusive marketing rights or data protection or other exclusivity rights (other than Patents) conferred by any Regulatory Authority with respect to a product in a country or jurisdiction in the Territory that prohibits the Commercialization of a Generic Product, including orphan drug exclusivity or pediatric exclusivity.



**1.1.248** “**Regulatory Lead Party**” for a given activity has the meaning set forth in Section 6.1 (Regulatory Lead Responsibilities).

**1.1.249** “**Regulatory Materials**” means (a) any submission to a Regulatory Authority, including all INDs, NDAs and other applications, registrations, licenses, authorizations and approvals (including Regulatory Approvals, Pricing and Reimbursement Approvals and product labeling) and designations (including designations of a product as an “orphan” drug or its equivalent outside of the United States), (b) correspondence, communication, materials, reports and documentation submitted to or received from Regulatory Authorities (including meeting requests, pre-meeting submissions, minutes and official contact reports relating to any communications with any Regulatory Authority) related to Developing, Manufacturing, obtaining marketing authorization, marketing, selling or otherwise Commercializing a pharmaceutical product in a particular country or jurisdiction, and all supporting documents with respect thereto, including all investigator brochures, regulatory drug lists, drug safety and signaling update reports, adverse event files and complaint files (including product technical complaints communications and handling) and other material regulatory submissions and (c) Clinical Data contained in any of the foregoing, and any supplement or amendment to any of the foregoing.

**1.1.250** “**Related Party(ies)**” means, (a) with respect to Biogen, Biogen’s Affiliates and Sublicensees, and (b) with respect to Sage, Sage’s Affiliates and Sublicensees.

**1.1.251** “**Returned Country**” has the meaning set forth in Section 11.1.6 (\*\*).

**1.1.252** “**Reversion License**” has the meaning set forth in Section 14.6.2 (Reversion License).

**1.1.253** “**Reversion Technology**” means, with respect to a Terminated Product in the Terminated Territory, \*\*.

**1.1.254** “**Reversion Trademarks**” has the meaning set forth in Section 14.6.9 (Biogen Trademarks).

**1.1.255** “**[\*\*]**” has the meaning set forth in Section 11.6 (\*\*).

**1.1.256** “**Royalty Bearing Patents**” means, with respect to a Licensed Product, the Sage Licensed Patents, Biogen Collaboration Patents and Joint Collaboration Patents, in each case, that \*\* of such Licensed Product.

**1.1.257** “**Royalty Term**” means, with respect to a Licensed Product and a country, the period commencing upon the First Commercial Sale of such Licensed Product in such country and continuing until the later of: (a) expiration of the last Valid Claim of the last to expire of the Royalty-Bearing Patents that would be infringed (absent a license granted hereunder) by the sale of such Licensed Product in such country, (b) expiration of the Regulatory Exclusivity for such Licensed Product in such country, and (c) 12 years after the First Commercial Sale of such Licensed Product in such country.

**1.1.258** “**[\*\*]**” has the meaning set forth in Section 3.10.1 (Licensed \*\* Product Development).

**1.1.259** “**Sage**” has the meaning set forth in the preamble.

**1.1.260** “**SAGE-[\*\*]**” means (a) the molecule described on Schedule 1.1.260 (SAGE-[\*\*]) or (b) any metabolite, salt, ester, hydrate, solvate, crystalline form, co-crystalline form, amorphous

form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, tautomer, stereoisomer, enantiomer, conjugate, complex, free acid, free base or optically active form thereof.

**1.1.261** “**SAGE-217**” means (a) the molecule described on Schedule 1.1.261 (SAGE-217) or (b) any metabolite, salt, ester, hydrate, solvate, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, tautomer, stereoisomer, enantiomer, conjugate, complex, free acid, free base or optically active form thereof.

**1.1.262** “**SAGE-324**” means (a) the molecule described on Schedule 1.1.262 (SAGE-324) or (b) any metabolite, salt, ester, hydrate, solvate, crystalline form, co-crystalline form, amorphous form, pro-drug (including ester pro-drug) form, racemate, polymorph, chelate, tautomer, stereoisomer, enantiomer, conjugate, complex, free acid, free base or optically active form thereof.

**1.1.263** “**Sage Collaboration Patents**” means all Collaboration Patents that claim any Sage Collaboration Know-How, but expressly excluding Sage’s interest in any Joint Collaboration Patents.

**1.1.264** “**Sage Collaboration Know-How**” has the meaning set forth in Section 13.2.1 (Ownership).

**1.1.265** “**Sage Collaboration Technology**” means the Sage Collaboration Know-How and Sage Collaboration Patents.

**1.1.266** “**Sage Indemnitees**” has the meaning set forth in Section 12.1 (General Indemnification by Biogen).

**1.1.267** “**Sage Licensed Know-How**” means any and all Know-How, other than Joint Collaboration Know-How, Controlled by Sage or any of its Affiliates (solely or jointly with any Third Party) as of the Execution Date or during the Term, that (a) is necessary for the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of a Licensed Product in the Field in the Territory, or (b) is reasonably useful for the Development, Manufacture, performance of Medical Affairs with respect to or Commercialization of a Licensed Product in the Field in the Territory; [\*\*]. The Sage Licensed Know-How includes all Sage Collaboration Know-How.

**1.1.268** “**Sage Licensed Patents**” means any and all Patents, other than Joint Collaboration Patents, Controlled by Sage or any of its Affiliates (solely or jointly with any Third Party) as of the Execution Date or during the Term that (a) are necessary for or Cover the Development, Manufacture, performance of Medical Affairs with respect to or Commercialization of a Licensed Product in the Field in the Territory, or (b) are reasonably useful for the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of a Licensed Product in the Field in the Territory [\*\*]. The Sage Licensed Patents include all Sage Collaboration Patents. The Sage Licensed Patents existing as of the Execution Date are set forth on Schedule 1.1.268 (Sage Licensed Patents as of the Effective Date). Sage Licensed Patents exclude Sage’s interest in the Joint Collaboration Patents.

**1.1.269** “**Sage Licensed Technology**” means, collectively, the Sage Licensed Know-How, the Sage Licensed Patents and Sage’s interest in the Joint Collaboration Technology and Joint Collaboration Technology.

**1.1.270** “**Sage Molecule**” means SAGE-217 or SAGE-324.

**1.1.271** “**Sage Prosecuted Patents**” has the meaning set forth in Section 13.4.3.1 (General).

**1.1.272** “**Sales & Marketing Costs**” means the FTE Costs and Out-of-Pocket Costs incurred in the performance of the following sales and marketing activities for a Licensed Product in the Profit-Share Territory to the extent in accordance with applicable Law and applicable industry codes, including the PhRMA Code: (a) activities directed to the advertising and marketing of a Licensed Product in the Profit-Share Territory; (b) public relations with respect to a Licensed Product in the Profit-Share Territory; (c) peer-to-peer activities with respect to a Licensed Product in the Profit-Share Territory, such as ‘lunch and learns’; (d) promotional speaker programs with respect to a Licensed Product in the Profit-Share Territory, including the training of such speakers; (e) developing, obtaining and providing training with respect field-based personnel and patient support with respect to a Licensed Product in the Profit-Share Territory, as well as training packages; (f) generating Promotional Materials; (g) developing and performing market research with respect to a Licensed Product in the Profit-Share Territory and developing branding and communications plans; (h) conducting promotional symposia with respect to a Licensed Product in the Profit-Share Territory; (i) developing and implementing reimbursement programs with respect to a Licensed Product in the Profit-Share Territory; (j) patient support costs; and (k) developing information and materials specifically intended for national accounts, managed care organizations and group purchasing organizations with respect to a Licensed Product in the Profit-Share Territory and related interactions; but, in each case ((a)-(k)), excluding the costs and expenses of any activity the costs and expenses of which are already included in the any Detail Costs.

**1.1.273** “**Sales Representative**” means a pharmaceutical sales representative engaged or employed by either Party to conduct Detailing and other promotional efforts with respect to the Licensed Products in the Profit-Share Territory in accordance with the terms of this Agreement.

**1.1.274** “**Samples**” means a Licensed Product that is not intended to be sold and that is instead intended to promote the sale of such Licensed Product in the Profit-Share Territory in accordance with applicable Law.

**1.1.275** “**Second Source**” has the meaning set forth in Section 7.6 (Second Source and Biogen Manufacturing Sites).

**1.1.276** “**Securitization Transaction**” has the meaning set forth in Section 15.1.2 (Securitization).

**1.1.277** “**Selling Party**” has the meaning set forth in Section 1.1.184 (Net Sales).

**1.1.278** “**Serious Adverse Event**” has the meaning set forth in 21 C.F.R. § 312.32 and generally means an adverse drug experience or circumstance that results in any of the following outcomes (a) death, (b) life threatening condition, (c) inpatient hospitalization or a prolongation of existing hospitalization, (d) persistent or significant disability or incapacity or substantial disruption of the ability to conduct normal life functions, (e) a congenital anomaly/birth defect or (f) based upon appropriate medical judgment is considered an important medical event that may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

**1.1.279** “**Shared Resource**” has the meaning set forth in Section 5.10 (Joint Commercialization Costs Allocation).

**1.1.280** “**SPA**” has the meaning set forth in Section 9.2 (Equity Investment).

**1.1.281** “**Strategic Enforcement or Defense Reasons**” has the meaning set forth in Section 13.5.2.1 (Rights to Enforce; In the Territory).

**1.1.282** “**Strategic Prosecution Reasons**” has the meaning set forth in Section 13.4.2.2 (Sage Step-In).

**1.1.283** “**Subcontractor**” means a Third Party contractor (including contract research organizations, contract manufacturing organizations or Third Party distributors) engaged by a Party or its Affiliates on a fee-for-service basis to perform certain services or activities on behalf of and for the benefit of such Party or its Affiliates or exercise certain rights on behalf of such Party or its Affiliates, in each case, under this Agreement.

**1.1.284** “**Sublicensee**” means a Third Party to which a Party or its Affiliate has granted or grants rights under the rights granted to such Party pursuant to this Agreement to Develop, perform Medical Affairs Activities for or Commercialize a Licensed Product, or any further sublicensee of such rights (regardless of the number of tiers, layers or levels of sublicenses of such rights), other than any Subcontractor that is granted any such sublicense or other rights solely for the purpose of performing specific limited services or activities solely on behalf of and for the benefit of a Party or its Affiliate.

**1.1.285** “**Supply Agreement**” has the meaning set forth in Section 7.5 (Supply Agreement).

**1.1.286** “**Supply Price**” has the meaning set forth in Section 7.3 (Manufacturing Costs).

**1.1.287** “**Substitution Termination Date**” means, unless otherwise agreed by the Parties, the date on which [\*\*].

**1.1.288** “**Tax**” and “**Taxation**” means any U.S. and non-U.S. federal, state, local, regional, municipal, or other tax or taxation, levy, duty, charge, withholding or other assessment of any kind (including any related fine, penalty, addition to tax, surcharge, or interest) imposed by, or payable to, a Governmental Authority, including sales, use, excise, stamp, transfer, property, value added, goods and services, withholding, and franchise taxes (whether imposed directly or through withholding, and whether or not disputed).

**1.1.289** “**Tax Partnership**” has the meaning set forth in Section 15.21.1.1 (Tax Matters).

**1.1.290** “**Term**” has the meaning set forth in Section 14.1 (Term).

**1.1.291** “**Terminated Products**” means all Licensed Products within a Product Class with respect to which this Agreement has been terminated pursuant to Article 14 (Term and Termination). All Licensed 217 Products will be deemed Terminated Products if this Agreement is terminated with respect to the Product Class of Licensed 217 Products and all Licensed 324 Products will be deemed Terminated Products if this Agreement is terminated with respect to the Product Class of Licensed 324 Products. All Licensed Products will be deemed Terminated Products if this Agreement is terminated in its entirety.

**1.1.292** “**Terminated Territory**” means, on a Product Class-by-Product Class basis, those countries with respect to which this Agreement has been terminated for such Product Class in accordance with Article 14 (Term and Termination). The Terminated Territory will be worldwide if this Agreement is terminated in its entirety with respect to a Product Class.

**1.1.293** “**Territory**” means, collectively, the Profit-Share Territory and the Biogen Territory.

- 1.1.294 “**Third Party**” means any Person other than Biogen, Sage or their respective Affiliates.
- 1.1.295 “**Third Party Action**” has the meaning set forth in Section 13.5.3 (Defense and Post-Grant Proceedings).
- 1.1.296 “**Third Party Claims**” has the meaning set forth in Section 12.1 (General Indemnification by Biogen).
- 1.1.297 “**Third Party Manufacturing Agreements**” has the meaning set forth in Section 7.8.2 (Third Party Agreements).
- 1.1.298 “**Third Party Payments**” has the meaning set forth in Section 8.3.2 (After Effective Date Executed In-License Agreements).
- 1.1.299 “**Trademark**” means any trademark, trade name, service mark, service name, brand, domain name, trade dress, logo, slogan or other indicia of origin or ownership, including the goodwill and activities associated with each of the foregoing.
- 1.1.300 “**Trademark Costs**” means the fees and expenses paid to outside counsel and other Third Parties, in each case, in connection with the establishment and maintenance of rights for Trademarks, including costs of filing, registration, maintenance and renewal fees, actions to enforce or defend a Trademark and other Trademark proceedings, but expressly excluding all Sales and Marketing Costs.
- 1.1.301 “**TRD**” means the Indication that is Treatment-Resistant Depression.
- 1.1.302 “**United States**” means the United States and its territories, possessions and commonwealths.
- 1.1.303 “**United States Royalties**” has the meaning set forth in Section 9.8.2 (United States Royalties).
- 1.1.304 “**Valid Claim**” means (a) a claim of an issued, unexpired patent that has not been rejected, revoked or held to be invalid, unenforceable or unpatentable by a court or other authority of competent jurisdiction, from which decision no appeal can be further taken, and which claim has not been finally abandoned, disclaimed or admitted to be invalid, unenforceable or unpatentable, including through reissue or disclaimer or (b) a pending claim of an unissued, pending patent application that has been prosecuted in good faith and has not been pending for more than [\*\*] and which claim has not been revoked, cancelled, withdrawn, held invalid or abandoned in the country of question, in which case it will cease to be considered a Valid Claim, unless the patent application issues and recites said claim and otherwise satisfies clause (a) of this definition.
- 1.1.305 “**VAT**” means, within the European Union, such Tax as may be charged in accordance with (but subject to derogations from) Directive 2006/112/EC and, outside the European Union, value added Tax or any form of consumption Tax, as well as all other forms of Taxes charged on the supply of a good or a service, including but not limited to sales Tax and goods and services Tax.
- 1.1.306 “**VAT Restructuring**” has the meaning set forth in Section 9.11.5.2 (VAT).

**1.1.307** “**WATERFALL Study**” means a placebo-controlled Phase 3 Study evaluating a two-week course of zuranolone 50 mg in patients with MDD, with additional short-term follow-up.

**1.1.308** “**Withholding Taxes**” has the meaning set forth in Section 9.11.5.1 (General).

## **2.GOVERNANCE**

**2.1 Alliance Manager.** Promptly following the Effective Date, each Party will designate an individual to facilitate communication and coordination of the Parties’ activities under this Agreement relating to the Licensed Products (each, an “**Alliance Manager**”). For clarity, an Alliance Manager will not be a representative of its respective Party on any Committee, and will have no voting right on any Committee, unless otherwise agreed in writing by the Parties.

### **2.2 Joint Steering Committee.**

**2.2.1 Formation; Composition; Dissolution.** Within [\*\*] after the Effective Date, the Parties will establish a committee (the “**Joint Steering Committee**” or “**JSC**”) to provide strategic oversight of the Parties’ activities under this Agreement. Each Party will initially appoint [\*\*] representatives to the JSC, with each representative having knowledge and expertise in the Development, Manufacture, performance of Medical Affairs with respect to and Commercialization of molecules and products similar to the Licensed Products, and having sufficient decision-making authority and seniority within the applicable Party to provide meaningful input and make decisions arising within the scope of the JSC’s responsibility. The JSC may change its size from time to time by agreement of the Parties, *provided* that the JSC will consist at all times of an equal number of representatives of each of Sage and Biogen. Each Party may replace its JSC representatives at any time upon written notice to the other Party. The JSC will be chaired by co-chairpersons designated by Sage and Biogen, respectively. The JSC co-chairpersons may invite non-members to participate in the discussions and meetings of the JSC, if necessary, *provided* that such participants have no voting authority at the meetings of the JSC and are bound under enforceable obligations of confidentiality and non-use no less protective of the Parties’ Confidential Information than those set forth in this Agreement. The JSC co-chairpersons’ responsibilities will include conducting meetings, including, when feasible, ensuring that objectives for each meeting are set and achieved. The JSC will exist for so long as the JDC or JCC exists or there is at least one Licensed Product being Commercialized under this Agreement.

**2.2.2 Specific Responsibilities of the JSC.** The JSC will have the following responsibilities:

**2.2.2.1** reviewing, discussing and determining whether to approve all annual and interim amendments to each Joint Development Plan and each corresponding Joint Development Budget for the Licensed 217 Products and the Licensed 324 Products (including the designation of Development Lead Party between the Parties for each of the activities thereunder, changes to the Major Development Activities, and the proposed allocation of responsibility between the Parties for each of the activities thereunder), as proposed by the JDC, including, in each case, to add to the applicable Joint Development Plan any Clinical Study or Indication, as described in Section 3.2 (Joint Development Plans) and Section 3.3 (Operational Responsibilities for Development; Additional Development);

**2.2.2.2** determining whether any proposed Additional Indication Development would result in a Material Adverse Product Effect, as described in Section 3.3.2 (Additional Indications Development);

**2.2.2.3** reviewing, discussing and determining whether to approve each Joint Medical Affairs Plan and corresponding Joint Medical Affairs Budget for the Licensed 217 Products and the Licensed 324 Products and all annual and interim amendments thereto (including the designation of Medical Affairs Lead Party between the Parties for each of the activities thereunder, changes to the Major Medical Affairs Activities and the proposed allocation of responsibility between the Parties for each of the activities thereunder), as recommended by the Joint Medical Affairs Subcommittee, as described in Section 4.2 (Joint Medical Affairs Plan), as described in Section 4.2.2 (Amendments to Joint Medical Affairs Plans);

**2.2.2.4** reviewing, discussing and determining whether to approve each Joint Commercialization Plan and the corresponding Joint Commercialization Budget for the Licensed 217 Products and the Licensed 324 Products and all annual and interim amendments thereto (including the designation of Commercialization Lead Party between the Parties for each of the activities thereunder, changes to the Major Commercialization Activities, and the proposed allocation of responsibility between the Parties for each of the activities thereunder), as recommended by the JCC, each as described in Section 5.2 (Joint Commercialization Plans), as such plans and amendments may be submitted to the JSC by the JCC, as described in Section 5.2.2 (Amendments to Joint Commercialization Plans);

**2.2.2.5** reviewing, discussing and determining whether to approve each Distribution Plan for the Licensed 217 Products and the Licensed 324 Products, as such plans and amendments may be submitted to the JSC by the JCC, as described in Section 5.7.3 (Distribution in the Profit-Share Territory);

**2.2.2.6** approving FTE rates included in clause (b) of Section 1.1.101 (FTE Rate) and approving [\*\*];

**2.2.2.7** reviewing, discussing and determining whether to approve the Pricing Matters for Licensed Products for the Profit-Share Territory submitted to the JSC by the JCC; [\*\*];

**2.2.2.8** reviewing, discussing and determining whether to approve the rate to be applied to determine Detail Costs that are included in the Joint Commercialization Costs for Licensed Products in the Profit-Share Territory, as described in Section 5.9 (Detail Costs; Authority over Sales Forces);

**2.2.2.9** reviewing and discussing [\*\*];

**2.2.2.10** reviewing, discussing and determining whether to approve the Branding Strategy recommended by the JCC for each Licensed Product in the Profit-Share Territory, including the selection and use of all LP U.S. Trademarks, as described in Section 5.11.1 (Branding);

**2.2.2.11** reviewing, discussing and determining whether to approve the packaging and labeling recommended by the applicable Regulatory Lead Party for each Licensed Product in the Profit-Share Territory, as described in Section 5.11.3 (Licensed Product Packaging);

**2.2.2.12** reviewing, discussing and determining whether to approve the LP U.S. TM Strategy recommended by the JCC, as described in Section 5.11.4.1 (Profit-Share Territory);

**2.2.2.13** developing the process by which the Parties will approve the Promotional Materials relating to each Licensed Product to be used in the Profit-Share Territory such that, unless

the Parties otherwise agree, appropriate representatives of each Party will approve such Promotional Materials, and reviewing, discussing and determining whether to approve the key messaging to be included in such Promotional Materials (the “**Promotional Materials Rules**”), as described in [Section 5.11.2](#) (Promotional Materials);

**2.2.2.14** in addition to those responsibilities set forth in [Section 2.2.2.6](#) (with respect to changes to Pricing Matters) and [Section 2.2.2.10](#) (with respect to changes to Branding Strategy), reviewing, discussing and determining whether to approve decisions for and any changes to the Major Commercialization Activities;

**2.2.2.15** discussing and determining whether to approve the Regulatory Strategy for the Licensed Products in the Profit-Share Territory, as described in [Section 6.1](#) (Regulatory Lead Responsibilities);

**2.2.2.16** serving as a forum for the Parties to exchange information relating to NDAs for the Licensed Products in the Territory, as described in [Section 6.6](#) (Submissions);

**2.2.2.17** discussing and determining whether to conduct a recall of a Licensed Product in the Profit-Share Territory, as described in [Section 6.9](#) (Recalls, Market Withdrawals or Corrective Actions);

**2.2.2.18** determining whether [\*\*];

**2.2.2.19** reviewing, discussing and determining whether to approve [\*\*];

**2.2.2.20** reviewing, discussing and determining whether to approve the engagement of a Second Source by Sage during the period for which Sage is the Manufacturing Lead Party and reviewing and discussing the engagement of a Second Source by Biogen, in each case, as described in [Section 7.6](#) (Second Source and Biogen Manufacturing Sites);

**2.2.2.21** reviewing, discussing and determining whether to approve the execution by either Party of any agreement for New Technology for the Profit-Share Territory (including the terms thereof), as described in [Section 8.3.2](#) Licensed Product (After Effective Date Executed In-License Agreements);

**2.2.2.22** reviewing, discussing and determining whether to approve a Publications Plan for each Product Class, and any additions or other amendments to an existing Publications Plan, as described in [Section 10.2.1](#) (Publication) and create a process to operationalize the implementation of a Publications Plan;

**2.2.2.23** reviewing, discussing and determining how to resolve any disagreement between the Parties as to the contents of any Publication relating to any Licensed Product in the Profit-Share Territory, which resolution must be consistent with the applicable Publications Plan (unless otherwise agreed by the Parties), as described in [Section 10.2.1](#) (Right to Review);

**2.2.2.24** reviewing, discussing and determining how to resolve any issues escalated by, or disputes within, the JDC, Joint Medical Affairs Subcommittee, JCC or the Finance Working Group;



**2.2.2.25** establishing such additional committees or subcommittees of the JSC as it deems necessary to oversee activities relating to the Licensed Products under this Agreement; and

**2.2.2.26** performing such other functions expressly allocated to the JSC in this Agreement or by the written agreement of the Parties.

**2.2.3** *Meetings.* The JSC will meet at least [\*\*] times per Calendar Year, unless the Parties agree in writing to a different frequency. The JSC may meet in person, by videoconference, or by teleconference, *provided* that at least [\*\*] of the JSC per Calendar Year will be in person unless the Parties otherwise agree. In-person JSC meetings will be held at locations in Massachusetts alternately selected by Sage and by Biogen, or at any other location agreed by the members of the JSC. The first JSC meeting will be held within [\*\*] of the Effective Date. Meetings of the JSC will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative from each Party. Each Party will bear the expense of its respective JSC members' participation in JSC meetings. No later than [\*\*] prior to any meeting of the JSC (or such shorter time period as the Parties may agree), the JSC co-chairpersons will work with the Alliance Managers to prepare and circulate an agenda for such meeting; *provided, however,* that additional topics may be included on such agenda prior to the meeting, and the Party or the Committee proposing an item will provide materials to the JSC representatives no later than [\*\*] prior to the JSC meeting to support discussion. A JSC co-chairperson may also call a special meeting of the JSC (by videoconference, teleconference or in person) if such JSC co-chairperson reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such JSC co-chairperson will work with the Alliance Managers to provide the members of the JSC, promptly after the decision is made to hold such special JSC meeting, with an agenda for the meeting and materials reasonably adequate to enable an informed decision. The Alliance Managers working with the JSC co-chairpersons will be responsible for preparing reasonably detailed written minutes of JSC meetings that reflect all decisions made and action items identified at such meetings within [\*\*] after each JSC meeting, and endeavor to finalize such minutes within [\*\*] after each JSC meeting.

**2.2.4** *Decision-Making.* The JSC will endeavor to reach decisions by consensus, with each Party, through its representative members of the JSC, having one (1) vote. Approvals of the JSC will require the unanimous agreement of the representatives. If the JSC cannot reach unanimous agreement on an issue that comes before the JSC within [\*\*] of the meeting at which such issue was raised and over which the JSC has oversight, then the Parties will refer such issue for resolution in accordance with Section 2.5 (Resolution of Committee Disputes).

### **2.3** **Joint Development Committee.**

**2.3.1** *Formation; Composition; Dissolution.* Within [\*\*] after the Effective Date, the Parties will establish (a) a committee to coordinate the Development of the Licensed 217 Products in the Territory, and (b) a committee to coordinate the Development of the Licensed 324 Products in the Territory (each, a “**Joint Development Committee**” or “**JDC**”). Each Party will initially appoint [\*\*] representatives to each JDC, with each representative having knowledge and expertise in the Development of molecules and products similar to, as applicable, the applicable Licensed Products, and having sufficient seniority and decision-making authority within the applicable Party to provide meaningful input and make decisions arising within the scope of such JDC's responsibilities. Each Party's JDC representatives may serve on one or more JDCs. Each JDC may change its size from time to time by agreement of the Parties, *provided* that each JDC will consist at all times of an equal number of representatives of each of Sage and Biogen. Each Party may replace its JDC representatives at any time upon written notice to the other Party. Each JDC may invite non-members to participate in the discussions and meetings of such JDC, *provided* that such participants have no voting authority at the meetings of such JDC and are bound under enforceable

obligations of confidentiality and non-use no less protective of the Parties' Confidential Information than those set forth in this Agreement. Each JDC will be chaired by co-chairpersons designated by Sage and Biogen, respectively, whose responsibilities will include conducting meetings, including, when feasible, ensuring that objectives for each meeting are set and achieved. The respective applicable JDC will exist for so long as at least one Licensed Product is being Developed under this Agreement.

**2.3.2** *Specific Responsibilities of the JDC.* The respective applicable JDC will have the following responsibilities:

**2.3.2.1** discussing, preparing and determining whether to approve for submission to the JSC each Joint Development Plan (including the designation of Development Lead Party between the Parties and changes to the Major Development Activities thereunder and the corresponding Joint Development Budget) for the Licensed 217 Products and the Licensed 324 Products, including, in each case, and all annual and interim amendments thereto to add to the applicable Joint Development Plan any Clinical Study or Indications, as described in Section 3.2 (Joint Development Plans) and Section 3.3 (Operational Responsibilities for Development; Additional Development);

**2.3.2.2** overseeing, reviewing and discussing the Development of each Licensed Product in the Profit-Share Territory, including (a) overseeing the conduct of all Clinical Studies and Nonclinical Studies, (b) discussing updates from the Parties regarding such Development, and (c) updating the JSC on such Development, in each case, in a manner consistent with Article 3 (Development);

**2.3.2.3** (a) determining whether and when to initiate or discontinue any Clinical Studies and any Nonclinical Study that is set forth under each Joint Development Plan, (b) reviewing, discussing and determining whether to approve the final protocols for Clinical Studies and Nonclinical Studies, and (c) reviewing, discussing and determining priorities for each Clinical Study and Nonclinical Study under each Joint Development Plan, *provided* that the foregoing is not intended to limit a Party's ability to comply with applicable Law or manage subject safety, in each case, in a manner consistent with Article 3 (Development);

**2.3.2.4** determining whether to conduct further Development of the Licensed [\*\*] Products, and, if the JDC so determines, then also determining each Party's responsibilities for the performance of such Development activities and the budget therefor, as described in Section 3.10.1 (Licensed [\*\*] Product Development);

**2.3.2.5** at any time during the period commencing as of the Effective Date and ending upon the Substitution Termination Date, determining whether to approve the substitution of the Licensed [\*\*] Product for the Licensed 217 Products or the Licensed 324 Products, as described in Section 3.10.1 (Licensed [\*\*] Product Development);

**2.3.2.6** determining the feasibility and timing of pursuing, and overseeing collaboration on, new formulations of any Licensed Product for the Profit-Share Territory, in a manner consistent with Article 3 (Development), for inclusion in the applicable Joint Development Plan;

**2.3.2.7** serving as a forum for exchange and discussion with respect to Development reports for the Licensed Products for the Profit-Share Territory, as described in Section 3.5 (Development Reports);

**2.3.2.8** [\*\*];

**2.3.2.9** establishing a process for each Party's disclosure of Regulatory Materials and Know-How to facilitate the technology and materials transfer described in Section 3.8 (Technology and Materials Transfer);

**2.3.2.10** reviewing and approving any [\*\*] that is not a [\*\*] and that a Party proposes to engage, as described in Section [\*\*];

**2.3.2.11** recommending to the JSC for approval the overall strategy for obtaining Regulatory Approval of the Licensed Products in the Profit-Share Territory, including the content of label or other prescribing information, and overseeing implementation of such strategy as approved by the JSC, in a manner consistent with Article 6 (Regulatory);

**2.3.2.12** developing and implementing procedures for the drafting and review of Regulatory Materials for the Licensed Products in the Profit-Share Territory, in a manner consistent with Article 6 (Regulatory);

**2.3.2.13** overseeing the Parties activities under the Pharmacovigilance Agreement, as described in Section 6.10 (Reporting Adverse Events);

**2.3.2.14** determining whether to Develop any EP-Enhanced 217 Product, as described in Section 8.3.1.3(b) (Third Party Payments owed to Existing Partner);

**2.3.2.15** [\*\*]; and

**2.3.2.16** performing such other functions expressly allocated to the JDC in this Agreement or by the written agreement of the Parties.

**2.3.3** *Meetings.* Each JDC will meet at least [\*\*] times per Calendar Year, unless the Parties agree in writing to a different frequency. Each JDC may meet in person, by videoconference, or by teleconference, *provided* that at least [\*\*] of each JDC per Calendar Year will be in person unless the Parties otherwise agree. In-person JDC meetings will be held at locations in Massachusetts alternately selected by Sage and by Biogen, or at any other location agreed by the members of the respective applicable JDC. Meetings of each JDC will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative of each Party. Each Party will bear the expense of its respective JDC members' participation in JDC meetings. No later than [\*\*] prior to the first meeting of the respective applicable JDC in the 2020 stub-Calendar Year and in each Calendar Year thereafter while such JDC exists, the co-chairpersons for such JDC will prepare a communication plan setting forth a schedule of the dates of each meeting of such JDC for that Calendar Year (a "**JDC Communication Plan**"). No later than [\*\*] prior to any meeting of the respective applicable JDC (or such shorter time period as the Parties may agree), the co-chairpersons of such JDC will work with the Alliance Managers to prepare and circulate an agenda for such meeting; *provided, however*, that additional topics may be included on such agenda prior to such meeting, and the Party proposing an item will provide detailed materials to the representatives of such JDC no later than [\*\*] prior to the JDC meeting to support discussion. A JDC co-chairperson may also call a special meeting of its JDC (by videoconference, teleconference or in person) if such JDC co-chairperson reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such JDC co-chairperson will work with the Alliance Managers to provide the members of such JDC, promptly after the decision is made to hold such special JDC meeting, with an agenda for the meeting and materials reasonably adequate to enable an informed decision. The co-chairpersons of their respective applicable JDC will be responsible for preparing reasonably detailed written minutes of meetings of such JDC that reflect all decisions made and action items identified at such meetings within [\*\*] after

each meeting of such JDC, and endeavor to finalize such minutes within [\*\*] after each meeting of such JDC.

**2.3.4** *Decision-Making.* The JDC will endeavor to reach decisions by consensus, with each Party, through its representative members of the JSC, having one (1) vote. Approvals of each respective applicable JDC matter will require the unanimous agreement of the representatives. If a JDC cannot reach unanimous agreement on a matter issue that comes before it within [\*\*] of the meeting at which such issue was raised and over which such JDC has oversight, then the Parties will refer such issue for resolution to the JSC.

## **2.4 Joint Commercialization Committee.**

**2.4.1** *Formation; Composition; Dissolution.* (a) Within [\*\*] after the Effective Date, the Parties will establish a committee to coordinate and oversee Commercialization activities with respect to the Licensed 217 Products for the Profit-Share Territory, and (b) within [\*\*] after the Initiation of the [\*\*] for the Licensed 324 Products or such other time as agreed by the Parties, the Parties will establish a committee to coordinate Commercialization activities with respect to the Licensed 324 Products for the Profit-Share Territory (each, a “**Joint Commercialization Committee**” or “**JCC**”). Each Party will initially appoint [\*\*] representatives to each JCC, with each representative having knowledge and expertise in the performance of Commercialization of products similar to the applicable Licensed Products, and having sufficient seniority and decision-making authority within the applicable Party to provide meaningful input and make decisions arising within the scope of such JCC’s responsibilities. Each Party’s JCC representatives may serve on one or more JCCs. Each JCC may change its size from time to time by agreement of the Parties, *provided* that each JCC will consist at all times of an equal number of representatives of each of Sage and Biogen. Each Party may replace its JCC representatives at any time upon written notice to the other Party. Each JCC may invite non-members to participate in the discussions and meetings of such JCC, *provided* that such participants have no voting authority at the meetings of such JCC and are bound under enforceable obligations of confidentiality and non-use no less protective of the Parties’ Confidential Information than those set forth in this Agreement. Each JCC will be chaired by co-chairpersons designated by Sage and Biogen, respectively, whose responsibilities will include conducting meetings, including, when feasible, ensuring that objectives for each meeting are set and achieved. The respective applicable JCC will exist for so long as at least one Licensed Product is being Commercialized or Commercialization is planned under this Agreement.

**2.4.2** *Specific Responsibilities of the JCC.* Subject to any limitations under applicable Law, the respective applicable JCC will have the following responsibilities:

**2.4.2.1** coordinating with the Joint Medical Affairs Subcommittee to discuss Medical Affairs Activities to the extent relevant to the Commercialization strategy (including the Medical Affairs Activities strategy) and the overall Commercialization strategy for the Licensed Products for the Profit-Share Territory (including the Medical Affairs Activities strategy);

**2.4.2.2** determining the anticipated date of First Commercial Sale of each Licensed Product in the Profit-Share Territory, as described in Section 1.1.150 (Launch Window);

**2.4.2.3** discussing, preparing and determining whether to approve for submission to the JSC each Joint Commercialization Plan for the Licensed 217 Products and the Licensed 324 Products (including the designation of Commercialization Lead Party between the Parties and changes to the Major Commercialization Activities thereunder and the corresponding Joint Commercialization Budget) and all annual and interim amendments thereto, as described in Section

5.2 (Joint Commercialization Plans) and Section 5.4 (Operational Responsibilities for Commercialization);

**2.4.2.4** overseeing the implementation of the Joint Commercialization Plans in a manner consistent with Article 5 (Commercialization);

**2.4.2.5** discussing, preparing and determining whether to approve for submission to the JSC each Distribution Plan for the Licensed 217 Products and the Licensed 324 Products and all annual and interim amendments thereto, as described in Section 5.7.3 (Distribution in the Profit-Share Territory);

**2.4.2.6** serving as a forum for exchange and discussion with respect to Commercialization reports for Licensed Products for the Profit-Share Territory, as described in Section 5.6 (Commercialization Reports);

**2.4.2.7** [\*\*], as described in Section [\*\*];

**2.4.2.8** reviewing, discussing and determining Pricing Matters, including the strategy with respect to Pricing Matters, for the Licensed Products for the Profit-Share Territory and [\*\*], as described in Section 5.7.1 (Pricing Matters);

**2.4.2.9** reviewing and approving any [\*\*] that is not a [\*\*] and that a Party proposes to engage, as described in Section [\*\*];

**2.4.2.10** reviewing and discussing a Party's promotion of [\*\*] using Shared Resources in the Profit-Share Territory [\*\*], as described in Section 5.10 (Joint Commercialization Costs Allocation);

**2.4.2.11** reviewing, discussing and determining whether to approve the Branding Strategy for the Licensed Products in the Profit-Share Territory and making a recommendation to the JSC on such strategy for the JSC to determine whether to approve, as described in Section 5.11.1 (Branding);

**2.4.2.12** discussing and determining whether to submit to the JSC to further review, discuss and determine whether to approve the LP U.S. TM Strategy, as described in Section 5.11.4.1 (Profit-Share Territory); and

**2.4.2.13** performing such other functions expressly allocated to the JCC in this Agreement or by the written agreement of the Parties.

**2.4.3** *Meetings.* Each JCC will meet at least [\*\*] times per Calendar Year, together with the applicable Joint Medical Affairs Subcommittee, unless the Parties agree in writing to a different frequency. Each JCC may meet in person, by videoconference, or by teleconference, *provided* that at least [\*\*] of each JCC per Calendar Year will be in person unless the Parties otherwise mutually agree. In-person JCC meetings will be held at locations in Massachusetts alternately selected by Sage and by Biogen, or at any other location agreed by the members of the respective applicable JCC. Meetings of each JCC will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative of each Party. Each Party will bear the expense of its respective JCC members' participation in JCC meetings. No later than [\*\*] prior to the first meeting of the respective applicable JCC in the 2020 stub-Calendar Year and in each Calendar Year thereafter while such JCC exists, the co-chairpersons for such JCC will prepare a communication plan setting forth a schedule of the dates of each meeting for such

JCC for that Calendar Year (a “**JCC Communication Plan**”). No later than [\*\*] prior to any meeting of the respective applicable JCC (or such shorter time period as the Parties may agree), the co-chairpersons of such JCC will work with the Alliance Managers to prepare and circulate an agenda for such meeting; *provided, however*, that additional topics may be included on such agenda, prior to the meeting, and the Party proposing an item will provide materials to the representatives of such JCC no later than [\*\*] prior to the JCC meeting to support discussion. A JCC co-chairperson may also call a special meeting of its JCC (by videoconference, teleconference or in person) if such JCC co-chairperson reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such JCC co-chairperson will work with the Alliance Managers to provide the members of such JCC, promptly after the decision is made to hold such special JCC meeting, with an agenda for the meeting and materials reasonably adequate to enable an informed decision. The co-chairpersons of their respective applicable JCC will be responsible for preparing reasonably detailed written minutes of meetings of such JCC that reflect all decisions made and action items identified at such meetings within [\*\*] after such meeting of such JCC, and endeavor to finalize such minutes within [\*\*] after each meeting of such JCC.

**2.4.4** *Decision-Making.* The JCC will endeavor to reach decisions by consensus, with each Party, through its representative members of the JCC, having one (1) vote. Approvals of each respective applicable JCC matter will require the unanimous agreement of the representatives. If a JCC cannot reach unanimous agreement on a matter that comes before it within [\*\*] of the meeting at which such issue was raised and over which such JCC has oversight, then the Parties will refer such issue for resolution to the JSC.

## **2.5 Joint Medical Affairs Subcommittee.**

**2.5.1** *Formation; Composition; Dissolution.* (a) Within [\*\*] after the Effective Date, the Parties will establish a subcommittee of the JCC to coordinate and oversee Medical Affairs Activities with respect to the Licensed 217 Products for the Profit-Share Territory, and (b) within [\*\*] after the Initiation of the [\*\*] for the Licensed 324 Products or such other time as agreed by the Parties, the Parties will establish a subcommittee of the JCC to coordinate and oversee Medical Affairs Activities with respect to the Licensed 324 Products for the Profit-Share Territory (each, a “**Joint Medical Affairs Subcommittee**”). Each Party will initially appoint [\*\*] representatives to the Joint Medical Affairs Subcommittee, with each representative having knowledge and expertise in the performance of Medical Affairs Activities with respect to products similar to the applicable Licensed Products, holding a position within such Party’s Medical Affairs or research and development departments (but not holding a position within such Party’s Commercialization department), and having sufficient seniority and decision-making authority within the applicable Party to provide meaningful input and make decisions arising within the scope of such Joint Medical Affairs Subcommittee’s responsibilities. Each Party’s Joint Medical Affairs Subcommittee’s representatives may serve on one or more Joint Medical Affairs Subcommittees. Each Joint Medical Affairs Subcommittee may change its size from time to time by agreement of the Parties, provided that each Joint Medical Affairs Subcommittee will consist at all times of an equal number of representatives of each of Sage and Biogen. Each Party may replace its Joint Medical Affairs Subcommittee representatives at any time upon written notice to the other Party. Each Joint Medical Affairs Subcommittee may invite non-members to participate in the discussions and meetings of such Joint Medical Affairs Subcommittee, provided that such participants have no voting authority at the meetings of such Joint Medical Affairs Subcommittee and are bound under enforceable obligations of confidentiality and non-use no less protective of the Parties’ Confidential Information than those set forth in this Agreement. Each Joint Medical Affairs Subcommittee will be chaired by co-chairpersons designated by Sage and Biogen, respectively, whose responsibilities will include conducting meetings, including, when feasible, ensuring that objectives for each meeting are set and achieved. The respective applicable Joint Medical Affairs Subcommittee will exist for so long as there are Medical Affairs Activities being conducted or planned to be conducted for at least one Licensed Product under this Agreement.

**2.5.2** *Specific Responsibilities of the Joint Medical Affairs Subcommittee.* Subject to any limitations under applicable Law, the respective applicable Joint Medical Affairs Subcommittee will have the following responsibilities:

**2.5.2.1** discussing, preparing and determining whether to approve for submission to the JSC each Joint Medical Affairs Plan for the Licensed 217 Products and the Licensed 324 Products, (including the designation of Medical Affairs Lead Party between the Parties, changes to the Major Medical Affairs Activities thereunder and the corresponding Joint Medical Affairs Budget) and all annual and interim amendments thereto, as described in Section 4.2 (Joint Medical Affairs Plan) and Section 4.3 (Operational Responsibilities for Medical Affairs Activities);

**2.5.2.2** serving as a forum for exchange and discussion with respect to Medical Affairs Activities reports for Licensed Products for the Profit-Share Territory and [\*\*], as described in Section 4.5 (Medical Affairs Reports);

**2.5.2.3** via the Joint Publications Working Group, reviewing, discussing and recommending to the JSC to further review, discuss and determine whether to approve, a Publications Plan for each Product Class, and any additions or other amendments to an existing Publications Plan, as described in Section 10.2.1 (Publication); and

**2.5.2.4** performing such other functions expressly allocated to the Joint Medical Affairs Subcommittee in this Agreement or by the written agreement of the Parties.

**2.5.3** *Meetings.* Each Joint Medical Affairs Subcommittee will meet at least [\*\*] times per Calendar Year, together with the applicable JCC (in which case the meeting logistics of Section 2.4.3 (Meetings) will apply), unless the Parties agree in writing to a different frequency, and will meet separately from the JCC on such frequency as is agreed by the Parties with respect to Medical Affairs Activities-specific matters. Each Joint Medical Affairs Subcommittee may meet in person, by videoconference, or by teleconference, *provided* that at least [\*\*] of each Joint Medical Affairs Subcommittee per Calendar Year will be in person unless the Parties otherwise mutually agree. With respect to any independent meetings of the Joint Medical Affairs Subcommittee regarding Medical Affairs Activities-specific matters, in-person meetings will be held at locations in Massachusetts alternately selected by Sage and by Biogen, or at any other location agreed by the members of the respective applicable Joint Medical Affairs Subcommittee. Meetings of each Joint Medical Affairs Subcommittee will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative of each Party. Each Party will bear the expense of its respective Joint Medical Affairs Subcommittee members' participation in Joint Medical Affairs Subcommittee meetings. No later than [\*\*] prior to the first meeting of the respective applicable Joint Medical Affairs Subcommittee in the 2020 stub-Calendar Year and in each Calendar Year thereafter while such Joint Medical Affairs Subcommittee exists, the co-chairpersons for such Joint Medical Affairs Subcommittee will prepare a communication plan setting forth a schedule of the dates of each meeting for such Joint Medical Affairs Subcommittee for that Calendar Year (a "**Joint Medical Affairs Subcommittee Communication Plan**"). No later than [\*\*] prior to any meeting of the respective applicable Joint Medical Affairs Subcommittee (or such shorter time period as the Parties may agree), the co-chairpersons of such Joint Medical Affairs Subcommittee will work with the Alliance Managers to prepare and circulate an agenda for such meeting; *provided, however*, that additional topics may be included on such agenda, prior to the meeting, and the Party proposing an item will provide materials to the representatives of such Joint Medical Affairs Subcommittee no later than [\*\*] prior to the Joint Medical Affairs Subcommittee meeting to support discussion. A Joint Medical Affairs Subcommittee co-chairperson may also call a special meeting of its Joint Medical Affairs Subcommittee (by videoconference, teleconference or in person) if such Joint Medical Affairs Subcommittee co-chairperson reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such Joint Medical Affairs Subcommittee

co-chairperson will work with the Alliance Managers to provide the members of such Joint Medical Affairs Subcommittee, promptly after the decision is made to hold such special Joint Medical Affairs Subcommittee meeting, with an agenda for the meeting and materials reasonably adequate to enable an informed decision. The co-chairpersons of their respective applicable Joint Medical Affairs Subcommittee will be responsible for preparing reasonably detailed written minutes of meetings of such Joint Medical Affairs Subcommittee that reflect all decisions made and action items identified at such meetings within [\*\*] after such meeting of such Joint Medical Affairs Subcommittee, and endeavor to finalize such minutes within [\*\*] after each meeting of such Joint Medical Affairs Subcommittee.

**2.5.4** *Decision-Making.* The Joint Medical Affairs Subcommittee will endeavor to reach decisions by consensus, with each Party, through its representative members of the Joint Medical Affairs Subcommittee, having one (1) vote. Approvals of each respective applicable Joint Medical Affairs Subcommittee matter will require the unanimous agreement of the representatives. If a Joint Medical Affairs Subcommittee cannot reach unanimous agreement on a matter that comes before it within [\*\*] of the meeting at which such issue was raised and over which such Joint Medical Affairs Subcommittee has oversight, then the Parties will refer such issue for resolution to the JSC.

## **2.6** **Joint Manufacturing Committee.**

**2.6.1** *Formation; Composition; Dissolution.* Within [\*\*] after the Effective Date, the Parties will establish a committee to coordinate and oversee Manufacturing activities with respect to the Licensed 217 Products for the Profit-Share Territory, and (b) within [\*\*] after the Effective Date, the Parties will establish a committee to coordinate and oversee Manufacturing Activities with respect to the Licensed 324 Products for the Profit-Share Territory (each, a “**Joint Manufacturing Committee**” or “**JMC**”). Each Party will initially appoint [\*\*] representatives to the JMC, with each representative having knowledge and expertise in the performance of Manufacturing activities with respect to products similar to the applicable Licensed Products, and having sufficient seniority and decision-making authority within the applicable Party to provide meaningful input and make decisions arising within the scope of such JMC’s responsibilities. Each Party’s JMC representatives may serve on one or more JMCs. Each JMC may change its size from time to time by agreement of the Parties, *provided* that each JMC will consist at all times of an equal number of representatives of each of Sage and Biogen. Each Party may replace its JMC representatives at any time upon written notice to the other Party. Each JMC may invite non-members to participate in the discussions and meetings of such JMC, *provided* that such participants have no voting authority at the meetings of such JMC and are bound under enforceable obligations of confidentiality and non-use no less protective of the Parties’ Confidential Information than those set forth in this Agreement. Each JMC will be chaired by co-chairpersons designated by Sage and Biogen, respectively, whose responsibilities will include conducting meetings, including, when feasible, ensuring that objectives for each meeting are set and achieved. The respective applicable JMC will exist for so long as there are Manufacturing activities being conducted or planned to be conducted for at least one Licensed Product under this Agreement.

**2.6.2** **Specific Responsibilities of the JMC.** Subject to any limitations under applicable Law, the respective applicable JMC will have the following responsibilities:

**2.6.2.1** in consultation with the Finance Working Group, as part of the Manufacturing Plan, allocating responsibilities as between the Parties with respect to the right to [\*\*], as described in Section 7.1 (Manufacturing Responsibilities);

**2.6.2.2** preparing and approving Manufacturing Plans and amendments to then-current Manufacturing Plans for each Product Class and submit such amendments to the JSC to



further review, discuss and determine whether to approve, as described in Section 7.2 (Manufacturing Plans);

**2.6.2.3** serving as a forum for the Parties to exchange information regarding the progress of all Manufacturing activities, including status of inventory and anticipated shortages of Licensed Product for the Profit-Share Territory and anticipated shortages of Licensed Product for the Territory, as described in Section 7.7 (Reporting; Shortages); and

**2.6.2.4** performing such other functions expressly allocated to the JMC in this Agreement or by the written agreement of the Parties.

**2.6.3** *Meetings.* Each JMC will meet at least [\*\*] times per Calendar Year, unless the Parties agree in writing to a different frequency, and otherwise as agreed by the Parties with respect to Manufacturing activities-specific matters. Each JMC may meet in person, by videoconference, or by teleconference, *provided* that at least [\*\*] of each JMC per Calendar Year will be in person unless the Parties otherwise mutually agree. In-person JMC meetings will be held at locations in Massachusetts alternately selected by Sage and by Biogen, or at any other location agreed by the members of the respective applicable JMC. Meetings of each JMC will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative of each Party. Each Party will bear the expense of its respective JMC members' participation in JMC meetings. No later than [\*\*] prior to the first meeting of the respective applicable JMC in the 2020 stub-Calendar Year and in each Calendar Year thereafter while such JMC exists, the co-chairpersons for such JMC will prepare a communication plan setting forth a schedule of the dates of each meeting for such JMC for that Calendar Year (a "**JMC Communication Plan**"). No later than [\*\*] prior to any meeting of the respective applicable JMC (or such shorter time period as the Parties may agree), the co-chairpersons of such JMC will work with the Alliance Managers to prepare and circulate an agenda for such meeting; *provided, however*, that additional topics may be included on such agenda, prior to the meeting, and the Party proposing an item will provide materials to the representatives of such JMC no later than [\*\*] prior to the JMC meeting to support discussion. A JMC co-chairperson may also call a special meeting of its JMC (by videoconference, teleconference or in person) if such JMC co-chairperson reasonably believes that a significant matter must be addressed prior to the next scheduled meeting, in which event such JMC co-chairperson will work with the Alliance Managers to provide the members of such JMC, promptly after the decision is made to hold such special JMC meeting, with an agenda for the meeting and materials reasonably adequate to enable an informed decision. The co-chairpersons of their respective applicable JMC will be responsible for preparing reasonably detailed written minutes of meetings of such JMC that reflect all decisions made and action items identified at such meetings within [\*\*] after such meeting of such JMC, and endeavor to finalize such minutes within [\*\*] after each meeting of such JMC.

**2.6.4** *Decision-Making.* The JMC will endeavor to reach decisions by consensus, with each Party, through its representative members of the JMC, having one (1) vote. Approvals of each respective applicable JMC matter will require the unanimous agreement of the representatives. If a JMC cannot reach unanimous agreement on a matter that comes before it within [\*\*] of the meeting at which such issue was raised and over which such JMC has oversight, then the Parties will refer such issue for resolution to the JSC.

## **2.7** Resolution of Committee Disputes.

**2.7.1** *Referral to the JSC.* If any subcommittee or working group of the JDC, JCC or JMC cannot reach consensus on any matter within its decision-making authority within [\*\*] after the meeting at which such failure to reach consensus occurred, then such matter will first be referred for attempted resolution to the applicable committee, *provided, however*, that any disputes arising out of the Joint Medical

Affairs Subcommittee will be referred for attempted resolution directly to the JSC. If the JDC, JCC, JMC or any other committee or subcommittee of the JSC cannot reach consensus on any matter within its decision-making authority within [\*\*] after the meeting at which such failure to reach consensus occurred, then the matter will be referred for attempted resolution to the JSC.

**2.7.2** *Referral to Executive Officers and Executive Management.* If the JSC cannot reach a consensus decision under Section 2.7.1 (Referral to the JSC), then the matter will be referred to the Executive Officers within [\*\*] of its determination under Section 2.7.1 (Referral to the JSC) that a consensus cannot be reached. If a matter is referred to the Executive Officers under this Section 2.7.2 (Referral to Executive Officers and Executive Management), then the JSC will submit in writing to their respective Executive Officers the respective positions of the Parties. Such Executive Officers will use good faith efforts to resolve such matter promptly, which good faith efforts will include at least [\*\*] between such Executive Officers within [\*\*] after such co-chairpersons' submission of their respective positions on such matter to them.

**2.7.3** *Final Decision-Making Authority.* If the Executive Officers are unable to reach unanimous agreement on any such matter within [\*\*] of the meeting between the Executive Officers, then no action will be taken as to the escalated matter until a joint decision can be made by the Parties, except that the following will apply:

**2.7.3.1** except as set forth in Section 3.3.2 (Additional Indications Development), if the escalated matter relates to [\*\*], then (a) [\*\*] or (b) with respect to a [\*\*];

**2.7.3.2** if the escalated matter relates to Development of a Licensed Product for a new Indication, then the [\*\*];

**2.7.3.3** if the escalated matter relates to any Major Commercialization Activity, then [\*\*];

**2.7.3.4** if the escalated matter relates to the inventory holding and ship to strategy with respect to any Licensed Product in the Profit-Share Territory, then [\*\*] will have final decision-making authority with respect to such matter; *provided* that [\*\*];

**2.7.3.5** the Development Lead Party for an activity will have final decision-making authority with respect to [\*\*];

**2.7.3.6** if the escalated matter relates to any Pricing Matter under a Joint Commercialization Plan as described in Section 5.7.1 (Pricing Matters), then the [\*\*];

**2.7.3.7** if the escalated matter relates to any dispute between the Parties with respect to the contents of any Biogen Publication, as described in Section 10.2.2 (Right to Review), then [\*\*] will have final decision-making authority with respect to such matter;

**2.7.3.8** if the escalated matter pertains to [\*\*]; and

**2.7.3.9** with respect to any matter set forth in this Section 2.7.3 (Final Decision-Making Authority) for which [\*\*] has final decision-making authority, [\*\*].

**2.7.4** *Exercise of Decision-Making Rights.* No exercise of a Party's decision-making authority on any matters may, without the other Party's prior written consent, (a) unilaterally waive its own

compliance with, modify or amend the terms or conditions of this Agreement, or (b) otherwise conflict with this Agreement.

**2.7.5** *Good Faith.* In conducting themselves on Committees, and in exercising their rights under this Section 2.5 (Resolution of Committee Disputes), all representatives of both Parties will consider reasonably and in good faith all input received from the other Party and will use good faith efforts to reach unanimous agreement on all matters before them.

**2.8** **General Committee Authority.** Each Committee has solely the powers expressly assigned to it in this Article 2 (Governance). No Committee will have any power to amend, modify, or waive the terms or conditions of this Agreement or compliance with the terms and conditions of this Agreement.

### 3.DEVELOPMENT

#### **3.1** **Diligence; Standards of Conduct.**

**3.1.1** *Profit-Share Territory.* Each of Sage and Biogen will use Commercially Reasonable Efforts to (a) Develop at least one Licensed 217 Product and at least one Licensed 324 Product in the Profit-Share Territory and [\*\*], and (b) [\*\*].

**3.1.2** *Biogen Territory.* Biogen will use Commercially Reasonable Efforts to (a) Develop at least one Licensed 217 Product and at least one Licensed 324 Product in the Biogen Territory and (b) [\*\*].

**3.1.3** *General.* Each of Sage and Biogen will perform the Development activities it undertakes with respect to the Licensed Products in the Territory in a good scientific manner and in compliance in all material respects with applicable Law.

#### **3.2** **Joint Development Plans.**

**3.2.1** *General.* All Development of the Licensed 217 Products and the Licensed 324 Products for the Profit-Share Territory will be conducted pursuant to a development plan and budget for the applicable Product Class (each such plan, a “**Joint Development Plan**”) that describes for each Product Class for the Profit-Share Territory: (a) [\*\*]; (b) the anticipated timelines for such activities, including [\*\*]; (c) the respective roles and responsibilities of each Party in connection with such activities, including which Party will have day-to-day operational responsibility with respect to such activities for the applicable Licensed Products in the Profit-Share Territory (for such activity, the “**Development Lead Party**”); and (d) the associated budget of the FTE Costs and Out-of-Pocket Costs anticipated to be incurred in the performance of the foregoing activities (each such included budget in a Joint Development Plan, a “**Joint Development Budget**”) and, starting with the annual update to the Joint Development Plan for 2021, a [\*\*], high-level budget with respect to the performance of activities in such Joint Development Plan (each such budget, a “**Long Term Joint Development Budget**”). Each Party will be allocated meaningful responsibility for Development activities under each Joint Development Plan, consistent with a 50:50 collaboration for the Licensed Products for the Profit-Share Territory. In the event of any inconsistency between a Joint Development Plan and this Agreement, the terms of this Agreement will prevail. The initial Joint Development Plan for the Licensed 217 Products and the initial Joint Development Plan for the Licensed 324 Products are attached hereto, respectively, as Schedule 3.2.1 (Joint Development Plans); *provided, however*, that for each such initial Joint Development Plans, the corresponding Joint Development Budgets will be (i) agreed between the Parties within [\*\*] after the Effective Date and (ii) unless agreed otherwise by the JSC, consistent with the applicable initial Joint Development Plan and

Sage's current and anticipated spend with respect to the activities included in such initial Joint Development Plan.

**3.2.2** *Amendments to Joint Development Plans.* On an annual basis, (a) no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the JDC will prepare amendments to each then-current Joint Development Plan (including the corresponding Joint Development Budget) for the Licensed 217 Products and the Licensed 324 Products, and submit such each such amendment to the JSC to review, discuss and determine whether to approve by no later than [\*\*] of each Calendar Year, and (b) no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the JDC will prepare amendments to each then-current Long Term Joint Development Budget corresponding to each Joint Development Plan and submit each such amendment to the JSC to review, discuss and determine whether to approve by no later than [\*\*] of each Calendar Year. Each such amended Joint Development Plan will specify the items described in Section 3.2.1 (Joint Development Plans; General) for each Product Class for the next Calendar Year (and additional periods as reasonably determined by the Parties) and the Joint Development Budget included therein will appropriately itemize the FTE Costs and Out-of-Pocket Costs for the activities undertaken pursuant to each Joint Development Plan. Such updated and amended Joint Development Plan will reflect any changes, re-prioritization or termination of Clinical Studies or Nonclinical Studies within, reallocation of resources with respect to, or additions to (including reprioritization of Indications, additions of Indications for Development and Regulatory Approval, in each case, not included currently therein) the then-current corresponding Joint Development Plan. Once approved by the JSC, an amended annual Joint Development Plan (including its corresponding Joint Development Budget and Long Term Joint Development Budget) will become effective for the applicable period on the date approved by the JSC (or such other date as the JSC will specify). Any JSC-approved amended Joint Development Plan (including its corresponding Joint Development Budget and Long Term Joint Development Budget) will supersede the previous Joint Development Plan (including its corresponding Joint Development Budget and Long Term Joint Development Budget) for the applicable period.

### **3.3 Operational Responsibilities for Development; Additional Development.**

#### **3.3.1 *Operational Responsibilities for Development.***

**3.3.1.1** *Profit-Share Territory.* Unless the Parties agree in writing upon an alternate allocation of responsibility, for the Profit-Share Territory, (a) Sage will be the Development Lead Party with respect to conducting and completing the Ongoing 217 Studies and the KINETIC Study, (b) [\*\*], and (c) Sage and Biogen will have joint responsibility for all other Development activities for the Licensed Products, with each Party serving as the Development Lead Party as designated in the applicable Joint Development Plan, as the same may be amended and expanded in accordance with Section 3.2.2 (Amendments to Joint Development Plans). As part of the preparation of the initial Joint Development Plans and any amendments thereto as described in Section 3.2 (Joint Development Plans), the JDC will identify any changes to the Major Development Activities in such Joint Development Plan and assign a Development Lead Party that will be responsible for each Major Development Activity. In the event that a Development Lead Party is unable to perform any of its material responsibilities in accordance with the applicable Joint Development Plan (including the applicable timeline set forth therein for the performance of such activities) and fails to cure any such non-performance within [\*\*] after receipt of written notice from the non-Development Lead Party regarding such non-performance, then the other Party will have the right to become the Development Lead Party with respect to the applicable non-performed responsibilities for purposes of this Agreement, and any FTE Costs and Out-of-Pocket Costs that such other Party incurs in connection with its performance of such responsibilities (or the assumption thereof) will be included as Joint Development Costs. [\*\*].

**3.3.1.2** *Biogen Territory.* For the Biogen Territory, Biogen will have sole control over and decision-making authority with respect to all Development of the Licensed Products solely for the Biogen Territory.

**3.3.2** *Additional Indications Development.* As contemplated under Section 3.2.2 (Amendments to Joint Development Plans), each Party may propose (the “**Proposing Party**”) for addition under the applicable then-current Joint Development Plan (and corresponding Joint Development Budget) Development of a Licensed Product for the Profit-Share Territory in an Indication not included in such then-current Joint Development Plan (“**Additional Indications Development**”). In such a case, the Proposing Party will prepare a proposed amendment to the applicable then-current Joint Development Plan (and corresponding Joint Development Budget) for the applicable Licensed Product setting forth the additional Indication proposed to be included for Development for the Profit-Share Territory, the proposed Development activities to be conducted in furtherance of such Indication, the proposed Development Lead Party designations as between the Parties for the performance thereof and the proposed budget of FTE Costs and Out-of-Pocket Costs associated with the performance of such additional Development activities (each, an “**Additional Development Proposal**”). The Proposing Party will submit each Additional Development Proposal to the JDC to review and discuss and then the JDC will submit each Additional Development Proposal (as may be revised by the JDC) to the JSC to review, discuss and determine whether to approve in accordance with Section 2.3.2.1 (Specific Responsibilities of the JDC). As soon as reasonably practicable, but in no event more than [\*\*] following such time as the JSC approves an Additional Development Proposal, the Parties, through the JDC, will prepare an amendment to the applicable Joint Development Plan to contemplate the Development of such Additional Indications Development that is consistent with such approved Additional Development Proposal, and submit such amendment to the JSC to review, discuss and determine whether to approve. If the JSC cannot reach consensus on approving any aspect of an Additional Development Proposal or the update to the Joint Development Plan related thereto (e.g., the additional Indication proposed to be included for Development and Regulatory Approval, [\*\*]).

### **3.4** Development Costs.

**3.4.1** *Profit-Share Territory.* Subject to Section 3.3.2 (Additional Indications Development) and Section 9.4 (Sage Opt Out), Sage will be responsible for fifty percent (50%) and Biogen will be responsible for fifty percent (50%) of all Joint Development Costs. The Parties will reconcile such Joint Development Costs they have incurred to reflect the foregoing allocation of Joint Development Costs according to the procedures in Section 9.3.1 (Reconciliation/Reimbursement Prior to First Commercial Sale) or Section 9.3.3 (Profit Sharing Following First Commercial Sale), as applicable.

**3.4.2** *Biogen Territory.* Biogen will be responsible for one hundred percent (100%) of all costs and expenses incurred by or on behalf of Biogen in the performance of the Development of the Licensed Products solely for the Biogen Territory.

**3.5** Development Reports. For Development activities conducted for the Profit-Share Territory, each Party will provide to the JDC: (a) no later than [\*\*] after the same becomes available, any material information and data arising from the Development of Licensed Products for the Profit-Share Territory by such Party, including [\*\*] and (b) at least [\*\*] in advance of each regularly scheduled meeting of the JDC, any other relevant information and data arising from the performance of Development activities by such Party for the Licensed Products for the Profit-Share Territory since the last such meeting to the extent not previously disclosed in connection with day-to-day interactions between the Parties. In addition, at the first JDC meeting in the following Calendar Year, each Party will provide an annual review for the Calendar Year-ended of results versus goals of Development activities for the Licensed Products for the Profit-Share Territory (as such goals are set forth in the applicable Joint Development Plans). Biogen will provide, (A) promptly after the same become available, [\*\*], (B) [\*\*], and (C) [\*\*].

**3.6 Clinical Study Reporting.** Each Party agrees that each Clinical Study conducted for a Licensed Product pursuant to this Agreement that is required to be posted pursuant to applicable Law or applicable industry codes in the Territory, and all results of any such Clinical Study, as the case may be, for a Licensed Product, in the Territory, will be so posted. All information posted pursuant to this [Section 3.6](#) (Clinical Study Reporting) will be subject to prior review pursuant to [Section 10.2.1](#) (Publication) as if such posting were a publication or presentation.

**3.7 Joint Program Activities Records.** Each Party will maintain complete and accurate records (in the form of technical notebooks or electronic files where appropriate) of all Development, Manufacturing, Medical Affairs Activities and Commercialization activities conducted by or on behalf of it under this Agreement and all information, data and results resulting from such activities for the Licensed Products for the Profit-Share Territory. Such records will fully and properly reflect all work done and results achieved in the performance of such Development, Manufacturing, Medical Affairs Activities or Commercialization activities, in each case, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes. Each Party will provide copies of such records (including in electronic format if maintained in such format) to the other Party to the extent related to the Development of Licensed Products for the Profit-Share Territory on a [\*\*] basis (or as more frequently as may be reasonably requested by such other Party) to enable such other Party to perform its obligations or exercise its rights under this Agreement.

**3.8 Technology and Materials Transfer.** Sage will provide to Biogen copies of all Sage Licensed Know-How that is necessary, has been used prior to the Effective Date, or [\*\*] is reasonably useful, in each case, for the performance of Development, Manufacturing, Medical Affairs Activities or Commercialization activities for Licensed Products for the Profit-Share Territory or the Biogen Territory, as applicable, no later than [\*\*] after the Effective Date. Thereafter, Sage will provide to Biogen copies of all Sage Licensed Know-How that is made, conceived, discovered or otherwise generated following the Effective Date or such initial transfer of Sage Licensed Know-How and that is licensed to Biogen pursuant to [Section 8.1.1.1](#) (License Grant to Biogen) to continue to enable Biogen to perform Development, Manufacturing, Medical Affairs Activities or Commercialization activities for Licensed Products for the Profit-Share Territory or the Biogen Territory, as applicable. [\*\*]. In addition to providing copies of the Sage Licensed Know-How and the Biogen Licensed Know-How, as applicable, in accordance with this [Section 3.8](#) (Technology and Materials), Sage and Biogen, respectively, will make its personnel reasonably available to the other Party so as to enable such Party to practice under, respectively, the Sage Licensed Technology, in case of Biogen, and the Biogen Licensed Technology, in case of Sage, in connection with its performance of the Development, Manufacture, Medical Affairs Activities or Commercialization activities for Licensed Products.

**3.9 Development Subcontracts.** Subject to this [Section 3.9](#) (Development Subcontracts), each Party may perform any of its Development obligations under this Agreement with respect to any Licensed Product in the Territory through one or more Subcontractors, [\*\*]. Prior to engaging any Subcontractor that is not a [\*\*] to perform any Development obligation relating to the conduct of [\*\*] assigned to such Party under a Joint Development Plan, (a) [\*\*], and (b) if [\*\*]. If the JDC approves the engagement of such [\*\*] to perform the activities set forth in the applicable proposal, then the applicable Party may engage such [\*\*] to perform such activities, and if the JDC does not approve the engagement of such [\*\*] to perform the activities set forth in the applicable proposal, then the proposing Party may not engage such [\*\*] to perform the activities within the scope of the proposal. Any subcontract permitted under this [Section 3.9](#) (Development Subcontracts) must be consistent with the terms of this Agreement, including that the Subcontractor undertakes in writing commercially reasonable obligations of confidentiality and non-use regarding Confidential Information that are substantially the same as those undertaken by the Parties with respect to Confidential Information pursuant to [Article 10](#) (Confidentiality and Publication) hereof, and each Party will use reasonable efforts to require that the Subcontractor

undertakes in writing to assign or exclusively license back (with the right to sublicense) to such Party all intellectual property with respect to the Licensed Products developed in the course of performing any such work. Without limitation of the foregoing, during the Term, each Party will keep the other Party reasonably informed with respect to any Development activities for the Licensed Products related to [\*\*] that such Party intends to subcontract for the Profit-Share Territory. However, in respect of any and all subcontracts entered into by either Party pursuant to this [Section 3.9](#) (Development Subcontracts), subject to [Section 12.4](#) (Certain Third Party Claims Related to Licensed Products in the Profit-Share Territory) and [Section 3.4](#) (Development Costs), such Party will remain responsible for the work allocated to, and payment to, such Subcontractors to the same extent it would if it had done such work itself and compliance by its Subcontractors with the applicable provisions of this Agreement.

### **3.10 Licensed [\*\*] Product Development**

**3.10.1 Licensed [\*\*] Product Development.** Sage may[\*\*]. Within [\*\*] after the [\*\*] for the [\*\*] become available to Sage, if any, Sage will (a) notify the JSC in writing of the completion of the [\*\*] and (b) provide the [\*\*] to the JSC.

**3.10.2 [\*\*] Substitution.** At any time during the period commencing as of the Effective Date and ending upon the Substitution Termination Date, the JDC may review, discuss and determine whether to approve the substitution of the Licensed [\*\*] Product for [\*\*] (the “[\*\*] Substitution”).

**3.10.3 Effects of [\*\*] Substitution.** If the JDC determines to make the [\*\*] Substitution, then the Parties will, for a period of [\*\*] following the date of the [\*\*] Substitution, negotiate the [\*\*] with respect to replacing the Licensed [\*\*] Products for [\*\*]. If the Parties agree on such [\*\*] and enter into a new agreement or an amendment of this Agreement within such [\*\*] period (the date of such agreement, the “[\*\*] Products Substitution Date”), then:

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**3.10.4 Failure of [\*\*] Substitution or Substitution Termination Date.** In the event that (a) the JDC agrees to a [\*\*] Substitution, but the Parties are unable to agree on [\*\*] with respect to the Licensed [\*\*] Products as described in [Section 3.10.3](#) (Effects of [\*\*] Substitution) or (b) the Substitution Termination Date occurs without the Licensed [\*\*] Products Substitution Date having first occurred, then, in each case ((a) or (b)), (i) each Party’s rights and obligations under this Agreement with respect to all Licensed [\*\*] Products will terminate, and (ii) Sage will be free to Develop, Manufacture, perform Medical Affairs Activities with respect to and Commercialize, alone or with one or more Third Parties, any and all Licensed [\*\*] Products anywhere in the world without any further obligation to Biogen.

## **4.MEDICAL AFFAIRS ACTIVITIES**

**4.1 Diligence; Standards of Conduct.** Each of Biogen and Sage will use Commercially Reasonable Efforts to carry out the tasks for which it is responsible for under the applicable corresponding Joint Medical Affairs Plan in accordance with the applicable timelines set forth in such plan.

### **4.2 Joint Medical Affairs Plans.**

**4.2.1 General.** All Medical Affairs Activities to be conducted for the Licensed 217 Products and the Licensed 324 Products in the Profit-Share Territory will be conducted pursuant to separate written plans and budgets for each Product Class (each such plan, a “[\*\*] Joint Medical Affairs Plan”) that describes for each Product Class for the Profit-Share Territory: (a) the pre-launch, launch and subsequent

Medical Affairs Activities to be conducted for such Licensed Products in the Profit-Share Territory (including anticipated Phase IV Optional Studies; when applicable, investigator initiated and scientific research agreements and post-hoc analyses of pivotal studies; the publications strategy and planning and medical content creation, including internal and external education); real-world evidence strategy and data generation planning; Key Medical Expert (KME) engagement through congress, face-to-face and digital, including the development of a KME engagement plan; advisory boards based on appropriate needs assessment; building and training of medical science liaisons and the engagement of medical science liaisons with providers; external disease-state awareness activities; and the key tactics and strategies for implementing such activities, (b) the development of a Medical Information call center and standard responses to ensure consistent communication and single point of contact for product-related customer service for health care providers and triage of product complaints, (c) the respective roles and responsibilities of each Party in connection with such activities, including which Party will have day-to-day operational responsibility with respect to each such activity for the applicable Licensed Product in the Profit-Share Territory (for such activity, the “**Medical Affairs Lead Party**”), and (d) the associated budget of the FTE Costs and Out-of-Pocket Costs anticipated to be incurred in the performance of the foregoing activities (each such included budget in a Joint Medical Affairs Plan, a “**Joint Medical Affairs Budget**”) and a [\*\*], high-level budget with respect to the performance of activities under such Joint Medical Affairs Plan (each such budget, a “**Long Term Joint Medical Affairs Budget**”). Each Party will be allocated meaningful responsibility for Medical Affairs Activities under each Joint Medical Affairs Plan, consistent with a 50:50 collaboration. In the event of any inconsistency between a Joint Medical Affairs Plan and this Agreement, the terms of this Agreement will prevail. The Parties will prepare initial Joint Medical Affairs Plans (including the corresponding Joint Medical Affairs Budgets) (a) for the Licensed 217 Products, no later than [\*\*] prior to the anticipated completion date of the WATERFALL Study and (b) for the Licensed 324 Products, no later than [\*\*] prior to the anticipated completion date of the first Phase 3 Study for the first Licensed 324 Product, and (in each case (i) and (ii)) submit such initial Joint Medical Affairs Plans to the JSC to review, discuss, and determine whether to approve.

**4.2.2** *Amendments to Joint Medical Affairs Plans.* On an annual basis, (a) no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the Joint Medical Affairs Subcommittee will prepare amendments to each then-current Joint Medical Affairs Plan, including the corresponding Joint Medical Affairs Budget, for the Licensed 217 Products and the Licensed 324 Products, and submit each such amendment to the JSC to review, discuss and determine whether to approve by no later than [\*\*] of each Calendar Year and (b) no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the Joint Medical Affairs Subcommittee will prepare amendments to each then-current Long Term Joint Medical Affairs Budget corresponding to each Joint Medical Affairs Plan and submit each such amendment to the JSC to review, discuss and determine whether to approve by no later than [\*\*] of each Calendar Year. Each such amended Joint Medical Affairs Plan will specify the items described in Section 4.2.1 (General) for each Product Class for the next Calendar Year (and additional periods as reasonably determined by the Parties) and the Joint Medical Affairs Budget included therein will appropriately itemize the FTE Costs and Out-of-Pocket Costs for the activities undertaken pursuant to such Joint Medical Affairs Plan. Such updated and amended Joint Medical Affairs Plan will reflect any changes, re-prioritization or termination of Medical Affairs Activities within, or additions to, the then-current corresponding Joint Medical Affairs Plan. Once approved by the JSC, an amended annual Joint Medical Affairs Plan (including its corresponding Joint Medical Affairs Budget and Long Term Joint Medical Affairs Budget) will become effective for the applicable period on the date approved by the JSC (or such other date as the JSC will specify). Any JSC-approved amended Joint Medical Affairs Plan (including its corresponding Joint Medical Affairs Budget and Long Term Joint Medical Affairs Budget) will supersede the previous Joint Medical Affairs Plan (including its corresponding Joint Medical Affairs Budget and Long Term Joint Medical Affairs Budget) for the applicable period.

### **4.3 Operational Responsibilities for Medical Affairs Activities.**



**4.3.1.1** *Profit-Share Territory.* Unless the Parties agree in writing upon an alternate allocation of responsibility, (a) for the Profit-Share Territory, the Parties will have joint responsibility for all Medical Affairs Activities in support of the Licensed Products, with each Party serving as the Medical Affairs Lead Party as designated in the applicable Joint Medical Affairs Plan, as the same may be amended and expanded in accordance with Section 4.2.2 (Amendments to Joint Medical Affairs Plan). As part of the preparation of the initial Joint Medical Affairs Plans and any amendments thereto as described in Section 4.2 (Joint Medical Affairs Plans), the Joint Medical Affairs Subcommittee will identify any changes to the Major Medical Affairs Activities in such Joint Medical Affairs Plan and assign a Medical Affairs Lead Party that will be responsible for each Major Medical Affairs Activity. In the event that a Medical Affairs Lead Party is unable to perform any of its material responsibilities in accordance with the applicable Joint Medical Affairs Plan (including the applicable timeline set forth therein for the performance of such activities) and fails to cure any such non-performance within [\*\*] after receipt of written notice from the non-Medical Affairs Lead Party regarding such non-performance, then the other Party will have the right to become the Medical Affairs Lead Party with respect to the non-performed activities for purposes of this Agreement, and any FTE Costs and Out-of-Pocket Costs that such other Party incurs in connection with its performance of such activities (or the assumption thereof) will be included as Joint Medical Affairs Costs. The Parties will resolve any dispute regarding whether any such responsibility that a Medical Affairs Lead Party is does not perform is “material”, as described in the foregoing sentence, in accordance with Section 15.3.5 (Expert Arbitration).

**4.3.1.2** *Biogen Territory.* For the Biogen Territory, Biogen will have sole control over and decision-making authority with respect to the performance of Medical Affairs Activities in support of the Licensed Products.

#### **4.4** Medical Affairs Costs.

**4.4.1** *Profit-Share Territory.* Subject to Section 9.4 (Sage Opt-Out), Sage will be responsible for fifty percent (50%) and Biogen will be responsible for fifty percent (50%) of all Joint Medical Affairs Costs in support of the Licensed Products for the Profit-Share Territory. The Parties will reconcile such Joint Medical Affairs Costs they have incurred to reflect the foregoing applicable allocation of Joint Medical Affairs Costs according to the procedures in Section 9.3.1 (Reconciliation/Reimbursement Prior to First Commercial Sale) or Section 9.3.3 (Profit Sharing Commercialization), as applicable.

**4.4.2** *Biogen Territory.* Biogen will be responsible for one hundred percent (100%) of all costs and expenses incurred by or on behalf of Biogen for Medical Affairs Activities in support of the Licensed Products solely for the Biogen Territory.

**4.5** Medical Affairs Reports. For Medical Affairs Activities conducted for the Profit-Share Territory, each Party will provide to the JSC, (a) within [\*\*] after the same becoming available, any material information and data arising from the Medical Affairs Activities with respect to the Licensed Products for the Profit-Share Territory by such Party, and (b) at least [\*\*] in advance of each regularly scheduled meeting of the Joint Medical Affairs Subcommittee, all other relevant information and data arising from Medical Affairs Activities for the Licensed Products for the Profit-Share Territory conducted by or on behalf of such Party since the last such meeting to the extent not previously disclosed in connection with day-to-day interactions between the Parties. In addition, at the first JSC meeting in the following Calendar Year, each Party will provide an annual review for the Calendar Year-ended of results versus goals of Medical Affairs Activities for the Licensed Products for the Profit-Share Territory (as such goals are set forth in the corresponding Joint Medical Affairs Plans). Biogen will provide (i) to the JSC [\*\*], and (ii) [\*\*].

## 5.COMMERCIALIZATION

### 5.1 Diligence; Standards of Conduct.

**5.1.1** *Profit-Share Territory.* Each of Sage and Biogen will use Commercially Reasonable Efforts to (a) Commercialize the Licensed 217 Products and the Licensed 324 Products in the Profit-Share Territory after Regulatory Approval and, if applicable, Pricing and Reimbursement Approval therefor has been obtained and (b) [\*\*].

**5.1.2** *Biogen Territory.* Biogen will use Commercially Reasonable Efforts to (a) obtain Pricing and Reimbursement Approval for a Licensed Product, where applicable, in each of the Major European Countries in which Regulatory Approval therefor has been obtained, and (b) following receipt of Pricing and Reimbursement Approval for a Licensed Product in any such Major European Country, where applicable, Commercialize such Licensed Product in each such country.

### 5.2 Joint Commercialization Plans.

#### 5.2.1 *General.*

**5.2.1.1** As further described in this Section 5.2 (Joint Commercialization Plans), the tactics and strategy for the Commercialization of the Licensed 217 Products and the Licensed 324 Products for the Profit-Share Territory will be set forth in and conducted pursuant to a commercialization plan and budget for each Product Class (each such plan, a “**Joint Commercialization Plan**”) that describes for each Product Class in the Profit-Share Territory: (a) the pre-launch, launch and subsequent Commercialization activities of the applicable Licensed Products in the Profit-Share Territory, including the field force size, structure, allocation and deployment; patient support size and structure; product positioning; market access plans; anticipated activities relating to messaging, branding, Pricing Matters, advertising, planning, marketing, and training; managed care contracting and account management and the plan for negotiation of managed care arrangements; Distribution Matters; CMC Activities and the quantities of Licensed Product to be supplied to the Parties for the Profit-Share Territory and the estimated delivery date for such Licensed Product, which quantities will be consistent with the forecast provided by the applicable Party in accordance with a forecasting schedule to be agreed by the Parties in an applicable Supply Agreement; and the key tactics and strategies for implementing the foregoing activities; (b) subject to Section 5.4 (Operational Responsibilities for Commercialization), the respective roles and responsibilities of each Party in connection with the performance of such activities, including which Party will have day-to-day operational responsibility with respect to such activities for the applicable Licensed Product in the Profit-Share Territory (for such activity, the “**Commercialization Lead Party**”); and (c) the associated budget of the FTE Costs and Out-of-Pocket Costs anticipated to be incurred in the performance of the foregoing activities (each such included budget, a “**Joint Commercialization Budget**”) and [\*\*], high-level budget with respect to the performance of activities under such Joint Commercialization Plan (each such budget, a “**Long Term Joint Commercialization Budget**”). In the event of any inconsistency between a Joint Commercialization Plan and this Agreement, the terms of this Agreement will prevail.

**5.2.1.2** (a) No later than [\*\*] following the Effective Date for the Licensed 217 Products and (b) no later than [\*\*] following Initiation of the [\*\*] for the first Licensed 324 Product, in each case, in the Profit-Share Territory, the JCC will prepare the applicable initial Joint Commercialization Plan therefor (including the corresponding initial Joint Commercialization

Budget and Long Term Joint Commercialization Budget) and submit such initial Joint Commercialization Plan(s) to the JSC to review, discuss and determine whether to approve.

**5.2.2** *Amendments to Joint Commercialization Plans.* On an annual basis, (a) no later than [\*\*] of each Calendar, or more often as the Parties deem appropriate, the JCC will prepare amendments to each then-current Joint Commercialization Plan, including the corresponding Joint Commercialization Budget, for the Licensed 217 Products and the Licensed 324 Products, and submit each such amendment to the JSC to review, discuss and determine whether to approve by no later [\*\*] of each Calendar Year and (b) no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the JCC will prepare amendments to each then-current Long Term Joint Commercialization Budget corresponding to each Joint Commercialization Plan and submit each such amendment to the JSC to review, discuss and determine whether to approve by no later than [\*\*] of each Calendar Year. Each such amended Joint Commercialization Plan will specify the items described in Section 5.2.1.1 (General) for each Product Class for the next Calendar Year (and additional periods as reasonably determined by the Parties) and the Joint Commercialization Budget included therein will appropriately itemize FTE Costs and Out-of-Pocket Costs for the activities undertaken pursuant to such Joint Commercialization Plan. Once approved by the JSC, an amended annual Joint Commercialization Plan (including its corresponding Joint Commercialization Budget and Long Term Joint Commercialization Budget) will become effective for the applicable period on the date approved by the JSC (or such other date as the JSC will specify). Any JSC-approved amended Joint Commercialization Plan (including its corresponding Joint Commercialization Budget and Long Term Joint Commercialization Budget) will supersede the previous Joint Commercialization Plan (including its corresponding Joint Commercialization Budget and Long Term Joint Commercialization Budget) for the applicable period.

**5.3** **Commercialization Principles.** With respect to Commercialization activities for Licensed Products for the Profit-Share Territory, the Parties hereby acknowledge and agree that: (a) each Party will be allocated meaningful responsibility for Commercialization activities under each Joint Commercialization Plan, consistent with a 50:50 collaboration and Sage's intent to build experience and expertise with respect to Commercialization activities, (b) [\*\*], and (c) [\*\*]. The Parties will perform all Commercialization activities under any Joint Commercialization Plan consistent with and in furtherance of the principles set forth in this Section 5.3 (Commercialization Principles).

#### **5.4** **Operational Responsibilities for Commercialization.**

**5.4.1** *Profit-Share Territory.* Unless the Parties agree in writing upon an alternate allocation of responsibility, for the Profit-Share Territory: (a) Sage will be the Commercialization Lead Party in the Profit-Share Territory with respect to Distribution Matters for the Licensed 324 Product and Biogen will be the Commercialization Lead Party in the Profit-Share Territory with respect to Distribution Matters for the Licensed 217 Product, (b) the JMC, in consultation with the Finance Working Group, will determine the allocation of responsibility with respect to [\*\*] for any Licensed Product in the Profit-Share Territory, and (c) the Parties will have joint responsibility for Commercializing the Licensed Products after Regulatory Approval therefor has been obtained, with each Party serving as the Commercialization Lead Party as designated in the applicable Joint Commercialization Plan, as the same may be amended and expanded in accordance with Section 5.2.2 (Amendments to Joint Commercialization Plans). As part of the preparation of the initial Joint Commercialization Plans and any amendments thereto as described in Section 5.2 (Joint Commercialization Plans), the JCC will identify any changes to the Major Commercialization Activities in such Joint Commercialization Plan and assign a Commercialization Lead Party that will be responsible for such Major Commercialization Activity. In the event that a Commercialization Lead Party is unable to perform any of its material responsibilities in accordance with the applicable Joint Commercialization Plan (including the applicable timeline set forth therein for the performance of such activities) and fails to cure any such non-performance within [\*\*] after receipt of

written notice from the non-Commercialization Lead Party regarding such non-performance, then the other Party will have the right to become the Commercialization Lead Party with respect to the non-performed activities for purposes of this Agreement, and any FTE Costs and Out-of-Pocket Costs that such other Party incurs in connection with its performance of such activities (or the assumption thereof) will be included as Joint Commercialization Costs. The Parties will resolve any dispute regarding whether any such responsibility that a Commercialization Lead Party does not perform is “material”, as described in the foregoing sentence, in accordance with Section 15.3.5 (Expert Arbitration).

**5.4.2** *Biogen Territory.* For the Biogen Territory, Biogen will have sole control over and decision-making authority with respect to all Commercialization activities for the Licensed Products.

## **5.5 Commercialization Costs.**

**5.5.1** *Profit-Share Territory.* Subject to Section 9.4 (Sage Opt-Out), Sage will be responsible for fifty percent (50%) and Biogen will be responsible for fifty percent (50%) of all Joint Commercialization Costs. The Parties will reconcile such Joint Commercialization Costs they have incurred to reflect the foregoing applicable allocation of Joint Commercialization Costs according to the procedures in Section 9.3.1 (Reconciliation/Reimbursement Prior to First Commercial Sale) or Section 9.3.3 (Profit Sharing Following First Commercial Sale), as applicable.

**5.5.2** *Biogen Territory.* Biogen will be responsible for one hundred percent (100%) of all costs and expenses incurred by or on behalf of Biogen for the Commercialization of the Licensed Products solely for the Biogen Territory.

**5.6** **Commercialization Reports.** For Commercialization activities conducted for the Profit-Share Territory, each Party will provide (a) within [\*\*] of the same becoming available, any material information and data arising from the Commercialization activities for the Licensed Products in the Profit-Share Territory by such Party, and (b) at least [\*\*] in advance of each regularly scheduled meeting of the Joint Commercialization Committee, all other relevant information and data arising from Commercialization activities for the Licensed Products for the Profit-Share Territory conducted by or on behalf of such Party since the last such meeting to the extent not previously disclosed in connection with day-to-day interactions between the Parties. In addition, at the first JCC meeting in the following Calendar Year, each Party will provide an annual review for the Calendar Year-ended of results versus goals of Commercialization activities for the Licensed Products for the Profit-Share Territory (as such goals are set forth in the corresponding Joint Commercialization Plans) and Biogen will provide (i) to the JCC [\*\*], except with respect to [\*\*], which will be discussed as forth in Section [\*\*], and (ii) [\*\*].

## **5.7 Pricing Matters; Distribution.**

**5.7.1** *Pricing Matters.*

**5.7.1.1** In conjunction with [\*\*]. The Parties agree that [\*\*].

**5.7.2** Biogen will have sole control and decision-making authority with respect to Pricing Matters for Licensed Products in the Biogen Territory; [\*\*].

**5.7.3** *Distribution in the Profit-Share Territory.* Subject to this Section 5.7.3 (Distribution in the Profit-Share Territory), with respect to Distribution Matters in the Profit-Share Territory, Biogen will be the Commercialization Lead Party for the Licensed 217 Products and Sage will be the Commercialization Lead Party for the Licensed 324 Products, and in each case, the applicable Commercialization Lead Party will be responsible for such Distribution Matters for the applicable Licensed Products, including (a) [\*\*],

(b) [\*\*], and (c) [\*\*] (as may be amended in accordance with this Agreement, the “**Distribution Plan**”), the other aspects of the applicable Joint Commercialization Plan and the decisions made by the JSC with respect to Pricing Matters. No later than (i) [\*\*] following the Effective Date for the Licensed 217 Products and (b) [\*\*] following Initiation of the first [\*\*] for the first Licensed 324 Product, the JCC will prepare the applicable initial Distribution Plan(s) therefor and submit such initial Distribution Plan(s) to the JSC to review, discuss and determine whether to approve. Each Party will be solely responsible for [\*\*] percent ([\*\*]%) of all costs and expenses (including Distribution Costs) incurred in connection with building and making operational any systems and infrastructure required to perform its responsibilities under the Distribution Plan, including [\*\*]. To the extent consistent with the Distribution Plan and the applicable Joint Commercialization Plan, any Distribution Costs incurred after the applicable Party has built and made operational such systems and infrastructure will be included as Joint Commercialization Costs. Each Party will provide reasonable assistance to the other Party in connection with such other Party’s performance of activities in accordance with the Distribution Plan. In the event that a Commercialization Lead Party is unable to perform any of its material responsibilities in accordance with the Distribution Plan (including the applicable timeline set forth therein for the performance of such activities) and fails to cure any such deficiency within [\*\*] after receipt of written notice from the non-Commercialization Lead Party regarding such deficiency, then the other Party will have the right to become the Commercialization Lead Party with respect to the affected responsibilities for purposes of this Agreement, and any FTE Costs and Out-of-Pocket Costs that such other Party incurs in connection with its performance of such responsibilities (or the assumption thereof) will be included as Joint Commercialization Costs. The Parties will resolve any dispute regarding whether any such responsibility that a Commercialization Lead Party does not perform is “material”, as described in the foregoing sentence, in accordance with Section 15.3.5 (Expert Arbitration).

**5.8 Uniform Training.** For training purposes, the Parties will treat the Sage and Biogen field-based representatives, including field-facing medical personnel, medical science liaisons, medical value liaisons, medical directors and patient support personnel, in each case, in the Profit-Share Territory as a combined field force within the applicable function and will cooperate to provide the foregoing Sage and Biogen personnel in the Profit-Share Territory with the same training, support, and assistance.

**5.9 Detail Costs; Authority over Sales Forces.** Each Party may include the applicable Detail Costs determined using the rate as agreed by the JSC as Joint Commercialization Costs in accordance with this Agreement, but otherwise each Party will be responsible for all costs and expenses incurred in connection with its respective Sales Representatives performing Details in the Profit-Share Territory, including salaries, incentive compensation, travel expenses and other expenses, providing benefits, deducting federal, state and local payroll taxes, Federal Insurance Contribution Act taxes, unemployment insurance taxes, and any similar taxes and paying workers’ compensation premiums, unemployment insurance contributions and any other payments required by applicable Law to be made on behalf of employees. Nothing in this Agreement will be construed to conclude that any of Biogen’s Sales Representatives or any other agents or employees of Biogen in the Profit-Share Territory are agents or employees of Sage or subject to Sage’s direction and control. Biogen will have sole authority over the terms and conditions of employment of Biogen’s Sales Representatives in the Profit-Share Territory, including their selection, management, compensation (including incentive plans) and discharge. Nothing in this Agreement will be construed to conclude that any of Sage’s Sales Representatives or any other agents or employees of Sage in the Profit-Share Territory are agents or employees of Biogen or subject to Biogen’s direction and control. Sage will have sole authority over the terms and conditions of employment of Sage’s Sales Representatives in the Profit-Share Territory, including their selection, management compensation (including incentive plans) and discharge.

**5.10 Joint Commercialization Costs Allocation.** Subject to this Section 5.10 (Joint Commercialization Costs Allocation) and to the extent consistent with the applicable Joint Commercialization Budget, Sage may use certain Commercialization resources (“Shared Resources”) that

are engaged both in the performance of activities under a Joint Commercialization Plan and in the performance of similar Commercialization activities for the benefit of [\*\*]. Subject to this Section 5.10 (Joint Commercialization Costs Allocation) and to the extent consistent with the applicable Joint Commercialization Budget, Biogen may use Shared Resources that are engaged both in the performance of activities under a Joint Commercialization Plan and in the performance of similar Commercialization activities for the benefit of [\*\*]. Prior to engaging any such Shared Resources with respect to [\*\*]. For each Shared Resource that also engages in Commercialization activities for [\*\*] during the relevant Calendar Quarter, the cost of such Shared Resource (for purposes of calculating Joint Commercialization Costs) will be [\*\*]. For the purposes of calculating the FTE Costs of each Party's Shared Resource performing Commercialization activities in the Profit-Share Territory under the applicable Joint Commercialization Plan, the FTEs of any contractor sales force will be reported in the same FTE category as any employee sales force and the FTE Rate for such contractor sales force FTEs will be calculated in accordance with Section 1.1.101 (FTE Costs). Notwithstanding any provision to the contrary in this Agreement, neither Party may share Commercialization resources between [\*\*] and [\*\*] in a manner that would result [\*\*].

## **5.11 Advertising and Promotional Materials in Profit-Share Territory.**

**5.11.1** *Branding.* From time to time during the Term, the Parties will jointly develop via the JCC (and thereafter modify and update) and submit to the JSC to review, discuss and determine whether to approve a branding strategy (including positioning, messages, timing, logo, colors, and other visual branding elements) for each Product Class in the Profit-Share Territory (a "**Branding Strategy**"). The JCC will allocate between the Parties responsibility for preparing the initial draft of the various sections of the Branding Strategy for each Product Class.

**5.11.2** *Promotional Materials.* The Parties will have joint responsibility for the creation, preparation, production, reproduction, review (medical, legal and regulatory) of, in compliance with the Promotional Materials Rules approved by the JSC the Promotional Materials relating to each Licensed Product in the Profit-Share Territory. The Party that [\*\*] will be responsible for filing the applicable Promotional Materials Rules with the FDA. All such Promotional Materials will be compliant with applicable Law and consistent with the applicable Joint Commercialization Plan for such Licensed Product and will be reviewed in accordance with the Promotional Materials Rules. The Parties will own jointly all rights, title and interests in and to any and all Promotional Materials for any Licensed Product for use in the Profit-Share Territory. Sage and Biogen will each: (a) require that its Sales Representatives do not make any representation, statement, warranty or guaranty with respect to a Licensed Product that is not consistent with the applicable product labeling for such Licensed Product, including approved limited warranty and disclaimers approved by each Party, if any, (b) require that its Sales Representatives do not make any statements, claims or undertakings to any person with whom they discuss or promote Licensed Products that are not consistent with, nor provide or use any labeling, literature or other materials other than those Promotional Materials provided by the Parties, and (c) if, at any time, either Party no longer approves of the use of specified Promotional Materials in the Profit-Share Territory, take appropriate action to remove the Promotional Materials from use and destroy such Promotional Materials or otherwise modify such Promotional Materials for an approved use. Neither Party will have the obligation to use any Promotional Material for any Licensed Product that such Party has not approved. Each Party will be responsible for its respective use of such Promotional Materials, and neither Party may use Promotional Materials that have not been approved by the JSC.

**5.11.3** *Licensed Product Packaging.* The applicable Regulatory Lead Party will develop and submit to the JSC to review, discuss and determine whether to approve the packaging and labeling for each Licensed Product in the Profit-Share Territory, which in all cases will be consistent with the applicable Profit-Share Regulatory Strategy and in compliance with applicable Law.

**5.11.4.1** *Profit-Share Territory.* The Parties will jointly develop via the JCC (and thereafter modify and update) and submit to the JSC to review, discuss and determine whether to approve a strategy to govern the registration, maintenance, enforcement and defense of LP U.S. Trademarks (the “**LP U.S. TM Strategy**”). The Parties will select (through the JCC) the Trademarks for use with each Licensed Product for the Profit-Share Territory in accordance with the applicable Branding Strategy and the LP U.S. TM Strategy, including which Party will own each such Trademark, and the JCC will submit all such Trademarks to the JSC to review, discuss and determine whether to approve. Neither Party will, directly or indirectly: (a) use in its respective businesses, any Trademark that is confusingly similar to, misleading or deceptive with respect to or that dilutes any LP U.S. Trademark in the Profit-Share Territory; or (b) do any act that endangers, destroys or similarly affects the value of the goodwill pertaining to the LP U.S. Trademarks in the Profit-Share Territory. Each Party agrees that it and its Affiliates and Sublicensees will (i) require that all Licensed Products that are sold bearing any LP U.S. Trademark are of a high quality consistent with industry standards for global pharmaceutical and biologic therapeutic products; (ii) not use such LP U.S. Trademarks in a way that might materially prejudice their distinctiveness or validity or the goodwill therein and includes the trademark registration symbol ® or ™ as appropriate; and (iii) not use any trademarks or trade names so resembling any of the LP U.S. Trademarks as to be likely to cause confusion or deception.

**5.11.4.2** *Biogen Territory.* Biogen will have sole control over and decision-making authority with respect to the selection of the product name and Trademarks for use with all Licensed Products in the Biogen Territory. Biogen may elect to use any LP U.S. Trademark as the Trademark for the corresponding Licensed Product in the Biogen Territory, and if Sage is the owner of such LP U.S. Trademark, then Sage will and hereby does grant Biogen the exclusive right and license to use such LP U.S. Trademark in connection with the Commercialization of the applicable Licensed Product in the Biogen Territory. Biogen will register and maintain the LP U.S. Trademark in the Biogen Territory that it determines reasonably necessary in Sage’s name, at Biogen’s cost and expense.

**5.12** **Coordination of Operational Activities.** The Parties recognize that each Party may benefit from discussing and sharing information and strategies with respect to Medical Affairs Activities for the Licensed Products between the Profit-Share Territory and the Biogen Territory. Accordingly, the Parties may discuss and share such information and strategies (a) through the Joint Medical Affairs Subcommittee, JCC or JSC, as applicable, with respect to the Profit-Share Territory and (b) through the appropriate Medical Affairs Activities or Commercialization activities representatives of each Party, with respect to the Biogen Territory, in each case ((a) and (b)) to the extent that the Parties agree that such coordination is appropriate (but in any event, no Committee will have any decision-making authority with respect to any Commercialization or Medical Affairs Activities for the Licensed Products in the Biogen Territory).

**5.13** **Territorial Restrictions.**

**5.13.1** *Cross-Territorial Restrictions.*

**5.13.1.1** Biogen hereby covenants and agrees that, insofar as permitted by applicable Law, it will not, and will require its Affiliates and Sublicensees not to, knowingly promote, market, distribute, import, sell or have sold any Licensed 217 Product, including via internet or mail order, into countries in the Existing Partner Territory or from the Biogen Territory into the Profit-Share Territory. As to such countries in the Existing Partner Territory, Biogen will

not, and will require its Affiliates and Sublicensees not to: (a) establish or maintain any branch, warehouse or distribution facility for any Licensed 217 Product in such countries, (b) engage in any advertising or promotional activities relating to any Licensed 217 Product that are directed primarily to customers or other purchasers or users of such Licensed 217 Product located in such countries, (c) solicit orders from any prospective purchaser located in such countries, (d) conduct any Distribution Matters with respect to Licensed 217 Products in such countries or (e) sell or distribute any Licensed 217 Product to any Person in the Biogen Territory who it knows intends to sell such Licensed 217 Product in such countries. If Biogen receives any order from a prospective purchaser located in a country in the Existing Partner Territory, insofar as permitted by applicable Law, Biogen will immediately refer that order to Sage, and Biogen will not accept any such orders. Biogen will not deliver or tender (or cause to be delivered or tendered) any Licensed 217 Product into a country in the Existing Partner Territory.

**5.13.1.2** Sage hereby covenants and agrees that, insofar as permitted by applicable Law, it will not, and will require that its Affiliates and Sublicensees do not, either directly or indirectly, knowingly promote, market, distribute, import, sell or have sold any Licensed Product, including via internet or mail order, into countries in the Biogen Territory. As to such countries in the Biogen Territory, Sage will not, and will require that its Affiliates and Sublicensees do not: (a) establish or maintain any branch, warehouse or distribution facility for any Licensed Product in such countries, except as permitted for the purposes of Section 8.1.2.1(a) (License Grants to Sage) or Section 8.1.2.1(b) (License Grants to Sage), (b) engage in any advertising or promotional activities relating to any Licensed Product that are directed primarily to customers or other purchasers or users of such Licensed Product located in such countries, (c) solicit orders from any prospective purchaser located in such countries, (d) conduct any Distribution Matters with respect to Licensed Products in such countries or (e) sell or distribute any Licensed Product to any Person outside the Biogen Territory who it knows intends to sell such Licensed Product in such countries. If Sage receives any order from a prospective purchaser located in a country in the Biogen Territory, insofar as permitted by applicable Law, Sage will immediately refer that order to Biogen, and Sage will not accept any such orders. Sage will not deliver or tender (or cause to be delivered or tendered) any Licensed Product into a country in the Biogen Territory.

**5.13.2** *Profit-Share Territory Restrictions.* Within the Profit-Share Territory, the Party that is not the Commercialization Lead Party with respect to Distribution Matters for a Licensed Product hereby covenants and agrees that, insofar as permitted by applicable Law, it will not, and will require that its Affiliates and Sublicensees do not, either directly or indirectly, knowingly undertake any activities relating to recalls, returns or other similar matters with respect to any such Licensed Product. If the Party that is not the Commercialization Lead Party with respect to Distribution Matters for a Licensed Product within the Profit-Share Territory receives any order from a prospective purchaser in the Profit-Share Territory for such Licensed Product, then such Party will immediately refer that order to the Commercialization Lead Party, and such Party will not accept any such orders. If Sage receives any order for a Licensed 217 Product in the Profit-Share Territory, then it will refer such order to Biogen, and if a Licensed 217 Product sold in the Profit-Share Territory is returned to Sage, then Sage will promptly ship such Licensed 217 Product to a facility designated by Biogen. If Biogen receives any order for a Licensed 324 Product in the Profit-Share Territory, then it will refer such order to Sage, and if a Licensed 324 Product sold in the Profit-Share Territory is returned to Biogen, then Biogen will promptly ship such Licensed 324 Product to a facility designated by Sage.

**5.14** **Commercialization Subcontracts.** Subject to this Section 5.14 (Commercialization Subcontracts), each Party may perform any of its Commercialization obligations under this Agreement with respect to any Licensed Product in the Territory through one or more Subcontractors, and each Party will [\*\*]. Each Party may [\*\*]. Prior to engaging any Subcontractor that is not a [\*\*] to perform any



Commercialization obligations assigned to such Party under a Joint Commercialization Plan, (a) [\*\*], and (b) [\*\*], then:

(i) if the proposed Subcontractor is a [\*\*], such Party will first submit such proposal to the JCC to review and determine whether to approve the engagement of such [\*\*] to perform the activities set forth in the applicable proposal. If the JCC approves the engagement of such [\*\*] to perform the activities set forth in the applicable proposal, then the applicable Party may engage such contract sales organization to perform such activities, and if the JCC does not approve the engagement of such [\*\*] to perform the activities set forth in the applicable proposal, then the proposing Party may not engage such [\*\*] to perform the activities within the scope of the proposal; and

(ii) if the proposed Subcontractor is not [\*\*], then the Party proposing such engagement will have the right to proceed with entering into such subcontract without submitting such engagement to the JCC for review and approval [\*\*].

Any subcontract permitted under this Section 5.14 (Commercialization Subcontracts) must be consistent with the terms of this Agreement, including that the Subcontractor undertakes in writing commercially reasonable obligations of confidentiality and non-use regarding Confidential Information that are substantially the same as those undertaken by the Parties with respect to Confidential Information pursuant to Article 10 (Confidentiality and Publication) hereof, and each Party will use reasonable efforts to require that the Subcontractor undertakes in writing to assign or exclusively license back (with the right to sublicense) to such Party all intellectual property with respect to the Licensed Products developed in the course of performing any such work. Without limitation of the foregoing, during the Term, each Party will, within a reasonable time thereafter, notify the other Party with respect to any Commercialization activities for the Licensed Products that such Party has subcontracted to any [\*\*] for the Profit-Share Territory. However, in respect of any and all subcontracts entered into by either Party pursuant to this Section 5.14 (Commercialization Subcontracts), subject to Section 12.4 (Certain Third Party Claims Related to Licensed Products in the Profit-Share Territory) and Section 5.5 (Commercialization Costs), such Party will remain responsible for the work allocated to, and payment to, such Subcontractors to the same extent it would if it had done such work itself and compliance by its Subcontractors with the applicable provisions of this Agreement.

## 6. REGULATORY

**6.1 Regulatory Lead Responsibilities.** The JSC will discuss and determine whether to approve the regulatory strategy for the Licensed Products in the Profit-Share Territory (the “**Profit-Share Regulatory Strategy**”). The Regulatory Lead Party as determined by Section 6.1.1 (Regulatory Lead Responsibilities) or Section 6.1.2 (Regulatory Lead Responsibilities) or as otherwise designated by the JSC (the “**Regulatory Lead Party**”) will have [\*\*].

**6.1.1** (a) [\*\*] will be the Regulatory Lead Party for the [\*\*] in the Profit-Share Territory from the Effective Date and until [\*\*] and (b) after [\*\*] will become the Regulatory Lead Party for the [\*\*] in the Profit-Share Territory, in each case ((a) and (b)), subject to the Profit-Share Regulatory Strategy and the input and joint participation of the other Party as set forth in Sections 6.3 (Biogen Territory), 6.4 (Communications with Regulatory Authorities), 6.5 (Regulatory Meetings), 6.6 (Submissions), 6.8 (Right of Reference) and 6.9 (Recalls, Market Withdrawals or Corrective Actions). (i) [\*\*] will be the Regulatory Lead Party for the [\*\*] in the Profit-Share Territory from the Effective Date and until [\*\*] and (ii) after [\*\*] will become the Regulatory Lead Party for the [\*\*] in the Profit-Share Territory, in each case, subject to the Profit-Share Regulatory Strategy and the input and joint participation of the other Party as set forth in Section 6.4 (Communications with Regulatory Authorities), Section 6.5 (Regulatory Meetings), 6.6

(Submissions), 6.8 (Right of Reference) and 6.9 (Recalls, Market Withdrawals or Corrective Actions). Biogen will be the Regulatory Lead Party for any [\*\*] with respect to the Licensed Products for the Profit-Share Territory, subject to the Profit-Share Regulatory Strategy and the input and joint participation of Sage as set forth in Section 6.4 (Communications with Regulatory Authorities), Section 6.5 (Regulatory Meetings), Section 6.6 (Submissions), Section 6.8 (Right of Reference) and Section 6.9 (Recalls, Market Withdrawals or Corrective Actions).

**6.1.2** Subject to applicable Laws, the Regulatory Lead Party designated under this Section 6.1 (Regulatory Lead Responsibilities) will own, or be assigned as set forth in Section 6.2 (Assignment), all INDs, NDAs, Regulatory Approvals and other Regulatory Materials for the applicable Licensed Products in the Profit-Share Territory, *provided* that, subject to Section 3.3.1.1 (Profit-Share Territory), in all cases [\*\*] will own any [\*\*] for the purposes of [\*\*] that may be available. Subject to applicable Laws, Biogen will own all INDs, NDAs, Regulatory Approvals and other Regulatory Materials for the applicable Licensed Products in the Biogen Territory.

**6.2** **Assignment.** Upon [\*\*] will promptly [\*\*], (a) the transfer and assignment to [\*\*] all of [\*\*] and (b) [\*\*] the transfer and assignment under clause (a) [\*\*] such transfer and assignment. Upon [\*\*] will promptly [\*\*], the transfer and assignment to [\*\*] all of [\*\*], and (ii) within [\*\*] to transfer and assignment under clause (i) [\*\*] will, in each case ((a) and (b)), [\*\*] with respect to the applicable transfer and assignment described in this Section 6.2 (Assignment).

**6.3** **Biogen Territory.** Subject to Section 6.4 (Communications with Regulatory Authorities), Section 6.5 (Regulatory Meetings), Section 6.6 (Submissions), 6.8 (Right of Reference) and 6.9 (Recalls, Market Withdrawals or Corrective Actions), Biogen will have sole control and decision-making authority over all regulatory matters, including filing all Regulatory Materials, with respect to the Licensed Products in the Biogen Territory. Biogen will own, and may file in its name or the name of its designee, all Regulatory Materials with respect to the Licensed Products throughout the Biogen Territory. Starting on the Effective Date, Sage will [\*\*] begin and [\*\*] complete no later than [\*\*] after the Effective Date, the assignment and transfer to Biogen of all Regulatory Materials related to any Licensed 217 Product or any Licensed 324 Product solely for the Biogen Territory, in each case, that are not necessary for Sage's performance of the Ongoing 217 Studies or the KINETIC Study. Sage will provide reasonable and ongoing updates to Biogen regarding Sage's process with respect to such transfer and assignment. Starting from the Effective Date and until [\*\*] becomes the Regulatory Lead Party with respect to the Licensed 217 Products or Licensed 324 Products, as applicable, [\*\*] will provide [\*\*] with access to all Regulatory Materials relating to the Ongoing 217 Studies or the KINETIC Study, in each case, as may be required for [\*\*] to conduct regulatory matters with respect to Licensed Products in the [\*\*] Territory.

**6.4** **Communications with Regulatory Authorities.** Each Regulatory Lead Party will provide to the other Party for review and discussion a copy of each Material Communication with any Regulatory Authorities with respect to any Licensed Product for which such Party is the Regulatory Lead Party. [\*\*] such Material Communication [\*\*] such Material Communication [\*\*] such Material Communication. With respect to any Material Communication with the FDA or the EMA or a Regulatory Authority in [\*\*] related to a Licensed Product, the Regulatory Lead Party will allow the other Party [\*\*]. Any Material Communication to a Regulatory Authority with respect to any Licensed Product in the Profit-Share Territory must be consistent with the Profit-Share Regulatory Strategy for such Licensed Product approved by the JSC.

**6.5** **Regulatory Meetings.** Each Regulatory Lead Party will provide notice to the other Party within [\*\*] after becoming aware of all meetings with the FDA [\*\*], related to a Licensed Product for which it is the Regulatory Lead Party, or with as much advance notice as practicable under the circumstances. The Regulatory Lead Party will, to the extent reasonably practicable, permit the other Party

to have, at such other Party's expense, [\*\*] of such other Party attend, solely as non-participating observers, any such meetings with such Regulatory Authorities that are substantive; *provided, however*, that (a) if required by such Regulatory Authority, attendance by the other Party will be permitted; (b) attendance by the representatives of the other Party may not prevent participation of the reasonably necessary representatives of the Regulatory Lead Party due to restrictions imposed by such Regulatory Authority on the number of attendees at such meeting; and (c) the Regulatory Lead Party will not be obligated to change the schedule of such meeting in order to accommodate the schedule of such other Party's representatives.

**6.6 Submissions.** The Regulatory Lead Party will provide the other Party with a copy of all substantive Regulatory Materials for any Licensed Product proposed to be submitted to the FDA [\*\*] for such other Party's review and comment sufficiently in advance of such Regulatory Lead Party's filing or submission thereof, and such Regulatory Lead Party will [\*\*] all comments timely provided by such other Party in connection therewith. Regulatory Materials with respect to any Licensed Product in the Profit-Share Territory must be consistent with the Profit-Share Regulatory Strategy for such Licensed Product approved by the JSC. Each Regulatory Lead Party will also provide the other Party, through the JSC, with written notice of each of the following events with regard to each Licensed Product for which it is the Regulatory Lead Party (a) within a reasonable period of time following the occurrence thereof (and in any event reasonably in advance of any public disclosure thereof), to the extent notice was not previously provided: (i) [\*\*]; and (ii) [\*\*]; and (b) on a [\*\*] basis at regularly scheduled meetings of the JSC or on such other frequency as is determined by the JSC, (i) [\*\*] and (ii) [\*\*].

**6.7 Costs of Regulatory Affairs.** The Parties will share as Joint Development Costs the FTE Costs and Out-of-Pocket Costs incurred in the performance of regulatory activities for Licensed Products in the Profit-Share Territory to the extent in accordance with the applicable Joint Development Budget. Biogen will be solely responsible for all costs and expenses incurred in connection with the performance of regulatory activities solely related to applying for and maintaining Regulatory Approval for the Licensed Products in the Biogen Territory.

**6.8 Right of Reference.** Each Party hereby grants to the other Party, and at the request of the other Party will grant to the other Party's Affiliates, licensees and Sublicensees (to the extent engaged in accordance with this Agreement), a "Right of Reference," as that term is defined in 21 C.F.R. § 314.3(b) (or any successor rule or analogous Law recognized outside of the United States), to, and a right to copy, access, and otherwise use, all information and data (including all CMC information) as well as data made, collected, or otherwise generated in the conduct of any Clinical Studies, or early access/named patient programs for the Licensed Products included in or used in support of any Regulatory Materials or drug master file Controlled by such Party or its Affiliates, licensees or Sublicensees that relates to any Licensed Product, (a) [\*\*] or (b) as otherwise agreed by the JSC. Each Party will take such actions as may be reasonably requested by the other Party to give effect to the intent of this Section 6.8 (Right of Reference) and to give the other Party the benefit of the granting Party's Regulatory Materials in the other Party's territory as provided in the preceding sentence. Such actions may include (i) [\*\*], or (ii) providing the other Party with [\*\*].

**6.9 Recalls, Market Withdrawals or Corrective Actions.** In the event that any Regulatory Authority issues or requests a recall or takes a similar action in connection with a Licensed Product in the Field in the Territory, or in the event either Party determines that an event, incident or circumstance has occurred that may result in the need for a recall or market withdrawal of a Licensed Product in the Field in the Territory, the Party notified of such recall or similar action, or the Party that desires such recall or similar action, will as promptly as possible, notify the other Party by telephone or e-mail. [\*\*] decide via the JSC whether to conduct a recall of, market withdrawal of or similar action with respect to a Licensed Product in the Profit-Share Territory and the manner in which such recall, market withdrawal or similar action will be conducted. [\*\*]. Biogen will have the sole right to determine whether and when to conduct a recall of,

market withdrawal of or similar action with respect to a Licensed Product in the Biogen Territory and the manner in which any such recall, market withdrawal or similar action will be conducted; [\*\*]. Except as may otherwise be agreed to by the Parties, Biogen will bear the costs and expenses of any such recall, market withdrawal or similar action to the extent related to the Biogen Territory. Each Party will make available all of its pertinent records that may be reasonably requested by the other Party in order for a Party to effect a recall of a Licensed Product anywhere in the Territory. The Parties' rights and obligations under this Section 6.9 (Recalls, Market Withdrawals or Corrective Actions) will be subject to the terms of any Pharmacovigilance Agreement or Supply Agreement entered into between the Parties. In the event of a conflict between the provisions of any Pharmacovigilance Agreement or Supply Agreement, as applicable, and this Section 6.9 (Recalls, Market Withdrawals or Corrective Actions), the provisions of such Pharmacovigilance Agreement or Supply Agreement, as applicable, will govern.

**6.10 Reporting Adverse Events.** The Parties will cooperate with regard to the reporting and handling of safety information involving the Licensed Products in the Territory, in each case, in accordance with the applicable regulatory Laws and regulations on pharmacovigilance and clinical safety. As soon as practicable after the Effective Date (but in no event longer than [\*\*] after the Effective Date), the Parties will negotiate in good faith and execute an agreed pharmacovigilance agreement specifying the procedures and timeframes for complying with applicable Law pertaining to safety reporting for each Licensed Product and their related activities (a "**Pharmacovigilance Agreement**"), which Pharmacovigilance Agreement will be overseen by the JDC. The Pharmacovigilance Agreement will set forth each Party's responsibilities and obligations pertaining to safety collection, assessment and reporting of the Licensed Products based on relevant guidelines and applicable Law. The allocation of responsibilities between the Parties will be governed by the Pharmacovigilance Agreement. The Party that [\*\*] with respect to a Licensed Product will own the global safety database for such Licensed Product.

**6.11 Priority Review Voucher.** If either Party receives a Rare Pediatric Disease Priority Review Voucher for a Licensed Product pursuant to Section 529 of the FD&C Act enabling priority review, then the Parties agree that [\*\*].

## 7.MANUFACTURE

**7.1 Manufacturing Responsibilities.** Subject to Section 7.4 (Biogen Manufacturing Assumption Rights), [\*\*] will be the Manufacturing Lead Party (a) for the [\*\*] and (b) [\*\*], unless and until Biogen assumes responsibility as the Manufacturing Lead Party for the [\*\*] pursuant to Section 7.4 (Biogen Manufacturing Assumption Rights) and, in each case ((a) and (b)), [\*\*] will be solely responsible for, and will, Manufacture (or have Manufactured) Licensed Products in accordance with the applicable Manufacturing Plan, the Supply Agreement to be entered into by the Parties pursuant to Section 7.5 (Supply Agreement). The Manufacturing Lead Party will have decision making authority over all day-to-day operational matters related to Manufacturing for Licensed Products for the Territory, subject to (i) the terms of the applicable Supply Agreement, (ii) with respect to [\*\*], the Manufacturing Plan approved by the JSC, and (iii) in any applicable jurisdiction, the NDA- or marketing authorization-holding Party for a Licensed Product will have final decision-making authority sufficient to [\*\*].

**7.2 Manufacturing Plans.** The JMC will develop a manufacturing plan (a) to ensure continuity and adequacy of supply of the active pharmaceutical ingredient and bulk drug product dosage form of each Product Class of Licensed Products for the Profit-Share Territory (and whether such Licensed Product will be supplied by Sage or by Biogen (if both Parties will be Manufacturing)) and, for so long as [\*\*] is the Manufacturing Lead Party, for the [\*\*] and (b) for final packaging and labeling in the Profit-Share Territory, which plan will also include the estimated associated budget of FTE Costs and Out-of-Pocket Costs anticipated to be incurred in the performance of activities under such plan (such included budget, a "**Manufacturing Budget**"), and the JMC will submit such manufacturing plan to the JSC to

review, discuss and determine whether to approve (each, a “**Manufacturing Plan**”). The initial Manufacturing Plans for the Licensed 217 Products and the Licensed 324 Products will be approved by the JSC no later than [\*\*] after the Effective Date. On an annual basis no later than [\*\*] of each Calendar Year, or more often as the Parties deem appropriate, the Parties, through the JMC, may prepare and approve amendments to the then-current Manufacturing Plans for each Product Class and will submit such amendments to the JSC to review, discuss and determine whether to approve. Each such amended Manufacturing Plan will specify the information described in this Section 7.2 (Manufacturing Plans) for the next Calendar Year (and additional periods as reasonably determined by the Parties) and the Manufacturing Budget included therein will appropriately itemize the costs and expenses for the activities undertaken pursuant to such Manufacturing Plan. Once approved by the JSC, an amended Manufacturing Plan (including its corresponding Manufacturing Budget) will become effective and supersede the previous Manufacturing Plan (including its corresponding Manufacturing Budget). In the event of any inconsistency between the Manufacturing Plan and this Agreement, the terms of this Agreement will prevail.

**7.3 Manufacturing Costs.** Active pharmaceutical ingredient and drug product dosage form, along with packaging and labeling, of the Licensed Products will be supplied for the [\*\*] at [\*\*] by [\*\*] or by [\*\*] (if [\*\*] has assumed any portion of Manufacturing for the [\*\*] pursuant to Section 7.4 ([\*\*] Manufacturing Assumption Rights) and the Manufacturing Plan provides that [\*\*] will supply Licensed Product for use in the [\*\*]). Active pharmaceutical ingredient and bulk drug product of the Licensed Products for which [\*\*] is the Manufacturing Lead Party will be supplied by [\*\*] for the [\*\*] at [\*\*]. The cost specified in this Section 7.3 (Manufacturing Costs) is referred to in this Agreement as the “**Supply Price.**” All Manufacturing Costs incurred by the Parties related to the Manufacture of the Licensed Products (whether supplied by Sage or Biogen) (i) [\*\*], and (ii) [\*\*].

**7.4 [\*\*] Manufacturing Assumption Rights.** Notwithstanding any provision to the contrary set forth in this Agreement, (a) at any time during the Term, [\*\*] may, in its sole discretion, become the Manufacturing Lead Party and assume responsibility for, and Manufacture or have Manufactured, for the [\*\*] and, to the extent provided in the applicable Manufacturing Plan, the supply of active pharmaceutical ingredient for, as applicable, one or more Product Classes, and (b) within a reasonable period of time after the Effective Date, [\*\*] will become the Manufacturing Lead Party and assume responsibility for, and Manufacture or have Manufactured, for the [\*\*] for both Product Classes. If [\*\*] exercises its rights under this Section 7.4 ([\*\*] Manufacturing Assumption Rights), then (i) the Parties will amend via the JSC the Manufacturing Plan to reflect that [\*\*] is the Manufacturing Lead Party for such Product Class with respect to the [\*\*], (ii) [\*\*], (iii) [\*\*] will be deemed the Manufacturing Lead Party in the [\*\*], solely with respect to the applicable Product Class for which [\*\*] has become the Manufacturing Lead Party pursuant to this Section 7.4 ([\*\*] Manufacturing Assumption Rights), and (iv) Sage or Biogen will have the right to request through the JSC to source [\*\*] Licensed Product from [\*\*] for the [\*\*], and, if the JSC so approves, then, [\*\*] will supply the requesting Party for the [\*\*], and, if applicable, the Parties will negotiate in good faith a supply agreement to cover such supply to [\*\*] consistent with the terms of this Agreement and any Supply Agreement between the Parties.

**7.5 Supply Agreement.** Within [\*\*] after the Effective Date (as such period may be extended by written agreement of the Parties or otherwise agreed by the JMC), the Parties will negotiate in good faith and enter into a supply agreement pursuant to which [\*\*] will supply (a) all [\*\*], in the case of the [\*\*] and (b) [\*\*], in the case of the [\*\*], in each case ((a) and (b)), of the Licensed Products in sufficient quantity as is necessary for (i) each Party’s Development purposes in the Profit-Share Territory in accordance with the Joint Development Plans and Biogen’s Development purposes in the Biogen Territory, consistent with the forecast in accordance with a forecasting schedule to be agreed by the Parties in the applicable Supply Agreement, and (ii) each Party’s Commercialization purposes in the Profit-Share Territory in accordance with the Joint Commercialization Plans and Biogen’s Commercialization activities with respect to Licensed Product for the Biogen Territory, which agreement will be consistent with the material terms set forth on

Schedule 7.5 (Supply Agreements Material Terms) (each, a “**Supply Agreement**”). Each such Supply Agreement also will contain such other customary terms and conditions, including quality and business continuity protections, and will otherwise be consistent with the terms of this Agreement. If the Parties are unable to reach agreement on such provisions of the Supply Agreement within [\*\*] after the Effective Date (which [\*\*] period may be extended upon the agreement of the Parties), then upon request by either Party, the same shall be determined pursuant to Section 15.3.5 (Expert Arbitration).

**7.6 Second Source and Biogen Manufacturing Sites.** At either Party’s request, the JMC will discuss in good faith engaging one or more Third Party contract manufacturers, including the identity of all Third Party contract manufacturers, as second sources (each, a “**Second Source**”) in order to ensure adequate supply of any Licensed Product for the Profit-Share Territory or the Biogen Territory, as may be so requested by such Party, *provided* that following discussion with the JMC, (a) [\*\*] and (b) [\*\*], (i) [\*\*] and (ii) [\*\*]. If the JMC does not approve the engagement by a Party of any additional Second Sources [\*\*], then [\*\*]. The requesting Party will be the Party to enter into a supply agreement with any Second Source; *provided* that if the Manufacturing Lead Party is the requesting Party, then such requesting Party must use reasonable efforts to ensure that such supply agreement will contain a provision permitting the free assignment of such supply agreement to the other Party in the event that the non-requesting Party becomes the Manufacturing Lead Party with respect to, as the case may be, the Licensed Products being Manufactured under such agreement. [\*\*].

**7.7 Reporting; Shortages.** Each Party will keep the other reasonably informed, through the JMC, regarding the status and progress of all Manufacturing activities for Licensed Products for the Territory (with respect to Licensed Product Manufactured by or on behalf of Sage) and for the Profit-Share Territory (with respect to Licensed Product Manufactured by or on behalf of Biogen). Within [\*\*] after the end of each [\*\*], (a) Sage will prepare and provide written reports to update the JMC on the status of [\*\*] Licensed Products for the Territory [\*\*] and (b) Biogen will prepare and provide written reports to update the JMC on the status of [\*\*] Licensed Products [\*\*], and each Party will provide written reports to update the JMC in the event of any [\*\*] for the current or upcoming [\*\*]. In the event of a shortage of any active pharmaceutical ingredient or bulk drug product dosage form of any Licensed Products for the Territory, the Parties will notify the JMC and in good faith discuss and seek to agree upon a plan to increase supply volume as necessary, which plan may include utilization of one or more Second Sources to be engaged in accordance with Section 7.6 (Second Source and Biogen Manufacturing Sites).

## **7.8 Technology Transfer to Biogen.**

**7.8.1 Manufacturing Technology Transfer.** If [\*\*] exercises its right under Section 7.4 ([\*\*] Manufacturing Assumption Rights) and becomes the Manufacturing Lead Party with respect to a Product Class in the [\*\*] or if [\*\*] elects to Manufacture Licensed Product for the [\*\*] at any [\*\*] or engages a Second Source pursuant to Section 7.6 (Second Source and Biogen Manufacturing Sites), then [\*\*] will promptly conduct a transfer of Manufacturing technology to [\*\*] or its designee, to enable [\*\*] or such designee at one or more locations as determined by [\*\*] or such designee, to Manufacture [\*\*], the applicable Licensed Products (for each Product Class, the “**Manufacturing Technology Transfer**”). The cost of such Manufacturing Technology Transfer for the first Second Source for the Profit-Share Territory for either Party or for any additional Second Source for the Profit-Share Territory for either Party approved by the JMC will be shared jointly by the Parties as Joint Development Costs; *provided* that [\*\*] will pay the cost of any Manufacturing Technology Transfer for the [\*\*]. Each such Manufacturing Technology Transfer will be conducted pursuant to and will be subject to a written plan developed by the Parties in good faith at least [\*\*] prior to the anticipated commencement of such Manufacturing Technology Transfer. The Parties will work to complete such Manufacturing Technology Transfer as quickly as reasonably practicable, with the transfer of documentation necessary to support a demonstration batch of, as applicable, active pharmaceutical ingredient, bulk drug product dosage form, or packaged/labeled drug product dosage

form, to be completed within [\*\*] after [\*\*] exercise of its right to assume Manufacturing responsibilities pursuant to Section 7.4 ([\*\*] Manufacturing Assumption Rights) or [\*\*] engagement of a Second Source pursuant to Section 7.6 (Second Source and Biogen Manufacturing Sites).

**7.8.2** *Third Party Agreements.* If [\*\*] agrees that [\*\*] will become the sole Manufacturing Lead Party, or, under the terms of the applicable Supply Agreement, [\*\*] has the right and elects to become the sole Manufacturing Lead Party, with respect to a Product Class for the Profit-Share Territory, then upon [\*\*] request, [\*\*] will assign to [\*\*] or its designee one or more (as requested by [\*\*]) those Manufacturing contracts entered into by [\*\*] or any of its Affiliates and any Third Party contract manufacturers that are solely related to the Manufacture of [\*\*], the Licensed Products of such Product Class (“**Third Party Manufacturing Agreements**”, those existing as of the Execution Date as set forth in Schedule 7.8.2), unless any such Third Party Manufacturing Agreement expressly prohibits such assignment, in which case [\*\*] will cooperate with [\*\*] in all reasonable respects to secure the consent of the applicable Third Party to such assignment. If any such consent is not obtained with respect to a Third Party Manufacturing Agreement for the applicable Product Class, then [\*\*] will, and cause its Affiliates to, obtain for [\*\*] the practical benefit of and burden under such Third Party Manufacturing Agreement by (a) entering into reasonable alternative arrangements on terms reasonably agreeable to [\*\*], and (b) subject to the consent and control of [\*\*], enforcing for the account of [\*\*], any and all rights of [\*\*] (or such Affiliate) against the Third Party counterparty arising out of the breach or cancellation thereof by such Third Party counterparty or otherwise.

**7.8.3** *During Pendency of Manufacturing Technology Transfer.* If [\*\*] has elected to assume Manufacturing Lead Party under Section 7.1 (Manufacturing Responsibilities) or Manufacturing Lead Party transfers to [\*\*] under Section 7.8.2 (Third Party Agreements), during the pendency of any Manufacturing Technology Transfer performed pursuant to Section 7.8.1 (Manufacturing Technology Transfer) with respect to the applicable Licensed Products, and through the completion of any related transfer activities, [\*\*] will continue to provide [\*\*] with Manufacturing services and otherwise supply Licensed Product in accordance with the most recently agreed-upon Supply Agreement for, as applicable, such Licensed Products.

## **8.LICENSES**

### **8.1 License Grants.**

#### **8.1.1** *License Grant to Biogen; Sage Retained Rights.*

**8.1.1.1** *License Grant to Biogen.* Subject to the terms and conditions of this Agreement (including Sage’s retained rights under Section 8.1.1.2 (Sage Retained Rights), Sage, on behalf of itself and its Affiliates, hereby grants Biogen a non-transferable (except as provided in Section 15.1 (Assignment)), sublicensable (as permitted in Section 8.2 (Sublicensing)) license under the Sage Licensed Technology to Develop, Manufacture, perform Medical Affairs Activities with respect to and Commercialize the Licensed Products in the Field in the Territory, which license will be (a) co-exclusive with Sage under the Sage Licensed Technology with respect to the Development, Manufacture, performance of Medical Affairs Activities with respect to and Commercialization of the Licensed Products in the Field in the Profit-Share Territory, and (b) exclusive (even as to Sage and its Affiliates) and royalty-bearing with respect to the Development, Manufacture, performance of Medical Affairs Activities with respect to and Commercialization of the Licensed Products in the Field for the Biogen Territory.

**8.1.1.2** *Sage Retained Rights.* Notwithstanding the exclusive licenses granted to Biogen pursuant to Section 8.1.1.1 (License Grant to Biogen), and without limiting the generality

of Section 8.5 (No Other Rights), Sage and its Affiliates will retain, under the Sage Licensed Technology, with the right to license (through multiple tiers, subject to Section 8.2 (Sublicensing), as applicable) to Sage's Affiliates and Third Parties, the following rights: (a) the right to Manufacture and have Manufactured the Licensed Products [\*\*] for the purpose of Developing and Commercializing the Licensed Products for the Profit-Share Territory and the Existing Partner Territory and supplying Licensed Product to Biogen for use in the Biogen Territory, subject to and in accordance with the terms of this Agreement and (b) the right to Develop the Licensed 217 Products [\*\*] solely for the purposes of obtaining Regulatory Approval for and Commercializing such Licensed 217 Products in the Existing Partner Territory, *provided* that [\*\*], but subject to the terms of this Agreement.

**8.1.2** *License Grants to Sage; Biogen Retained Rights.*

**8.1.2.1** *License Grants to Sage.*

(a) Subject to the terms and conditions of this Agreement, Biogen, on behalf of itself and its Affiliates, hereby grants Sage the following non-transferable (except as provided in Section 15.1 (Assignment)), sublicensable (as permitted in Section 8.2 (Sublicensing)) licenses: (i) a co-exclusive (with Biogen), royalty-free, fully paid-up license under the Biogen Collaboration Technology and Biogen's interest in the Joint Collaboration Technology and (ii) a non-exclusive, royalty-free, fully paid-up license under the Biogen Background Technology, in each case ((i) and (ii)), to perform (or to have performed by permitted Subcontractors hereunder) the Joint Program Activities allocated to Sage under this Agreement.

(b) Subject to the terms and conditions of this Agreement, Biogen, on behalf of itself and its Affiliates, hereby grants Sage a non-transferable (except as provided in Section 15.1 (Assignment)), sublicensable (as permitted in Section 8.2 (Sublicensing)), non-exclusive, royalty-free, fully paid-up license under the Biogen Collaboration Technology and the Biogen Background Technology, in each case, to (i) Manufacture each Licensed 217 Product [\*\*] for the purpose of Developing the Licensed 217 Products for and Commercializing Licensed 217 Products in the Existing Partner Territory, solely to the extent required under the Existing Partner Agreement, or (ii) [\*\*], to Develop each Licensed 217 Products [\*\*] for the purposes of obtaining Regulatory Approval for and Commercializing the Licensed 217 Product in the Existing Partner Territory, and to Commercialize the Licensed 217 Products in the Existing Partner Territory.

**8.1.2.2** *Biogen Retained Rights.* Notwithstanding the exclusive nature of the foregoing license grant to Sage in Section 8.1.2.1(a) (License Grants to Sage), Biogen will retain, under the Biogen Collaboration Technology and Biogen's interest in the Joint Collaboration Technology, with the right to license (through multiple tiers and subject to Section 8.2 (Sublicensing), as applicable) to Biogen's Affiliates and Third Parties, the following rights: to Manufacture each Licensed Product [\*\*] for the purpose of Developing and Commercializing Licensed Products in the Biogen Territory, and to Develop the Licensed Products [\*\*] for the purposes of obtaining Regulatory Approval for and Commercializing any Licensed Product in the Territory, in each case, subject to and in accordance with the terms of this Agreement.

**8.2** **Sublicensing.**

**8.2.1** *Scope of Permissible Sublicensing.*



### **8.2.1.1**

#### *Sage.*

(a) *To Subcontractors.* Sage may grant a sublicense of the rights granted by Biogen to Sage under Section 8.1.2 (License Grants to Sage; Biogen Retained Rights) in the Profit-Share Territory to a Subcontractor engaged in accordance with Section 3.9 (Development Subcontracts) or Section 5.14 (Commercialization Subcontracts), as applicable, to perform Sage's responsibilities or exercise Sage's rights, in each case, under any Joint Development Plan, Joint Medical Affairs Plan, Joint Commercialization Plan or Manufacturing Plan or any Supply Agreement.

(b) *To Affiliates and Other Third Parties.* Sage may grant a sublicense of the rights granted by Biogen to Sage under Section 8.1.2 (License Grants to Sage; Biogen Retained Rights), which sublicensed rights may be further sublicensable through multiple tiers, to: (i) [\*\*], or (ii) [\*\*].

(c) *Responsibilities.* With respect to any sublicense granted pursuant to Section 8.2.1.1(a) (To Subcontractors) or Section 8.2.1.1(b) (To Affiliates and Other Third Parties), Sage will (i) remain responsible for the work allocated to, and payment to, such Subcontractor or Sublicensee to the same extent it would if it had done such work itself and compliance by such Subcontractor or Sublicensee with the applicable provisions of this Agreement, and Biogen will have the right to proceed directly against Sage without any obligation to first proceed against such Subcontractor or Sublicensee, as applicable, (ii) [\*\*], (iii) require that each Subcontractor or Sublicensee undertakes in writing commercially reasonable obligations of confidentiality and non-use regarding Confidential Information that are substantially the same as those undertaken by the Parties with respect to Confidential Information pursuant to Article 10 (Confidentiality and Publication) hereof, and (iv) without limitation of the foregoing clause (iii), include in any such sublicense terms consistent with Sage's obligations to Biogen under this Agreement.

### **8.2.1.2**

#### *Biogen.*

(a) *To Subcontractors.* Biogen may grant a sublicense of the rights granted by Sage to Biogen under Section 8.1.1 (License Grant to Biogen; Sage Retained Rights) in the Profit-Share Territory to a Subcontractor engaged in accordance with Section 3.9 (Development Subcontracts) or Section 5.14 (Commercialization Subcontracts), as applicable, to perform Biogen's responsibilities or exercise Biogen's rights, in each case, under any Joint Development Plan, Joint Medical Affairs Plan, Joint Commercialization Plan or Manufacturing Plan or any Supply Agreement.

(b) *To Affiliates and Other Third Parties.* Biogen may grant a sublicense of the rights granted by Sage to Biogen in Section 8.1.1 (License Grant to Biogen; Sage Retained Rights), which sublicensed rights may be further sublicensable through multiple tiers to: (i) [\*\*]; (ii) [\*\*]; and (iii) [\*\*].

(c) *Responsibilities.* With respect to any sublicense granted pursuant to this Section 8.2.1.2(a) (To Subcontractors) or Section 8.2.1.2(b) (To Affiliates and Other Third Parties), Biogen will (i) remain responsible for the work allocated to, and payment to, such Subcontractor or Sublicensee to the same extent it would if it had done such work itself and compliance by such Subcontractor or Sublicensee with the applicable provisions of this Agreement, and Sage will have the right to proceed directly against Biogen without any obligation to first proceed against such Subcontractor or Sublicensee, as applicable,

(ii) [\*\*], (iii) require that each Subcontractor or Sublicensee undertakes in writing commercially reasonable obligations of confidentiality and non-use regarding Confidential Information that are substantially the same as those undertaken by the Parties with respect to Confidential Information pursuant to Article 10 (Confidentiality and Publication) hereof, and (iv) without limitation of the foregoing clause (iii), include in any such sublicense terms consistent with Biogen's obligations to Sage under this Agreement.

### **8.3 Third Party In-Licenses Payments.**

#### **8.3.1 *Existing In-License Agreements.***

**8.3.1.1** *Sage.* Except as set forth in Section 8.3.1.3 (Third Party Payments owed to Existing Partner), Sage will be solely responsible for all Third Party Payments associated with any Existing Sage Agreement.

**8.3.1.2** *Biogen.* Biogen will be solely responsible for all Third Party Payments associated with any license agreement or other agreement of Biogen or any of its Affiliates that exists as of the Effective Date under which Biogen or such Affiliate has obtained rights to any Biogen Background Technology.

#### **8.3.1.3 *Third Party Payments owed to Existing Partner.***

(a) Sage owes to the Existing Partner (i) a royalty of [\*\*] percent ([\*\*]%) on annual Net Sales (as such term is defined in the Existing Partner Agreement) in the Territory by Sage, its Affiliates and its (sub)licensees of a Licensed 217 Product that [\*\*], and (ii) a [\*\*] royalty by Sage and the Existing Partner on annual Net Sales (as such term is defined in the Existing Partner Agreement) in the Territory by Sage, its Affiliates and its (sub)licensees [\*\*] and, in each case ((i) and (ii)), such royalty is owed, on a country-by-country basis in the Territory, from the first commercial sale of such a Licensed 217 Product in such country until the expiration of the last Valid Claim (as defined in the Existing Partner Agreement) of the EP Background Patents or EP CMC Patent, as applicable, Covering such Licensed 217 Product in such country (a product described in clause (i) or (ii), an "**EP-Enhanced 217 Product**").

(b) In the event the JDC elects to Develop for Commercialization in the Profit-Share Territory an EP-Enhanced 217 Product, then the associated corresponding royalty payments owed to the Existing Partner in connection with Net Sales of such EP-Enhanced 217 Product in the Profit-Share Territory [\*\*].

(c) In the event Biogen elects to Develop for Commercialization in the Biogen Territory an EP-Enhanced 217 Product, then subject to Section [\*\*] Biogen will be [\*\*] responsible for [\*\*], and Biogen will comply, and will require its Affiliates and its Sublicensees to comply, with any obligations under the Existing Partner Agreement that apply to Biogen, its Affiliates or its Sublicensees and of which Biogen was informed in writing by Sage. Biogen will pay all undisputed amounts for such payments to Sage within [\*\*] of receiving an applicable invoice from Sage for the same.

**8.3.2 *After Effective Date Executed In-License Agreements.*** The Parties hereby agree that all upfront, milestone, royalty and other payments to any Third Party in respect of any license agreement or other agreement entered into after the Effective Date in accordance with the subsections below of this

Section 8.3 (Third Party In-Licenses Payments) will be deemed “**Third Party Payments**” and be subject to this Section 8.3 (Third Party In-Licenses Payments).

**8.3.2.1** *New Technology.* After the Effective Date, a Party may wish to acquire a right or license under additional Patents or Know-How of Third Parties for the Development, Manufacture or Commercialization of Licensed Products for the Profit-Share Territory (“**New Technology**”). With respect to the New Technology for the Profit-Share Territory, such Party will (a) promptly notify the JSC in writing and keep the JSC reasonably informed of any negotiations with respect to such right or license, including the proposed terms of any such license, and consider in good faith any comments of the other Party with respect thereto, and (b) in any event comply with the procedures set forth in Section 8.3.2.2 (*Inclusion Process*).

**8.3.2.2** *Inclusion Process.* If, after the Effective Date, a Party wishes to acquire rights under any New Technology that would be Sage Licensed Technology or Biogen Licensed Technology, as applicable, then such Party will so notify the JSC and provide the JSC with a summary of the terms of any license or agreement, including any Third Party Payments owed to a Third Party as a result of the grant to the other Party of rights with respect to such New Technology or a Party’s practice or use of any such New Technology in the performance of activities under this Agreement, under which such Party would acquire the rights to such subject matter in accordance with Section 8.3.2.1 (New Technology) (such applicable terms, the “**New Technology Terms**”). In connection with the discussion of the New Technology Terms, the JSC may also discuss [\*\*]. In the event the JSC agrees to include such New Technology under this Agreement for the Profit-Share Territory, then such New Technology will be included in the Sage Licensed Technology or the Biogen Licensed Technology, as applicable and will be subject to the terms and conditions of this Agreement, and the Parties will be bound by such New Technology Terms. If the JSC does not agree to include such New Technology under this Agreement for the Profit-Share Territory as Sage Licensed Technology or Biogen Licensed Technology, as applicable, and one Party believes that such New Technology is [\*\*], then the resolution procedure of Section 8.3.2.4 (New Technology Disputes) will apply. For clarity, with respect to New Technology other than [\*\*], the Party proposing to acquire rights to such New Technology will have the right to obtain a license to such New Technology, but the other Party will not be bound by any agreement related to such New Technology or have any rights under, or cost-sharing obligations with respect to, such new Technology, unless such other Party agrees to include such New Technology under this Agreement.

**8.3.2.3** *Cost Sharing.* Prior to entering into an agreement for New Technology and its inclusion under this Agreement for the Profit-Share Territory as Sage Licensed Technology or Biogen Licensed Technology pursuant to Section 8.3.2.2 (Inclusion Process), the JSC must agree on the amount of any Third Party Payments to be paid to the applicable Third Party in consideration for such New Technology, (a) [\*\*], and (b) [\*\*]. Notwithstanding any provision set forth in this Agreement to the contrary, with respect to any [\*\*], Sage will bear fifty percent (50%) and Biogen will bear fifty percent (50%) of the Third Party Costs associated with such [\*\*] to the extent allocable to the Profit-Share Territory. Nothing herein will prevent Biogen from obtaining rights (whether by acquisition or license) under any intellectual property right that is necessary or reasonably useful to Exploit any Licensed Product in the Biogen Territory. Except as set forth in this Section 8.3.2.3 (Cost Sharing) and subject to Section 9.9.3 (Third Party Payments), Biogen will be solely responsible for any and all payments under an agreement to acquire a right or license under additional Patents or Know-How of Third Parties for the Development, Manufacture or Commercialization of Licensed Products solely for the Biogen Territory.

**8.3.2.4** *New Technology Disputes.* If a Party disputes whether certain New Technology is [\*\*], then each Party may [\*\*], then such New Technology will be included as Sage

Licensed Technology or Biogen Licensed Technology and licensed to the applicable Party pursuant to the terms of this Agreement, as applicable[\*\*].

**8.4 Combinations.** Notwithstanding any other provision of this Agreement, for purposes of the licenses grants under Section 8.1.1 (License Grant to Biogen; Sage Retained Rights) and Section 8.1.2 (License Grants to Sage; Biogen Retained Rights), with respect to any Licensed Product that is a Combination Product, such license will only include a license with respect to, respectively, the SAGE-217 component or the SAGE-324 component, as applicable, of such Combination Product (and not any Other Component Controlled by Sage or any of its Affiliates or Biogen or any of its Affiliates).

**8.5 No Other Rights.** Except as otherwise expressly provided in this Agreement, under no circumstances will a Party or any of its Affiliates, as a result of this Agreement, obtain any ownership interest, license or other right (whether by implication, estoppel or otherwise) in or to any Know-How, Patents or other intellectual property rights of the other Party or any of such other Party's Affiliates. Neither Party nor any of its Affiliates will use or practice any Know-How or Patents licensed or provided to such Party or any of its Affiliates outside the scope of or otherwise not in compliance with the rights and licenses granted to such Party and its Affiliates under this Agreement.

## 9. PAYMENTS

**9.1 Upfront Fee.** No later than five (5) Business Days after the Effective Date, Biogen will pay to Sage a one-time, non-refundable, non-creditable payment of Eight Hundred Seventy Five Million Dollars (\$875,000,000).

**9.2 Equity Investment.** On the Execution Date, the Parties will enter into a share purchase agreement (the "SPA") pursuant to which Sage will sell to BIMA in one transaction, and BIMA will purchase from Sage, Six Hundred Fifty Million Dollars (\$650,000,000) worth of shares of common stock of Sage, as more specifically set forth in such SPA.

### **9.3 Licensed Product Reconciliation of Shared Costs; Profit Sharing.**

**9.3.1 Joint Development Costs Reconciliation.** The terms and conditions of this Section 9.3.1 (Joint Development Costs Reconciliation) will govern the rights and obligations of Biogen and Sage with respect to sharing the Joint Development Costs with respect to a Product Class, unless and until Sage exercises an Opt-Out Right in accordance with Section 9.4 (Sage Opt-Out) for such particular Product Class. During the Term, for each Calendar Quarter in which a Party or its Affiliates performs Development activities under a Joint Development Plan, (a) within [\*\*] after the end of each such Calendar Quarter, such Party will submit to a finance officer designated by Sage and a finance officer designated by Biogen (the "Finance Officers") a report setting forth such Party's actual Joint Development Costs with respect to each Product Class of Licensed Products, which report will specify [\*\*] (a "Development Expense Report"), and (b) within [\*\*] after the end of each such Calendar Quarter, such Party will submit to the Finance Officers [\*\*]. Within [\*\*] after receipt of such Development Expense Reports, the Finance Officers will confer and agree in writing on whether a reconciliation payment is due from Sage to Biogen or Biogen to Sage, and if so, the amount of such reconciliation payment, for all Licensed Products in a Product Class in accordance with the applicable provisions of this Agreement, which payment in any event will be made such that Sage and Biogen share equally the Joint Development Costs. Sage or Biogen, as applicable, if required to pay such reconciliation payment, will submit the undisputed portion of any such payment to Biogen or Sage, as applicable, within [\*\*] after the end of such [\*\*] conferral period. In the event of any disagreement with respect to the calculation of such reconciliation payment, the owing Party will pay to the other Party any disputed portion within [\*\*] after the date on which Sage and Biogen, using good faith efforts, resolve the dispute. In addition, following the Effective Date, each Party will consider in good faith

other reasonable procedures proposed by the other Party for sharing financial information in order to permit each Party to close its books periodically in a timely manner.

**9.3.2** *Reconciliation/Reimbursement Prior to First Commercial Sale.* The terms and conditions of this Section 9.3.2 (Reconciliation/Reimbursement Prior to First Commercial Sale) will govern the rights and obligations of Biogen and Sage with respect to sharing the Joint Medical Affairs Costs and the Joint Commercialization Costs prior to the First Commercial Sale of a Licensed Product in the Product Class in the Profit-Share Territory, unless and until Sage exercises an Opt-Out Right in accordance with Section 9.4 (Sage Opt-Out) for such particular Product Class. During the Term, for each Calendar Quarter prior to the Calendar Quarter in which the First Commercial Sale of a Licensed Product in a Product Class occurs in the Profit-Share Territory, (a) within [\*\*] after the end of each such Calendar Quarter, Sage and Biogen will submit to the Finance Officers a report setting forth the Joint Medical Affairs Costs and Joint Commercialization Costs such Party incurred in such Calendar Quarter with respect to each Product Class of Licensed Products prior to First Commercial Sale in the United States, which report for a Product Class will specify [\*\*] (a “**Pre-Commercialization Expense Report**”), and (b) within [\*\*] after the end of each such Calendar Quarter, such Party will submit to the Finance Officers [\*\*]. Within [\*\*] after receipt of such Medical Affairs and Commercialization Expense Reports, the Finance Officers will confer and agree in writing on whether a reconciliation payment is due from Sage to Biogen or Biogen to Sage, and if so, the amount of such reconciliation payment, which payment in any event will be made such that Sage and Biogen share equally the Joint Medical Affairs Costs and Joint Commercialization Costs for all Licensed Products in a Product Class in accordance with the applicable provisions of this Agreement. Sage or Biogen, as applicable, if required to pay such reconciliation payment, will submit the undisputed portion of any such payment to Biogen or Sage, as applicable, within [\*\*] after the end of such [\*\*] conferral period. In the event of any disagreement with respect to the calculation of such reconciliation payment, the owing Party will pay to the other Party any disputed portion within [\*\*] after the date on which Sage and Biogen, using good faith efforts, resolve the dispute. In addition, following the Effective Date, each Party will consider in good faith other reasonable procedures proposed by the other Party for sharing financial information in order to permit each Party to close its books periodically in a timely manner.

**9.3.3** *Profit Sharing Following First Commercial Sale.* The terms and conditions of this Section 9.3.3 (Profit Sharing Following First Commercial Sale) will govern the rights and obligations of Biogen and Sage with respect to the OP&L Share with respect to a Product Class, unless and until Sage exercises an Opt-Out Right in accordance with Section 9.4 (Sage Opt-Out) for such Product Class.

**9.3.3.1** *Share of Operating Profits and Operating Losses.* For so long as (a) a Licensed Product in a Product Class is being sold in the Profit-Share Territory and (b) Sage has not exercised its Opt-Out Right in accordance with Section 9.4 (Sage Opt-Out) for the applicable Product Class, Sage and Biogen will share equally (50:50) all Operating Profits and all Operating Losses (as applicable) for all Licensed Products in such Product Class in the Profit-Share Territory.

**9.3.3.2** *Calculation and Payment.* During the Term, for each Calendar Quarter beginning with the Calendar Quarter in which the First Commercial Sale of a Licensed Product in a Product Class occurs in the Profit-Share Territory, within [\*\*] after the end of each such Calendar Quarter, (a) Biogen will report to the Finance Officers [\*\*]. and (b) Sage will report to the Finance Officers [\*\*], in each case ((a) and (b)), in the format of the Profit and Loss Statement set forth on Schedule 9.3.3.2 (Calculation and Payment), which report will specify for a Product Class [\*\*] (each, a “**Post-Commercialization Expense Report**”). During the Term, for each Calendar Quarter beginning with the Calendar Quarter in which the First Commercial Sale of a Licensed Product in a Product Class occurs in the Profit-Share Territory, within [\*\*] after the end of each such Calendar Quarter, (i) Biogen will report to the Finance Officers [\*\*], and Sage and Biogen will each report to the Finance Officers [\*\*], and (ii) Sage will report to the Finance Officers [\*\*],

and Sage and Biogen will each report to the Finance Officers [\*\*]. Within [\*\*] after receipt of such Post-Commercialization Expense Reports, the Finance Officers will confer and agree upon in writing a consolidated financial statement (i) setting forth the Operating Profit or Operating Loss for such Calendar Quarter for, as the case may be, for such Licensed Product, in the Profit-Share Territory, and (ii) calculating each Party's share of such Operating Profit or Operating Loss. Within [\*\*] after such [\*\*] conferral period, Biogen or Sage, as applicable, will make a payment to Sage or Biogen respectively, as applicable, so that each of Biogen and Sage has been compensated for its respective share of such Operating Profits, or has borne its respective share of such Operating Loss, as applicable, after giving effect to the Net Sales invoiced by, as applicable, Biogen or Sage and the Joint Medical Affairs Costs and Joint Commercialization Costs incurred by Sage and Biogen with respect to such Licensed Product in such Product Class in such Calendar Quarter; *provided, however*, that in the event of any disagreement with respect to the calculation of such payment, any undisputed portion of such payment will be paid in accordance with the foregoing timetable and the remaining, disputed portion will be paid within [\*\*] after the date on which Biogen and Sage, using good faith efforts, resolve the dispute. In addition, following the Effective Date, each Party will consider in good faith other reasonable procedures proposed by the other Party for sharing financial information in order to permit each Party to close its books periodically in a timely manner.

**9.4 Finance Working Group.** With respect to the financial reporting activities between the Parties, the JSC (or the Parties if the JSC does not exist) will establish a finance working group (the "Finance Working Group") to coordinate the activities and reporting by the Parties as set forth in Section 9.3.1 (Joint Development Costs) through Section 9.3.3 (Profit-Sharing Following Commercialization) and Section 9.11.2 (Reports and Royalty Payments) and to assist the JSC in its responsibilities with respect to the review and resolution of financial matters. In particular, the Finance Working Group will:

- (a) facilitate the creation of each Joint Development Budget, Long Term Joint Development Budget, Joint Medical Affairs Budget, Long Term Joint Medical Affairs Budget, Joint Commercialization Budget, Long Term Joint Commercialization Budget and Manufacturing Budget;
- (b) reconcile financial and accounting matters between the Parties;
- (c) initiate and execute an effective and efficient revenue and cost-sharing process (cross-charges);
- (d) review and recommend for the Parties' consideration modifications to the FTE Rate used to calculate Joint Development Costs, Joint Medical Affairs Costs or Joint Commercialization Costs;
- (e) discuss, prepare and determine whether to approve for submission to the JSC for approval a FTE time tracking approach to be following by each Party;
- (f) cooperate to ensure that all budgets referenced in Section 9.4(a) (Finance Working Group) agreed to for a Calendar Year (or any other given period) can be interpreted for the purposes of both Parties' internal financial and audit reporting requirements, including each Party's fiscal year reporting;
- (g) implement a series of reporting requirements for actual and forecasted financial information, available at times to be agreed by the Parties through the Finance Working Group, consistent with the need to report the results of the OP&L Share;

- (h) monitor the budget, expense and revenue reporting requirements between the Parties related to Licensed Products to ensure that each Party is able to comply with its respective internal financial and audit reporting requirements and, as appropriate, recommending to the JSC for approval, changes to the reporting requirements under this Agreement; and
- (i) undertake such other tasks with respect to the calculation, implementation and reporting for the Parties' sharing of Joint Development Costs, Joint Medical Affairs Costs, Joint Commercialization Costs and Net Revenues as the Parties agree.

## **9.5 Sage Opt-Out.**

**9.5.1** *Exercise of Opt-Out.* Sage may elect to opt-out of the OP&L Share set forth in Section 9.3.3 (Profit Sharing Following First Commercial Sale) on a Product Class-by-Product Class basis with respect to all Licensed Products in such Product Class in accordance with this Section 9.4 (Sage Opt-Out) (each such right to opt out, an “**Opt-Out Right**”, and all such Licensed Products in the applicable Product Class, the “**Opt-Out Products**”). At any time during the Term after [\*\*], Sage may elect to exercise an Opt-Out Right by providing written notice to Biogen, which notice must specify the Product Class to which Sage wishes the Opt-Out Right to apply. The date on which Sage exercises an Opt-Out Right for a specific Product Class as set forth in this Section 9.4 (Sage Opt-Out) will be deemed the “**Opt-Out Date**” for such Product Class (or for all Product Classes if Sage exercises an Opt-Out Right for all Product Classes on the same date).

**9.5.2** *Effect of Opt-Out.* If Sage exercises an Opt-Out Right pursuant to Section 9.5.1 (Exercise of Opt-Out) for a Product Class, then, from and after the Opt-Out Date with respect to the Opt-Out Products:

**9.5.2.1** Sage will continue to perform, as the case may be depending on when the Opt-Out Date occurs, (a) the Development activities under the then-applicable Joint Development Plan(s) for such Opt-Out Products, (b) the Medical Affairs Activities under the then-applicable Joint Medical Affairs Plan(s) for such Opt-Out Products or (c) the Commercialization activities under the then-applicable Joint Commercialization Plan(s) for such Opt-Out Products, in each case ((a), (b) and (c)), subject to Section 9.5.2.4 (Effect of Opt-Out), for which Sage was responsible thereunder for a single, consecutive transition of period of up to [\*\*] (such period, the “**Opt-Out Wind-Down Period**” and such activities, the “**Opt-Out Wind-Down Activities**”, and Biogen will pay Sage for the Joint Development Costs, Joint Medical Affairs Costs and Joint Commercialization Costs, as applicable, incurred by Sage to conduct the Opt-Out Wind-Down Activities, in each case, to the extent consistent with the corresponding Joint Development Budget, Joint Medical Affairs Budget or Joint Commercialization Budget approved and included in such Joint Development Plan, Joint Medical Affairs Plan or Joint Commercialization Plan prior to the Opt-Out Date or updated versions of one or more of such plans or budgets approved by the JSC to account for the Opt-Out Wind-Down Period for the applicable Product Class (collectively, the “**Opt-Out Wind-Down Costs**”), and Biogen will pay all undisputed invoiced amounts for such payments to Sage no later than [\*\*] after receiving an applicable invoice from Sage for the same. Notwithstanding the foregoing, if Sage exercises its Opt-Out Right during [\*\*] of any Product Class of Licensed Products, then [\*\*];

**9.5.2.2** Biogen will become the Regulatory Lead Party with respect to the applicable Licensed Products in the Profit-Share Territory in the Product Class for which Sage exercised its Opt-Out Right;

**9.5.2.3** Biogen will be solely responsible for all other costs and expenses incurred in connection with the further Development, performance of Medical Affairs Activities with respect to and Commercialization of the Opt-Out Products in the Profit-Share Territory after the Opt-Out Wind-Down Period, including (a) [\*\*] and (b) [\*\*];

**9.5.2.4** No later than [\*\*] after the Opt-Out Date for a Product Class, Biogen will notify Sage in writing if it desires the Opt-Out Wind Down Period to be less than [\*\*];

**9.5.2.5** Other than the performance of the Opt-Out Wind-Down Activities, Sage will not have any performance obligations or funding obligations with respect to the Opt-Out Products in the Profit-Share Territory under any then-applicable Joint Development Plan(s), Joint Medical Affairs Plan(s) or Joint Commercialization Plan(s), or any other right to the OP&L Share, including under Section 9.3 (Licensed Product Reconciliation of Shared Costs; Profit Sharing);

**9.5.2.6** Biogen will pay Sage the Territory Royalties (a) pursuant to Section 9.8.2 (United States Royalties) for Net Sales of the Opt-Out Products by Biogen and its Related Parties in the United States for their respective Royalty Terms and (b) pursuant to Section 9.8.1 (Biogen Territory Royalties) for Net Sales of the Opt-Out Products by Biogen and its Related Parties in the Biogen Territory (always excluding the United States) for their respective Royalty Terms;

**9.5.2.7** the Biogen Territory for the Opt-Out Products will be deemed to include the United States for purposes of this Agreement (except for royalties owed to Sage on Net Sales of the Opt-Out Products in the United States, which will be calculated in accordance with Section 9.8.2 (United States Royalties)); and

**9.5.2.8** the Parties will otherwise have the rights and obligations with respect to the Licensed Products as set forth in this Agreement.

## **9.6 Licensed Products Regulatory/Commercial Milestone Payments.**

**9.6.1** *Licensed 217 Products Regulatory/Commercial Milestones.* Subject to Section 9.6.3 (Payment Terms for 217/324 Regulatory Milestone Payments), Biogen will make one-time, non-refundable milestone payments to Sage (each, a “**217 Regulatory/Commercial Milestone Payment**”) upon the first achievement by Biogen or its Affiliates or Sublicensees or, if applicable, by Sage or any of its Related Parties in the case of the 217 Regulatory/Commercial Milestone Events of Rows 1, 2 and 3 of the regulatory/commercial milestone events set forth in this Section 9.6.1 (Licensed 217 Products Regulatory/Commercial Milestones) for the first Licensed 217 Product (each, a “**217 Regulatory/Commercial Milestone Event**”) to achieve the applicable 217 Regulatory/Commercial Milestone Event. For clarity, [\*\*].



217 Regulatory/Commercial Milestone Event	217 Regulatory/Commercial Milestone Payment			
	For the 1st of either MDD or [**] (but not both)	For PPD	For [**]	For [**]
[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]
4. First Commercial Sale in the United States of a Licensed 217 Product	[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]	[**]

The maximum total amount payable by Biogen to Sage under this Section 9.6.1 (Licensed 217 Products Regulatory/Commercial Milestones) for all Licensed 217 Products under this Agreement is Four Hundred Seventy Five Million Dollars (\$475,000,000).

**9.6.2** *Licensed 324 Products Regulatory/Commercial Milestones.* Subject to Section 9.6.3 (Payment Terms for 217/324 Regulatory Milestone Payments), Biogen will make one-time, non-refundable milestone payments to Sage (each, a “**324 Regulatory/Commercial Milestone Payment**”) upon the first achievement by Biogen or its Affiliates or Sublicensees or, if applicable, by Sage or any of its Related Parties in the case of the 324 Regulatory/Commercial Milestone Events of Rows 1, 2 and 3 of the regulatory/commercial milestone events set forth in this Section 9.6.2 (Licensed 324 Products *Regulatory/Commercial Milestones*) for the first Licensed 324 Product (each, a “**324 Regulatory/Commercial Milestone Event**”) to achieve the applicable 324 Regulatory/Commercial Milestone Event. For clarity, [\*\*].

324 Regulatory/Commercial Milestone Event	324 Regulatory/Commercial Milestone Payment		
	For [**]	For [**]	For [**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]
[**]	[**]	[**]	[**]

The maximum total amount payable by Biogen to Sage under this Section 9.6.2 (Licensed 324 Products *Regulatory/Commercial Milestones*) for all Licensed 324 Products under this Agreement is Five Hundred Twenty Million Dollars (\$520,000,000).

**9.6.3** *Payment Terms for 217/324 Regulatory Milestone Payments.* Biogen will provide Sage with written notice of the first achievement of each 217 Regulatory/Commercial Milestone Event and each 324 Regulatory/Commercial Milestone Event, and, if applicable, Sage will provide Biogen with written notice of the first achievement of each of 217 Regulatory/Commercial Milestone Events set forth in Rows 1, 2 and 3 of the table in Section 9.6.1 (Licensed 217 Products Regulatory/Commercial Milestones) and the first achievement of each of the 324 Regulatory/Commercial Milestone Events set forth in Rows 1, 2 and 3 in the table in Section 9.6.2 (Licensed 324 Products *Regulatory/Commercial Milestones*), in each case, no later than [\*\*] after such achievement. Thereafter, Biogen will pay to Sage, as applicable, the corresponding 217 Regulatory Milestone Payment or 324 Regulatory Milestone Payment within [\*\*] after

Biogen's receipt of an invoice for the same from Sage, which invoice may be delivered only after receipt of notice of achievement of the applicable milestone event.

**9.7 Licensed Products Sales Milestone Payments.**

**9.7.1 Licensed 217 Products Sales Milestones.**

**9.7.1.1** Subject to Section 9.7.3 (Payment Terms for Sales Milestone Payments), Biogen will make one-time, non-refundable milestone payments to Sage (each, a "**217 Sales Milestone Payment**") when annual Net Sales of all Licensed 217 Products across all Indications in the Territory in a given Calendar Year first reach the Dollar threshold values indicated below in one of the applicable tables set forth under either Section 9.7.1.1(a), (Licensed 217 Products Sales Milestones) or Section 9.7.1.1(b), (Licensed 217 Products Sales Milestones) during the Term (each, a "**217 Sales Milestone Event**"):

(a) if Sage has not exercised an Opt-Out Right for the Licensed 217 Products:

<b>Non-Opt-Out Right 217 Sales Milestone Event</b>	<b>217 Sales Milestone Payment</b>
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]

(b) if Sage has exercised an Opt-Out Right for the Licensed 217 Products, then beginning in the next Calendar Year after the exercise of such Opt-Out Right:

<b>Opt-Out Right 217 Sales Milestone Event</b>	<b>217 Sales Milestone Payment</b>
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 217 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]

(c) For clarity, the 217 Sales Milestone Payments will each only be paid once, such that, the maximum total amount payable by Biogen to Sage under this Section 9.7.1 (Licensed 217 Products Sales Milestones) is either (i) if Sage *has not* exercised an Opt-Out Right for the Licensed 217 Products: Three Hundred Million Dollars (\$300,000,000), or (ii) if Sage *has exercised* an Opt-Out Right for the Licensed 217 Products: Five Hundred Twenty Five Million (\$525,000,000). It being understood in each case ((i) and (ii)) that the 217 Sales Milestone Payments will be additive, such that if more than one 217 Sales Milestone Event set forth in the either table above is achieved in the same Calendar Year and the same 217 Sales Milestone Event has not been achieved in any prior Calendar Year, then Biogen will pay to Sage each of the 217 Sales Milestone Payments for such achieved 217 Sales Milestone Events in a Calendar Year in

accordance with Section 9.7.1 (Licensed 217 Products Sales Milestones) (e.g., if Sage *has not* exercised an Opt-Out Right for the Licensed 217 Products, and, if in one Calendar Year, all three (3) 217 Sales Milestone Events of the table in Section 9.7.1.1(a) (Licensed 217 Products Sales Milestone Payments) are achieved and no 217 Sales Milestone Events has been achieved in any prior Calendar Year, then Biogen would pay Sage Three Hundred Million Dollars (\$300,000,000) in accordance with Section 9.7.3 (Payment Terms for Sales Milestone Payments)).

**9.7.2** *Licensed 324 Products Sales Milestones.*

**9.7.2.1** Subject to Section 9.7.3 (Payment Terms for Sales Milestone Payments), Biogen will make one-time, non-refundable milestone payments to Sage (each, a “**324 Sales Milestone Payment**”) when annual Net Sales of all Licensed 324 Products across all Indications in the Territory in a given Calendar Year first reach the Dollar threshold values indicated below in one of the applicable tables set forth under either Section 9.7.2.1(a) (Licensed 324 Products Sales Milestones) or 9.7.2.1(b) (Licensed 324 Products Sales Milestones) during the Term (each, a “**324 Sales Milestone Event**”):

(a) if Sage has not exercised an Opt-Out Right for the Licensed 324 Products:

<b>Non-Opt-Out Right 324 Sales Milestone Event</b>	<b>324 Sales Milestone Payment</b>
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]

(b) if Sage has exercised an Opt-Out Right for the Licensed 324 Products, then beginning in the next Calendar Year after the exercise of such Opt-Out Right:

<b>Opt-Out Right 324 Sales Milestone Event</b>	<b>324 Sales Milestone Payment</b>
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]
annual Net Sales of Licensed 324 Products in the Territory in a Calendar Year first equaling or exceeding \$[**]	[**]

(c) For clarity, the 324 Sales Milestone Payments will only each be paid once, such that the maximum total amount payable by Biogen to Sage under this Section 9.7.2 (Licensed 324 Product Sales Milestones) is either (i) if Sage *has not* exercised an Opt-Out Right for the Licensed 324 Products: Three Hundred Million Dollars (\$300,000,000), and (ii) if Sage *has exercised* an Opt-Out Right for the Licensed 324 Products: Five Hundred Twenty Five Million (\$525,000,000). It being understood in each case ((i) and (ii)) that the 324 Sales Milestone Payments will be additive, such that if more than one 324 Sales Milestone Event set forth in the either table above is

achieved in the same Calendar Year and the same 324 Sales Milestone Event has not been achieved in any prior Calendar Year, Biogen will pay to Sage the total amount of the 324 Sales Milestone Payments for such achieved 324 Sales Milestone Events in a Calendar Year in accordance with Section 9.7.2 (Licensed 324 Product Sales Milestones) (e.g., if Sage *has not* exercised an Opt-Out Right for the Licensed 324 Products, and, if in one Calendar Year, all three (3) 324 Sales Milestone Events of the table in Section 9.7.2.1(a) (Licensed 324 Products Sales Milestones) are achieved and no 324 Sales Milestone Events has been achieved in any prior Calendar Year, then Biogen would pay Sage Three Hundred Million Dollars (\$300,000,000) in accordance with Section 9.7.3 (Payment Terms for Sales Milestone Payments)).

**9.7.3** *Payment Terms for Sales Milestone Payments.* Biogen will provide Sage with written notice of the first achievement of each 217 Sales Milestone Event and each 324 Sales Milestone Event, and, if applicable, Sage will provide Biogen with written notice of the first achievement of each of 217 Sales Milestone Event set forth in the table in Section 9.7.1.1(a) (Licensed 217 Products Sales Milestones) and the first achievement of each of the 324 Sales Milestone Event set forth in the table in Section 9.7.2.1(a) (Licensed 324 Products Sales Milestones), in each case, no later than **[\*\*]** after such achievement, and will pay to Sage, as applicable, the corresponding 217 Sales Milestone Payment or 324 Sales Milestone Payment within **[\*\*]** after Biogen’s receipt of an invoice for the same from Sage, which invoice may be delivered only after receipt of notice of achievement of the applicable milestone event.

**9.8** **Licensed 217 Product and Licensed 324 Product Royalties.**

**9.8.1** *Biogen Territory Royalties.* During the Royalty Term for each Licensed 217 Product and each Licensed 324 Product, Biogen will make royalty payments to Sage based on aggregate annual Net Sales made, respectively, for each Licensed 217 Product and for each Licensed 324 Product in the Field in the Biogen Territory (in all cases, excluding the United States) by Biogen and its Related Parties in a given Calendar Year at the royalty rates set forth in the table below in this Section 9.8.1 (Biogen Territory Royalties) (such royalties, “**Biogen Territory Royalties**”):

<b>Annual Net Sales in a Given Calendar Year of a Licensed 217 Product or a Licensed 324 Product in the Biogen Territory</b>	<b>Royalty Rate Paid on the Portion of Annual Net Sales of a Licensed 217 Product in the Biogen Territory</b>	<b>Royalty Rate Paid on the Portion of Annual Net Sales of a Licensed 324 Product in the Biogen Territory</b>
Portion less than \$ <b>[**]</b>	<b>[**]</b> %	<b>[**]</b> %
Portion equal to or greater than \$ <b>[**]</b> but less than \$ <b>[**]</b>	<b>[**]</b> %	<b>[**]</b> %
Portion equal to or greater than \$ <b>[**]</b>	<b>[**]</b> %	<b>[**]</b> %

**9.8.2** *United States Royalties.* In the event that Sage has exercised an Opt-Out Right with respect to either or both of the Product Classes for the Licensed 217 Products or the Licensed 324 Products, as applicable, then from and after the Opt-Out Date for the applicable Product Class, during the remainder of the Royalty Term in the United States for each Licensed 217 Product or each Licensed 324 Product in the Product Class(es) for which Sage exercised the Opt-Out Right, Biogen will make royalty payments to Sage based on aggregate annual Net Sales made, respectively, for each such Licensed 217 Product or for each Licensed 324 Product in the Field in the United States by Biogen and its Related Parties in a given

Calendar Year at the royalty rates set forth in the table below in this Section 9.8.2 (Territory Royalties) (such royalties, the “United States Royalties”):

<b>9.8.3 Annual Net Sales in a Given Calendar Year of a Licensed Product in the United States</b>	<b>Royalty Rate Paid on the Portion of Annual Net Sales of a Licensed 217 Product in the Territory in the United States</b>	<b>Royalty Rate Paid on the Portion of Annual Net Sales of a Licensed 324 Product in the Territory in the United States</b>
Portion less than \$[**]	[**]%	[**]%
Portion equal to or greater than \$[**] but less than \$[**]	[**]%	[**]%
Portion equal to or greater than \$[**]	[**]%	[**]%

## **9.9 Royalty Reductions.**

**9.9.1** *Royalty Reduction for No Valid Claim.* Subject to Section [\*\*], on a Licensed Product-by-Licensed Product and country-by-country basis, if, during any Calendar Quarter prior to the expiration of the Royalty Term for a Licensed 217 Product or Licensed 324 Product (as applicable) in such country in the Biogen Territory, there is no Valid Claim of a Royalty Bearing Patent that would be infringed by the sale of such Licensed 217 Product or Licensed 324 Product (as applicable) in such country, then, for the remainder of the Royalty Term for such Licensed 217 Product or Licensed 324 Product (as applicable) in such country, the Biogen Territory Royalties or the United States Royalties, as applicable, will be reduced by [\*\*] percent ([\*\*]%).

**9.9.2** *Reduction for Generic Approval.* On a Licensed Product-by-Licensed Product and country-by-country basis in the Biogen Territory, commencing in the first Calendar Quarter in which Generic Competition occurs and continuing thereafter for the remainder of the Royalty Term for such Licensed Product in such country:

**9.9.2.1** if the Generic Competition in such country with respect to such Licensed Product during such Calendar Quarter equals or exceeds [\*\*] percent ([\*\*]%) but is less than [\*\*] percent ([\*\*]%), then the Biogen Territory Royalties or the United States Royalties, as applicable, for such Licensed Product will be reduced by [\*\*] percent ([\*\*]%).

**9.9.2.2** if the Generic Competition in such country with respect to such Licensed Product during such Calendar Quarter equals [\*\*] percent ([\*\*]%), the Biogen Territory Royalties or the United States Royalties, as applicable, for such Licensed Product (a) will be reduced by [\*\*]%) and (b) will be further reduced by [\*\*] percent ([\*\*]%) for each additional percentage increase in Generic Competition above [\*\*] percent ([\*\*]%). For example, if the Generic Competition in a country with respect to a Licensed Product during a Calendar Quarter equals [\*\*] percent ([\*\*]%), then the total reduction for the Biogen Territory Royalties or the United States Royalties, as applicable, for such Licensed Product would be [\*\*] percent ([\*\*]%).

**9.9.3** *Licensed Third Party Payments.* Subject to Section 9.9.4 (Cumulative Reductions Floor), for any agreement with a Third Party pursuant to which Biogen is granted rights (whether by acquisition or license) under (a) any Patents of such Third Party or (b) any Patents and Know-How of such Third Party inseparably, in each case ((a) and (b)), that are [\*\*], as applicable, a Licensed 217 Product or a Licensed 324 Product in a country in the Biogen Territory, Biogen may credit [\*\*] percent ([\*\*]%) of [\*\*]

specifically owed for such Licensed 217 Product or Licensed 324 Product, as applicable, made by Biogen to such Third Party under such agreement in a given Calendar Quarter (to the extent attributable to a Licensed Product) against [\*\*], as applicable, payable by Biogen to Sage in such Calendar Quarter.

**9.9.4** *Cumulative Reductions Floor.* In no event will the Biogen Territory Royalties or the United States Royalties, as applicable, otherwise due to Sage for any Licensed 217 Product or any Licensed 324 Product in a Calendar Quarter during the applicable Royalty Term for such Licensed 217 Product or Licensed 324 Product be reduced by more than [\*\*] percent ([\*\*]%) of the amount that would otherwise be due in such Calendar Quarter for such Licensed 217 Product or Licensed 324 Product as a result of the reductions set forth in Section 9.9.1 (Royalty Reduction for No Valid Claim) or Section 9.9.3 (Licensed Product Third Party Payments). [\*\*].

**9.10** **Other Amounts Payable.** With respect to any amounts owed under this Agreement by one Party to the other for which no other invoicing and payment procedure is specified in this Article 9 (Payments), within [\*\*] after the end of each Calendar Quarter, each Party will provide an invoice, together with reasonable supporting documentation, to the other Party for such amounts owed in respect of such Calendar Quarter. The owing Party will pay any undisputed amounts within [\*\*] of receipt of the invoice, and any disputed amounts owed by a Party will be paid within [\*\*] of resolution of the dispute.

**9.11** **Payment Terms.**

**9.11.1** *Manner of Payment.* All payments to be made by each Party (the “**Paying Party**”) to the other Party hereunder will be made in Dollars by wire transfer to such bank account as such other Party may designate in writing.

**9.11.2** *Reports and Royalty Payments.* All amounts payable by Biogen to Sage pursuant to Section 9.8 (Licensed 217 Product and Licensed 324 Product Royalties) will be paid within [\*\*] after the end of each Calendar Quarter when such amounts become payable. Each such payment of royalties by Biogen will be accompanied by a written report that includes, at a minimum, the following information for the applicable Calendar Quarter, each listed by Licensed 217 Product and Licensed 324 Product and by country of sale: [\*\*].

**9.11.3** *Records and Audits.*

**9.11.3.1** **Record Retention; Audits.** Each Party will keep complete, true, and accurate books and records in accordance with GAAP, in reasonable detail to permit the other Party to confirm the accuracy of all payments or costs reported hereunder for at least the preceding [\*\*] in relation to this Agreement, including in relation to Joint Development Costs, Joint Commercialization Costs, Joint Medical Affairs Costs, Manufacturing Costs, all FTE Costs, Out-of-Pocket Costs and other costs and expenses incurred in its performance under this Agreement, and Net Sales. Upon reasonable (but in any case no less than [\*\*] advance notice) by one Party (the “**Auditing Party**”) to the other Party (the “**Audited Party**”) and not more than [\*\*] and [\*\*] per audited period (in each case, except for cause), the Audited Party and its Affiliates will permit, and will cause their Sublicensees to permit, an independent certified public accounting firm of internationally-recognized standing (the “**Auditor**”), selected by the Auditing Party and reasonably acceptable to the Audited Party, to have access during normal business hours to such of the records of the Audited Party and its Affiliates and, if applicable, their Sublicensees, as may be reasonably necessary to verify the payments made or costs reported by the other Party and the related reports, statements and books of accounts, as applicable for any year ending not more than [\*\*] prior to the date of such request. The Auditor will enter a confidentiality agreement reasonably acceptable to the Audited Party governing the use and disclosure of the Audited Party’s information disclosed to

such firm, and such firm will disclose to the Auditing Party only whether information provided by the Audited Party to the Auditing Party as described in the preceding sentences was accurate and the specific details concerning any discrepancies, which information will be Confidential Information of the Audited Party.

**9.11.3.2**            **Audit Disputes.** Any disputes with respect to the findings of such Auditor may be referred by either Party to the dispute resolution procedure set forth in Section 15.3 (Dispute Resolution). If either Party is found to have been underpaid any amounts payable to such Party hereunder or to have overpaid to the other Party any amounts payable hereunder, then such first Party will be entitled to recover any undisputed discrepancy, plus interest as set forth in Section 9.11.9 (Interest Due), no later than [\*\*] after delivery to the Parties of the final report of the Auditor. The fees charged by the Auditor will be paid by the Auditing Party; *provided* that if the audit discloses a net underpayment of amounts owed or overreporting of expenses by the Audited Party of more than [\*\*] percent ([\*\*]%) of total amounts owed or expenses reported by the Audited Party for any Calendar Year period covered by the audit, then the Audited Party will pay the reasonable fees and expenses charged by the Auditor. The Auditing Party will treat all financial information disclosed by the Auditor pursuant to this Section 9.11.3 (Records Retention and Audits) as Confidential Information of the Audited Party for purposes of Article 10 (Confidentiality and Publication) of this Agreement, and will cause the Auditor to do the same.

**9.11.4**            *Currency Exchange.* With respect to annual Net Sales invoiced in Dollars, the annual Net Sales and the amounts due by the Paying Party to the other Party hereunder will be expressed in Dollars. When conversion of payments from any foreign currency is required to be undertaken by the Paying Party, the Dollar equivalent will be calculated using the Paying Party's then-current standard exchange rate methodology as applied in its external reporting for the conversion of foreign currency sales into Dollars.

**9.11.5**            *Taxes.*

**9.11.5.1**            *General.* Each Party will be responsible for all Taxes imposed on such Party's net income, or on net income allocated to such Party under applicable Law. To the extent one Party pays Taxes imposed on net income of the other Party, the other Party will reimburse the paying Party for any such Taxes paid. The amounts payable pursuant to this Agreement ("Payments") will not be reduced on account of any Taxes unless required by applicable Law. A payor Party will deduct and withhold from the Payments any Taxes that it is required by applicable Law to deduct or withhold including from subsequent Payments ("Withholding Taxes"), and any such Withholding Taxes shall be treated as having been paid to the payee pursuant to this Agreement; provided that the payor Party will provide the payee with written notice of the required withholding as promptly as reasonably practical (and in any event, no later than [\*\*]) prior to making such payment and will cooperate with the payee as provided in this Section 9.11.5 (Taxes) in order to mitigate the imposition of such Withholding Taxes. Notwithstanding the foregoing, if the recipient Party is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, or recovery of, applicable Withholding Tax, it may deliver to the payor Party or the appropriate Governmental Authority the prescribed forms necessary to reduce the applicable rate of withholding or to relieve the payor Party of its obligation to withhold Tax. In such case the payor Party will apply the reduced rate of withholding, or not withhold, as the case may be, provided that the payor Party is in receipt of evidence, in a form reasonably satisfactory to the payor Party of the recipient Party's entitlement to a reduced or no withholding rate at least [\*\*] prior to the time that the applicable Payment is due. If a payor Party withholds any amount, it will pay to the recipient Party the balance (for the avoidance of doubt, net of the withholding) when due, make timely payment to the proper taxing authority of the withheld amount, and send the recipient Party

proof of such payment within [\*\*] following that payment. The Parties will reasonably cooperate to reduce or eliminate any withholding required under applicable Law, and to provide the other with reasonable assistance to enable the recovery, as permitted by Law, of Withholding Taxes, with recovery to be for the benefit of the payee Party. Sage will provide a complete and accurate IRS Form W-9 to Biogen prior to payment of the due date of the Upfront Payment and will promptly provide a new properly executed IRS Form W-9 if information provided on the previous IRS Form W-9 changes or if an updated IRS Form W-9 or its equivalent is required by law or requested by Biogen. Based on the foregoing, the Parties acknowledge and agree that, as of the date hereof, no Withholding Taxes (other than with respect to the Federal Republic of Germany) are expected to be deducted or withheld from any Payments.

**9.11.5.2** *VAT.* It is understood and agreed between the Parties that any payments made under this Agreement are exclusive of VAT. Where VAT is properly added to a payment made under this Agreement, the payor Party will pay the amount of such VAT only on receipt of a valid Tax invoice (or, where there is no provision in the legislation for the jurisdiction concerned that a VAT invoice is required to be issued, a written demand containing such information as is customary in that jurisdiction) issued in accordance with the Laws and regulations of the country in which the VAT is chargeable. If in the event of any amendment to VAT Laws the sums invoiced without VAT in accordance with this Agreement become or are subject to VAT, then the applicable invoices will be deemed to be exclusive of VAT and the payor Party will, in addition to the sums payable, pay the recipient Party, on receipt of an updated, valid VAT invoice, the full amount of VAT chargeable thereon. The Parties acknowledge and agree that, as at the date of this Agreement, no VAT is expected to be charged by Sage on amounts payable by Biogen pursuant to this Agreement, as Sage is not required to account for VAT as at the date of this Agreement in relation to the services, rights and licenses provided by Sage to Biogen pursuant to this Agreement. Notwithstanding anything in this Agreement to the contrary, Sage agrees that prior to establishing a taxable presence for VAT outside the United States of America, assigning, delegating, sublicensing or otherwise transferring (to include by merger) its rights or obligations under this Agreement to an assignee, delegate, sublicensee or other transferee (including by operation of a merger) which would require a charge to VAT (other than VAT chargeable by a Government Authority of the United States of America) on amounts payable by Biogen under this Agreement (either singly or together referred to as a “**VAT Restructuring**”), Sage will: (a) consult with Biogen; and (b) take account of reasonable representations made by Biogen where Biogen is able to demonstrate to Sage’s reasonable satisfaction that Sage’s proposed assignee, delegate, sublicensee or other transferee would give rise to irrecoverable VAT costs for Biogen which would not otherwise exist in the absence of any act, default, omission or transaction involving Biogen.

**9.11.5.3** *Tax Actions.* Notwithstanding anything in this Agreement to the contrary, if an action (including but not limited to a VAT Restructuring, any assignment, delegation or sublicense of a Party’s rights or obligations under this Agreement (including a subsequent transfer following such assignment, delegation or sublicense), a change or adoption of a Tax reporting position, a change in the corporate or tax status or location of a Party, or any failure to comply with applicable Laws or filing or record retention requirements) by a Party (a “**Tax Action**”) leads to the imposition or incidence of any Withholding Tax liability or VAT on the other Party that would not have been imposed in the absence of such Tax Action or in an increase in such liability above the liability that would have been imposed in the absence of such Tax Action (such additional or increased Withholding Tax liability or VAT, “**Incremental Taxes**”), such Party will indemnify and hold harmless the other Party (the “**Non-Acting Party**”) from any such Incremental Taxes (except to the extent that the other Party can reclaim or otherwise offset or recover such Incremental Taxes, *provided* that such other Party will be reimbursed for any reasonable out of pocket costs incurred in the reclaim). The indemnification obligation described in the preceding sentence shall



not apply, however, to the extent such Incremental Taxes (a) would not have been imposed but for a prior Tax Action taken by the Non-Acting Party or (b) are attributable to a the failure of the Non-Acting Party to comply with the requirements of this Section 9.11.5 (Taxes).

#### **9.11.6** Payment Allocation.

**9.11.6.1** Subject to the remainder of this Section 9.11.6 (Payment Allocation), payments under this Agreement will be paid by BIMA and BIG separately and in such proportions as determined solely by Biogen in its reasonable discretion and shall be invoiced separately by Sage; *provided* that separate invoices will only be provided by Sage if Biogen provides details of the allocations of such amounts between BIMA and BIG in writing and reasonably in advance of each such payment becoming due and failure to provide such invoices will not affect Biogen's obligations to make any such payments as and when due.

**9.11.6.2** With respect to the upfront payment described in Section 9.1 (Upfront Fee), BIG will pay a portion of such amount in consideration of the rights granted outside of the United States which will equal [\*\*] Dollars (\$[\*\*]), and BIMA will pay a portion of such amount in consideration of the rights granted in the United States which will equal [\*\*] Dollars (\$[\*\*]).

**9.11.6.3** With respect to the payments for the 217 Regulatory/Commercial Milestone Payments in Section 9.6.1 and the 324 Regulatory/Commercial Milestone Payments in Section 9.6.2 (Licensed 324 Products *Regulatory/Commercial Milestones*), BIG will pay a percentage of each such amount in consideration of the rights granted outside of the United States and BIMA will pay a percentage each such amount in consideration to the rights granted in the United States, such percentages, in each case, to be determined by Biogen at the time at which such amounts are due. Notwithstanding the foregoing, [\*\*].

**9.11.6.4** With respect to the 217 Sales Milestone Payments in Section 9.7.1 (Licensed 217 Products Sales Milestones) and 324 Sales Milestone Payments in and Section 9.7.2 (Licensed 324 Products Sales Milestones), BIG will pay a percentage of each such amount in consideration of the rights granted outside of the United States, and BIMA will pay a percentage of each such amount in consideration to the rights granted in the United States, such percentages, in each case, to be determined by Biogen at the time at which such amounts are due.

**9.11.6.5** With respect to Biogen Territory Royalties and the Territory Royalties, BIG will pay such Biogen Territory Royalties described in Section 9.8.1 (Biogen Territory Royalties), and in the event that Sage has exercised an Opt-Out Right with respect to either or both of the Product Classes for the Licensed 217 Products or the Licensed 324 Products, as applicable, then from and after the Opt-Out Date for the applicable Product Class, during the remainder of the Royalty Term for each Licensed 217 Product or each Licensed 324 Product in the Product Class(es) for which Sage exercised the Opt-Out Right, BIMA will pay such United States Royalties described in Section 9.8.2 (United States Royalties).

**9.11.6.6** With respect to all payments set forth in this Article 9 (Payments) that are not described in Section 9.11.6.2 (Payment Allocation) through Section 9.11.6.5 (Payment Allocation) above, BIG will pay such amount in consideration of the rights granted outside of the United States and BIMA will pay such amount in consideration to the rights granted in the United States, such percentages, in each case, to be determined by Biogen at the time in which such amounts are due.

**9.11.6.7** For clarity, nothing in this Section 9.11 (Payment Terms) is intended to limit Section 15.15 (Coordination between BIMA and BIG) of this Agreement.

**9.11.7** *Blocked Payments.* In the event that, by reason of applicable Law in any country, it becomes impossible or illegal for the Paying Party to transfer, or have transferred on its behalf, payments owed by the Paying Party to the other Party hereunder, the Paying Party will promptly notify the other Party of the conditions preventing such transfer and such payments will be deposited in local currency in the relevant country to the credit of the other Party in a recognized banking institution designated by the other Party or, if none is designated by the other Party within a period of [\*\*], in a recognized banking institution selected by the Paying Party, as the case may be, and identified in a written notice given to the other Party.

**9.11.8** *Right of Offset.* Upon notice to the other Party, each Party will have the right to offset any undisputed Payment not paid within the specified period owed by such Party to the other Party under this Agreement, including in connection with any breach or indemnification obligation by such Party, against any undisputed Payments owed by the other Party to such Party under this Agreement. Such offsets will be in addition to any other rights or remedies available to the offsetting Party under this Agreement and applicable Laws.

**9.11.9** *Interest Due.* The Paying Party will pay the other Party interest on any undisputed payments that are not paid on or before the date such payments are due under this Agreement at a rate equal to [\*\*] percentage points ([\*\*]%) per annum or, if lower, the maximum applicable legal rate, calculated on the total number of days payment is delinquent.

## 10. CONFIDENTIALITY AND PUBLICATION

### **10.1** Nondisclosure and Non-Use Obligations.

**10.1.1** All Confidential Information disclosed by one Party (the “**Disclosing Party**”) to the other Party (the “**Receiving Party**”) under this Agreement will be maintained in confidence by the Receiving Party and will not be disclosed to a Third Party or used for any purpose except pursuant to the licenses granted under this Agreement or as otherwise set forth herein, without the prior written consent of the Disclosing Party. Notwithstanding any provision to the contrary set forth in this Agreement, Confidential Information will not include any information that:

- (a) is known by the Receiving Party at the time of its receipt from the Disclosing Party, and not through a prior disclosure by the Disclosing Party, as documented by the Receiving Party’s business records;
- (b) is known to the public before its receipt from the Disclosing Party, or thereafter becomes generally known to the public through no breach of this Agreement by the Receiving Party;
- (c) is subsequently disclosed to the Receiving Party by a Third Party who is not known by the Receiving Party to be under an obligation of confidentiality to the Disclosing Party; or
- (d) is developed by the Receiving Party independently of Confidential Information received from the Disclosing Party, as documented by the Receiving Party’s business records.

For clarity, and notwithstanding any provision to the contrary set forth in this Agreement, [\*\*]. Specific aspects or details of Confidential Information will not be deemed to be within the public domain or in the possession of the Receiving Party merely because the Confidential Information is encompassed by more general information in the public domain or in the possession of the Receiving Party. Further, any combination of Confidential Information will not be considered in the public domain or in the possession of the Receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the Receiving Party unless the combination and its principles are in the public domain or in the possession of the Receiving Party.

The terms and conditions of this Agreement are hereby deemed to be the Confidential Information of each Party.

**10.1.2** *Permitted Disclosures.* Notwithstanding the obligations of confidentiality and non-use set forth in Section 10.1.1 (Nondisclosure and Non-Use Obligations) above, a Receiving Party may provide Confidential Information disclosed to it and disclose the existence and terms and conditions of this Agreement, in each case, as may be reasonably required in order to perform its obligations or to exercise its rights under this Agreement, and to the extent such disclosure is:

**10.1.2.1** to its Affiliates, Sublicensees or licensees, and their employees, directors, agents, consultants, or advisors to the extent necessary for the potential or actual performance of its obligations or exercise of its rights under this Agreement, in each case, who are under an obligation of confidentiality with respect to such information that is no less stringent than the terms and conditions of this Section 10.1 (Nondisclosure and Non-Use Obligations);

**10.1.2.2** to the Regulatory Authorities in connection with any filing, application or request for Regulatory Approval in accordance with the terms of this Agreement; *provided* that reasonable measures shall be taken to assure confidential treatment of such Confidential Information to the extent practicable and consistent with applicable Law;

**10.1.2.3** made in connection with the Prosecution and Maintenance of Sage Licensed Technology or Biogen Licensed Technology in an effort to secure, maintain, defend or enforce Patents, as contemplated by this Agreement, or, with respect to such activities only, otherwise with the prior written consent of the disclosing Party's intellectual property counsel;

**10.1.2.4** to bring or defend litigation and to enforce Patents in connection with the Receiving Party's rights and obligations pursuant to this Agreement;

**10.1.2.5** subject to Section 10.1.2.8 (Permitted Disclosures), required to be disclosed by applicable Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or listing entity;

**10.1.2.6** (a) with respect to the terms and conditions of this Agreement, any *bona fide* actual or prospective acquirers, underwriters, investors, lenders, other financing sources, licensors, Sublicensees or licensees and to employees, directors, agents, consultants or advisors of such Third Party, and (b) with respect to any other Confidential Information of the other Party, any *bona fide* actual or prospective acquirers, licensors, Sublicensees or licensees and to employees, directors, agents, consultants or advisors of such Third Party, *provided* that any entity or individual receiving Confidential Information under clause (a) or (b) has a need to know such information and is under obligations of confidentiality and non-use with respect to such information that are no less

stringent than the terms and conditions of this Section 10.1 (Nondisclosure and Non-Use Obligations) (but of duration customary in confidentiality agreements entered into for a similar purpose); and

**10.1.2.7** to any Third Party to the extent a Party is required to do so pursuant to the terms and conditions of an in-license agreement with such Third Party relating to the intellectual property rights sublicensed to such Party hereunder, *provided* that any such Third Party receiving Confidential Information is under obligations of confidentiality and non-use with respect to such information that are no less stringent than the terms and conditions of this Section 10.1 (Nondisclosure and Non-Use Obligations).

**10.1.2.8** if a Party, after consultation with counsel, determines it is required by Law to disclose Confidential Information of the other Party that is subject to the confidentiality or non-disclosure provisions of this Section 10.1 (Nondisclosure and Non-Use Obligations), then such Party will promptly inform the other Party of the disclosure that is being sought (and to the extent possible at least [\*\*] notice) in order to provide the other Party an opportunity to challenge or limit the disclosure and will reasonably cooperate with the other Party to do so. In the event that no such protective order or other remedy is obtained, or the Disclosing Party waives compliance with certain terms of this Article 10 (Confidentiality And Publication), then the Receiving Party will furnish only that portion of Confidential Information that the Receiving Party is advised by counsel is legally required to be disclosed. Notwithstanding Section 10.1.1 (Nondisclosure and Non-Use Obligations), Confidential Information that is permitted or required to be disclosed will remain otherwise subject to the confidentiality and non-use provisions of this Section 10.1 (Nondisclosure and Non-Use Obligations). If either Party concludes based on the reasonable opinion of counsel that a copy of this Agreement must be filed with the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States, such Party will, within a reasonable time prior to any such filing (and to the extent possible at least [\*\*] prior to any such filing), provide the other Party with a copy of this Agreement showing any provisions hereof as to which the Party proposes to request confidential treatment, will provide the other Party with an opportunity to comment on any such proposed redactions and to suggest additional redactions, and will take such Party's reasonable comments into consideration before filing such copy of this Agreement and use reasonable efforts to have terms identified by such other Party afforded confidential treatment by the applicable regulatory agency.

## **10.2 Publication and Publicity.**

**10.2.1** *Publication.* [\*\*]. Each Party via the Joint Publications Working Group will have the right to propose additions or other amendments to an existing Publications Plan for approval by the JSC. The Joint Publications Working Group will determine which of Sage or Biogen will have the first right (but not the obligation) to be responsible for each Joint Publication contemplated in each Publication Plan (such appointed Party, the "**Lead Publishing Party**"); *provided, however,* that, unless otherwise agreed by the Joint Publications Working Group in the Publications Plan, Sage will be the Lead Publishing Party for all Joint Publications contemplated in the applicable Publications Plan related to the Ongoing 217 Studies or the KINETIC Study. Upon Biogen becoming the Regulatory Lead Party with respect to the applicable Product Class, the Joint Publications Working Group will determine which of the Parties will be the Lead Publishing Party with respect to Joint Publications, including those related to the Ongoing 217 Studies or the KINETIC Study, as applicable. In the event that the Lead Publishing Party elects not to exercise such right with respect to a certain Publication, the responsibility for such Publication will pass to the other Party. [\*\*].

**10.2.2** *Right to Review.* Each Party will have the right to review any Publication that contains results arising from the performance of Development, Commercialization or Medical Affairs Activities with respect to any Licensed Product or that includes Confidential Information of the non-publishing Party. The publishing Party will provide the other non-publishing Party the opportunity to review such proposed Publication at least [\*\*] prior to the earlier of its intended submission for publication or publication, and the publishing Party will consider in good faith any reasonable and timely comments submitted by the non-publishing Party (it being understood and agreed that if there is a material amendment to such Publication after the publishing Party has provided such Publication to the non-publishing Party, such reviewing period will be extended to ensure that at least [\*\*] remain for the non-publishing Party to review subsequent to the date the non-publishing Party received the amended Publication). Further, the non-publishing Party will have the right (a) to propose modifications to the Publication to remove Confidential Information solely of such non-publishing Party, in which case the publishing Party will remove such Confidential Information solely of the non-publishing Party identified by the non-publishing Party, or (b) to request a reasonable delay in Publication in order to protect patentable information, in which case the publishing Party will delay submission for a period of [\*\*] (or such other period as may be mutually agreed by the Parties in writing) to enable the non-publishing Party to file Patent applications protecting the non-publishing Party's rights in such information. The publishing Party subsequently will provide the non-publishing Party a copy of the Publication at the time of its submission. Without limiting the foregoing, each publishing Party agrees to acknowledge the contributions of the other Party and the employees of the other Party, in all Publications, as scientifically appropriate. After the release of any Publication by a Party in accordance with this Section 10.2 (Publication and Publicity), such Party may further disclose the information contained in such Publication without the need for further notice to, or review by, the other Party under this Section 10.2.2 (Publication and Publicity) or otherwise. In the event of any dispute between the Parties with respect to the contents of any Joint Publication or any Biogen Publication, the Parties will submit such dispute to the Joint Publications Working Group to determine resolution.

**10.2.3** *Publicity.* Except as set forth in Section 10.1 (Nondisclosure and Non-Use Obligations), Section 10.2.1 (Publication) or Section 10.3 (Press Release, Public Announcements and Other Public Disclosure) and in this Section 10.2.3 (Publicity), the terms and conditions of this Agreement may not be disclosed by either Party, and neither Party will use the name or Trademark of the other Party or its employees in any publicity, news release or other disclosure relating to this Agreement, its subject matter, or the activities of the Parties under this Agreement without the prior express written permission of the other Party, *provided* that the Party making such disclosure or use of the name or Trademark of the other Party or its employees, not covered by Section 10.1 (Nondisclosure and Non-Use Obligations), Section 10.2.1 (Publication) or Section 10.3 (Press Release, Public Announcements and Other Public Disclosure) and in this Section 10.2.3 (Publicity), obtains the prior consent (not to be unreasonably withheld, conditioned or delayed) of such other Party if such disclosure references such other Party and otherwise complies with Section 10.1 (Nondisclosure and Non-Use Obligations) or (b) as expressly permitted by the terms and conditions hereof. Notwithstanding the foregoing, either Party may disclose information (a) that has already been made public through a press release, publication or other public statement made in accordance with the terms of this Agreement so long as such information remains true, correct and current, or (b) in connection with disclosures under a joint communication plan agreed upon by the Parties. The Parties, through their respective heads of Corporate Communications and Investor Relations, will agree on procedures to operationalize the provisions of Section 10.3 (Press Release, Public Announcements and Other Public Disclosure) and in this Section 10.2.3 (Publicity).

### **10.3 Press Release, Public Announcements and Other Public Disclosure.**

**10.3.1** On the Execution Date, the Parties will issue the joint press release substantially in the form attached as in Schedule 10.3.1 (Press Release).

**10.3.2** Except as provided in Section 10.2.3 (Publicity) or this Section 10.3 (Press Release), neither Party will issue a press release, public announcement or other public disclosure relating to this Agreement or the Parties' activities hereunder without the prior written approval of the other Party (such approval not to be unreasonably withheld, conditioned or delayed), except that a Party may (a) once a press release, public statement or other public statement has been made as permitted under the terms of this Agreement, make subsequent public disclosure of the information contained in such press release, publication or other public statement so long as such information remains true, correct and current, (b) make a disclosure expressly permitted in accordance with this Article 10 (Confidentiality and Publication), and (c) make any such other disclosure that is, in the opinion of the Receiving Party's counsel, required by applicable Law, including by the rules or regulations of the United States Securities and Exchange Commission or similar regulatory agency in a country other than the United States or of any stock exchange or listing entity on which securities of the Receiving Party are listed, *provided* that, solely with respect to clause (c), the Party issuing such press release, public announcement or other public disclosure gives reasonable prior written notice to the other Party of and the opportunity to comment on such press release, public announcement or other public disclosure will submit the same in writing to the other Party as far in advance as reasonably practicable (and in no event less than [\*\*] prior to the anticipated date of disclosure, unless such proposed disclosure is required under applicable Law or the rules of an applicable securities exchange, in each case, to be made in less than [\*\*]) so as to provide the Disclosing Party a reasonable opportunity to comment thereon.

## **11. REPRESENTATIONS, WARRANTIES AND COVENANTS**

**11.1 Mutual Representations and Warranties as of the Execution Date and Effective Date.** Each Party represents and warrants to the other Party that, as of the Execution Date and the Effective Date:

**11.1.1** such Party is a corporation duly organized, validly existing and in good standing under the laws of its jurisdiction of incorporation or formation;

**11.1.2** such Party has all requisite corporate power and corporate authority to enter into this Agreement and to carry out its obligations under this Agreement;

**11.1.3** all requisite corporate action on the part of such Party, its directors and stockholders required by applicable Law for the authorization, execution and delivery by such Party of this Agreement, and the performance of all obligations of such Party under this Agreement, has been taken;

**11.1.4** the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action, and compliance with the provisions of this Agreement, by such Party do not and will not: (a) violate any provision of applicable Law or any ruling, writ, injunction, order, permit, judgment, determination, award or decree of any Governmental Authority, (b) constitute a breach of, or default under (or an event which, with notice or lapse of time or both, would become a default under) or conflict with, or give rise to any right of termination, cancellation or acceleration of, any agreement, arrangement, contractual obligation or instrument, whether written or oral, by which such Party or any of its assets are bound, or (c) violate or conflict with any of the provisions of such Party's organizational documents (including any articles or memoranda of organization or association, charter, bylaws or similar documents); and

**11.1.5** except for any filings that may be required to comply with Antitrust Law, no consent, approval, authorization, license, exemption or other order of, or filing or registration with, or notice to, any Governmental Authority or other Third Party is required or will be necessary to be obtained or made by such Party for, or in connection with the authorization, execution and delivery by such Party of this

Agreement or any other agreement or instrument executed in connection herewith, or for the performance by such Party of its obligations under this Agreement and such other agreements;

**11.1.6** this Agreement is a legal, valid, and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency, or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance, and general principles of equity (whether enforceability is considered a proceeding at law or equity);

**11.1.7** such Party is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any material respect with the terms of this Agreement;

**11.1.8** neither party nor any of its employees nor to its knowledge, any of the agents performing hereunder, has ever been, is currently, or is the subject of a proceeding that could lead to it or such employees or agents becoming, as applicable, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual. For purposes of this provision, the following definitions shall apply:

**11.1.8.1** A “**Debarred Individual**” is an individual who has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from providing services in any capacity to a Person that has an approved or pending drug or biological product application.

**11.1.8.2** A “**Debarred Entity**” is a corporation, partnership or association that has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from submitting or assisting in the submission of any abbreviated drug application, or a subsidiary or Affiliate of a Debarred Entity.

**11.1.8.3** An “**Excluded Individual**” or “**Excluded Entity**” is (i) an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal health care programs such as Medicare or Medicaid by the Office of the Inspector General (OIG/HHS) of the U.S. Department of Health and Human Services, or (ii) is an individual or entity, as applicable, who has been excluded, debarred, suspended or is otherwise ineligible to participate in federal procurement and non-procurement programs, including those produced by the U.S. General Services Administration (GSA).

**11.1.8.4** A “**Convicted Individual**” or “**Convicted Entity**” is an individual or entity, as applicable, who has been convicted of a criminal offense that falls within the ambit of 21 U.S.C. §335a (a) or 42 U.S.C. §1320a - 7(a), but has not yet been excluded, debarred, suspended or otherwise declared ineligible.

**11.2** **Representations and Warranties of Sage as of the Execution Date and Effective Date.** Sage represents and warrants to Biogen that, as of the Execution Date and the Effective Date:

**11.2.1** to the knowledge of Sage, the Principal Mode of Action for (a) the SAGE-217 molecule described on Schedule 1.1.261, (b) the SAGE-324 molecule described on Schedule 1.1.262, and (c) the SAGE-[\*] molecule described on Schedule 1.1.260, in each case ((a)–(c)), is positive allosteric modulation of the GABA<sub>A</sub> Receptor;

**11.2.2** (a) Sage or one of its Affiliates is the sole and exclusive owner or exclusive licensee of the Sage Licensed Technology in the Field, and (b) to Sage’s knowledge: (i) Sage owns or has the right to use all Sage Technology necessary to conduct the activities under this Agreement with respect

to the Sage Molecules and Licensed Products (for each, as it exists as of the Execution Date or the Effective Date, as applicable); and (ii) the Development or Commercialization, as contemplated as of the Execution Date or the Effective Date, as applicable, of any Sage Molecule or Licensed Products will not conflict with any other license or agreement to which Sage or any of its Affiliates is a party;

**11.2.3** none of the issued Sage Licensed Patents existing as of the Execution Date or the Effective Date, as applicable, have been adjudged, in a final and non-appealable decision, invalid, unenforceable or unpatentable in whole or part by any Governmental Authority of competent jurisdiction, and to the knowledge of Sage, all such issued Sage Licensed Patents existing as of the Execution Date and the Effective Date are valid and enforceable;

**11.2.4** to the knowledge of Sage, the Development, Manufacture and Commercialization, each as contemplated by Sage and its Affiliates as of the Execution Date or the Effective Date, as applicable, of, respectively, the Licensed 217 Products and the Licensed 324 Products (for each, as such product exists as of the Execution Date or Effective Date, as applicable) in the Field in the Territory does not infringe, misappropriate or otherwise violate any valid and enforceable issued Patent or any other intellectual property right of any Third Party; and no written claim has been filed, or to Sage's knowledge, is or has been threatened in writing, against it by any Third Party alleging that the conception, development, or reduction to practice of the Sage Licensed Technology existing as of the Execution Date or the Effective Date, as applicable, owned by Sage involve the misappropriation of trade secrets or other violation of the rights or property of any Person;

**11.2.5** (a) the Sage Licensed Technology (including the Sage Licensed Patents listed on Schedule 1.1.268 (Sage Licensed Patents as of the Execution Date)) constitutes all of the Patents and Know-How Controlled by Sage or any of its Affiliates that are necessary for the Development, Manufacture or Commercialization, each as contemplated by Sage and its Affiliates as of the Execution Date or the Effective Date, as applicable, of, respectively, the Licensed 217 Products and the Licensed 324 Products (for each, as such product exists as of the Execution Date or the Effective Date, as applicable) in the Field in the Territory; (b) as of the Execution Date, Sage does not own or hold rights to any Patents that would otherwise qualify as a Sage Licensed Patent but for the fact that Sage does not Control such Patent; and (c) except as otherwise noted on Schedule 1.1.268 (Sage Licensed Patents as of the Execution Date), Sage exclusively owns all rights, title and interests in and to all Sage Licensed Patents existing as of the Execution Date or the Effective Date, as applicable;

**11.2.6** to Sage's knowledge, the Sage Licensed Patents with respect to which Sage controls Prosecution and Maintenance activities, have been prosecuted in the respective patent offices in the Territory in accordance with applicable Law;

**11.2.7** (a) all fees required to be paid in order to maintain a Patent in any jurisdiction where a Sage Licensed Patent has issued and with respect to which Sage controls Prosecution and Maintenance activities have been timely paid, and (b) to Sage's knowledge, all fees required to be paid in order to maintain a Patent in any jurisdiction where any other Sage Licensed Patent has issued have been timely paid, and to Sage's knowledge, the Sage Licensed Patents that have issued are subsisting, valid and enforceable;

**11.2.8** the inventorship of the Sage Licensed Patents is properly identified on each issued Patent or Patent application (in the form such patent application exists as of the Execution Date or the Effective Date, as applicable) within the existing Sage Licensed Patents;



**11.2.9** Sage has not previously assigned, transferred, conveyed or granted any license or other rights under the Sage Licensed Technology that would conflict with or limit the scope of any of the rights or licenses granted to Biogen hereunder;

**11.2.10** Sage's rights, title and interests to all Sage Licensed Technology are free of any lien or security interest;

**11.2.11** Sage has conducted, and to Sage's knowledge, its contractors and consultants have conducted, all Development and Manufacturing of the Sage Molecules in all material respects in accordance with applicable Law;

**11.2.12** Sage has obtained, or caused its Affiliates, as applicable, to have obtained, assignments from the inventors of any issued Patents within the Sage Licensed Technology, of all inventorship rights to such issued Patents within the Sage Licensed Technology, and, to Sage's knowledge, all such assignments are valid and enforceable;

**11.2.13** except for Existing Sage Agreements, there are no Third Party agreements pursuant to which Sage is granted an exclusive license under or otherwise Controls any Patents or Know-How included in the Sage Licensed Technology, and no Third Party has any rights, title or interests in or to, or any license under, any such Sage Licensed Technology that would conflict with the rights and licenses granted to Biogen hereunder;

**11.2.14** Schedule 1.1.110 (Existing Sage Agreements and Provisions) contains a true and complete list of all Existing Sage Agreements, and Sage has provided Biogen with a redacted copy of each Existing Sage Agreements, and each such agreement is in full force and effect, and no written notice of default or termination has been received or given under any such agreement, and, to Sage's knowledge, there is no act or omission by Sage or its Affiliates that would provide a right to terminate any such agreement;

**11.2.15** Sage and its Affiliates have taken commercially reasonable measures consistent with industry practices to protect the secrecy, confidentiality and value of all Sage Licensed Know-How that constitutes trade secrets under applicable Law (including requiring all employees, consultants and independent contractors to execute binding and enforceable agreements requiring all such employees, consultants, and independent contractors to maintain the confidentiality of such Sage Licensed Know-How), and, to Sage's knowledge, such Sage Licensed Know-How has not been used or disclosed to any Third Party except pursuant to such confidentiality agreements, and to Sage's knowledge, there has not been a material breach by any party to such confidentiality agreements;

**11.2.16** Sage has furnished or made available to Biogen (a) all information requested by Biogen in connection with the due diligence process, (b) all material safety and efficacy data, and (c) all material Regulatory Materials and other material correspondence with Regulatory Authorities, in each case ((a) through (c)), concerning the Sage Molecules, the Licensed Products (in each case in the form being Developed by Sage or any of its Affiliates as of the Execution Date or the Effective Date, as applicable) and the Sage Licensed Technology. To the knowledge of Sage, all such information and data, Regulatory Materials and other correspondence with Regulatory Authorities is accurate, complete and true in all material respects;

**11.2.17** except as set forth in Schedule 11.2.17 (Proceedings), no Proceeding, settlement, arbitration, citation, summons, or subpoena of any nature, civil, criminal, regulatory or otherwise, in law or in equity, has been brought or obtained, is pending, or, to the knowledge of Sage, threatened, against Sage or any of its Affiliates or relating to any of the Sage Licensed Technology,

including: (a) challenging the ownership, scope, duration, validity, enforceability, priority or right to the Sage Licensed Patents (including, by way of example, through the institution of or written threat of institution of interference, *inter partes* review, reexamination, protest, opposition, nullity, or similar invalidity proceeding before the United States Patent and Trademark Office or any foreign patent authority or court), (b) challenging or seeking to deny or restrict, any rights of Sage or any of its Affiliates in any Sage Licensed Technology and not already covered by clause (a), or (c) alleging that the use of any Sage Licensed Technology, or the disclosing, copying, making, or licensing of the Sage Licensed Technology, or the Development, Manufacture or Commercialization of the Sage Molecules or Licensed Products as contemplated herein, does or will misappropriate, infringe or otherwise violate, conflict with or interfere with any issued Patents or other intellectual property or proprietary right of any Third Party; *provided, however*, that, "Proceeding" for purposes of the representations and warranties of clauses (a) and (b) excludes office actions or similar communications issued by any patent office or comparable registration authority in the ordinary course of prosecution of any patent application within the Sage Licensed Patents; and

**11.2.18** to the knowledge of Sage, no Person is infringing or threatening to infringe or misappropriating or threatening to misappropriate or otherwise violating or threatening to violate Sage Licensed Technology, or has infringed, misappropriated or otherwise violated any Sage Licensed Technology in the Field in the Territory.

**11.3 Warranty Disclaimer.** EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY REPRESENTATION OR EXTENDS ANY WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER WARRANTIES, WHETHER WRITTEN OR ORAL, EXPRESS OR IMPLIED, TO THE OTHER PARTY WITH RESPECT TO ANY PATENTS, INFORMATION, KNOW-HOW, OTHER INTELLECTUAL PROPERTY, MATERIALS, LICENSED PRODUCTS, GOODS, SERVICES, RIGHTS OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND HEREBY DISCLAIMS ALL IMPLIED WARRANTIES OF QUALITY, MERCHANTABILITY, NONINFRINGEMENT, AND FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO ANY AND ALL OF THE FOREGOING. EACH PARTY HEREBY DISCLAIMS ANY REPRESENTATION OR WARRANTY THAT THE DEVELOPMENT, MANUFACTURE OR COMMERCIALIZATION OF ANY LICENSED PRODUCT PURSUANT TO THIS AGREEMENT WILL BE SUCCESSFUL.

#### **11.4 Certain Covenants.**

**11.4.1 Compliance.** Each Party and its Related Parties will conduct all activities under this Agreement, including the Development, Manufacture, performance of Medical Affairs Activities and Commercialization of the Licensed Products in the Territory, in accordance in all material respects with all applicable Laws.

**11.4.2 No Debarment.** Each Party will use reasonable efforts to not use, in any capacity in connection with the exercise of its rights or the performance of its obligations under this Agreement, any Person that has been debarred pursuant to Section 306 of the FD&C Act, as amended, or that is the subject of a conviction described in such section. Each Party agrees to inform the other Party in writing immediately if it or any Person that is performing activities under this Agreement, is debarred or is subject to debarment or is the subject of a conviction described in Section 306 of the FD&C Act, or if any Proceeding is pending or, to the best of the notifying Party's knowledge, is threatened, relating to the debarment or conviction of the notifying Party or any Person or entity used in any capacity by such Party or any of its Affiliates in connection with the exercise of its rights or the performance of its obligations under this Agreement.

**11.4.3** *Conflicting Transactions.* During the Term, Sage will not, and will cause its Affiliates not to, enter into any agreement (or amend any agreement that Sage is a party to as of the Execution Date) granting any license or other right under any Sage Licensed Technology that is inconsistent with this Agreement. During the Term, Biogen will not, and will cause its Affiliates not to, enter into any agreement (or amend any agreement that Biogen is a party to as of the Execution Date) granting any license or other right under the Biogen Background Technology, Biogen Collaboration Technology or Biogen's interest in the Joint Collaboration Technology that is inconsistent with this Agreement.

## **11.5 Additional Covenants of the Parties.**

**11.5.1** Sage will not assign, transfer, convey or grant any license or other rights to its rights, title and interests in or to the Sage Licensed Technology or any Sage Molecule that would conflict with or limit the scope of any of the options, rights or licenses granted to Biogen under this Agreement, and Sage and its Affiliates will remain the sole and exclusive owner or exclusive licensee, as applicable, of the Sage Licensed Technology in the Field in the Territory. Biogen will retain Control of the Biogen Licensed Technology incorporated into any Licensed Product so as not to materially and adversely affect the rights granted to Sage under this Agreement.

**11.5.2** Sage will not, directly or indirectly, alone, with or through any other Person, cause, induce, assist, authorize, or otherwise participate in any Proceeding against Biogen or its Affiliates based upon any assertion of direct or indirect infringement, due to Biogen or its Affiliates' performance of its or their permitted activities under this Agreement, of any Patents that are Controlled by Sage or any of its Affiliates (solely or jointly with any Third Party) that would be Sage Licensed Patents but for Sage's failure to use the subject matter claimed in such Patents at any time during the Term by Sage or any of its Affiliates in connection with the performance of any of the Joint Program Activities for a Licensed Product.

**11.5.3** Except with respect to any Securitization Transaction entered into by Sage in accordance with Section 15.1.2 (Securitization), Sage will not, and will cause its Affiliates not to incur or permit to exist, with respect to any Sage Licensed Technology, any lien, encumbrance, charge, security interest, mortgage, liability, or other restriction (including in connection with any indebtedness) that would conflict with any of the rights or licenses granted to Biogen under this Agreement.

**11.5.4** with respect to any Existing Sage Agreement or In-License Agreement entered into by Sage or its Affiliates after the Execution Date and to the extent relevant to the Profit-Share Territory, and with respect to any In-License Agreement entered into by Biogen or its Affiliates after the Execution Date: (a) such Party will not breach any such agreement in a manner that would give rise to the right of any Third Party to terminate such agreement; (b) such Party will promptly notify the other of any such breach by such Party or a Third Party of any such agreement, in each case, of which such Party is aware; and (c) in the event of any such breach by such Party that is not cured within [\*\*] after written notice to the other, (i) such Party will permit the other to cure such breach on such Party's behalf upon the other's reasonable written request, and (ii) the other may offset any reasonable amounts paid to cure such breach against amounts otherwise payable by the other to such Party under this Agreement;

**11.5.5** neither Party will amend, modify or terminate, in the case of Sage, any Existing Sage Agreement or In-License Agreement entered into by Sage or its Affiliates after the Execution Date, or, to the extent relevant to the Profit-Share Territory in the case of Biogen, any In-License Agreement entered into by Biogen or its Affiliates after the Execution Date, in a manner that would adversely affect the other Party's rights or licenses under this Agreement without first obtaining such other Party's written consent, which consent may be withheld in such other Party's sole discretion; and

**11.5.6** if a Party, or any of its employees (and to the extent a Party is aware of the situation, its agents performing hereunder), became, become or are the subject of a proceeding that could lead to a Person becoming, as applicable, a Debarred Entity or Debarred Individual, an Excluded Entity or Excluded Individual or a Convicted Entity or Convicted Individual, such Party shall promptly notify the other Party, and such other Party shall have the option, at its sole discretion, to prohibit such Person from performing work under this Agreement.

**11.6** [\*\*].

**11.7** Exclusivity.

**11.7.1** *Exclusivity.*

**11.7.1.1** *Sage.* Subject to Sections [\*\*] during the Term, Sage will not, and will cause its Affiliates not to (a) alone or with any Affiliates or Third Parties Develop, Manufacture, perform Medical Affairs Activities with respect to or Commercialize a Competing Product in the Field in the Territory, or (b) enter into an agreement or other arrangement with any Third Party pursuant to which Sage or one of its Affiliates grants such Third Party any license or other rights to Develop, Manufacture, perform Medical Affairs Activities with respect to or Commercialize a Competing Product, in each case, in the Field in the Territory.

**11.7.1.2** *Biogen.* Subject to Sections [\*\*], during the Term, Biogen will not, and will cause its Affiliates not to (a) alone or with any Affiliates or Third Parties Develop, Manufacture, perform Medical Affairs Activities with respect to or Commercialize a Competing Product in the Field in the Territory, or (b) enter into an agreement or other arrangement with any Third Party pursuant to which Biogen or one of its Affiliates grants such Third Party any license or other rights to Develop, Manufacture, perform Medical Affairs Activities with respect to or Commercialize a Competing Product in the Field in the Territory.

**11.7.1.3** [\*\*]. Notwithstanding Section 11.7.1 (Exclusivity), in the event that

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**11.7.2** [\*\*]. Notwithstanding Section 11.7.1 (Exclusivity), in the event that,

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**11.7.3** [\*\*]. For the avoidance of doubt, and notwithstanding anything in this Agreement to the contrary, nothing in this Section 11.7.1 (Exclusivity) [\*\*], *provided* that, [\*\*].

## **12. INDEMNIFICATION; LIMITATION OF LIABILITY; INSURANCE**

**12.1** General Indemnification by Biogen. Biogen will indemnify, hold harmless and defend each of Sage, its Related Parties, and their respective directors, officers, employees and agents (“**Sage Indemnitees**”) from and against any and all losses, liabilities, damages, costs, fees and expenses (including reasonable attorneys’ fees and litigation expenses) (collectively, “**Losses**”) incurred in connection with Third Party claims, investigations, demands or suits (“**Third Party Claims**”) incurred by or rendered against the Sage Indemnitees after the Effective Date to the extent arising out of or resulting from (a) any breach of this Agreement, including any breach of a representation or warranty made by Biogen in this Agreement, or any breach or violation of any covenant or agreement of Biogen in this Agreement, (b) the gross negligence, reckless conduct or willful misconduct by or on the part of Biogen or any of its Affiliates,

or any of their respective directors, officers, employees or agents in the performance of Biogen's or their obligations under this Agreement, or (c) the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of Licensed Products by or on behalf of Biogen or any of its Related Parties in the Biogen Territory pursuant to this Agreement. Notwithstanding the foregoing, Biogen will have no obligation to indemnify any of the Sage Indemnitees to the extent that any Losses arise out of or result from any matters for which Sage is obligated to indemnify the Biogen Indemnitees under Section 12.2 (General Indemnification by Sage).

**12.2 General Indemnification by Sage.** Sage will indemnify, hold harmless, and defend each of Biogen, its Related Parties and their respective directors, officers, employees and agents ("**Biogen Indemnitees**") from and against any and all Losses incurred in connection with Third Party Claims incurred by or rendered against the Biogen Indemnitees after the Effective Date to the extent arising out of or resulting from (a) any breach of this Agreement, including any breach of a representation or warranty made by Sage in this Agreement, or any breach or violation of any covenant or agreement of Sage in this Agreement, (b) the gross negligence, reckless conduct or willful misconduct by or on the part of Sage or any of its Affiliates, or any of and their respective directors, officers, employees or agents in the performance of Sage's obligations under this Agreement, (c) the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of Licensed 217 Products in the Existing Partner Territory whether before, after or during the Term, (d) the Development, Manufacture or Commercialization by or on behalf of Sage or any of its Related Parties (excluding such conduct by or on behalf of Biogen, its Affiliates and its Sublicensees as licensees or sublicensees of Sage hereunder) of any Licensed Product in the Territory whether before or after the Term, or (e) the conduct of the [\*\*] by or on behalf of Sage or any of its Related Parties. Notwithstanding the foregoing, Sage will have no obligation to indemnify any of the Biogen Indemnitees to the extent that any Losses arise out of or result from, directly or indirectly, any matters for which Biogen is obligated to indemnify the Sage Indemnitees under Section 12.1 (General Indemnification by Biogen).

**12.3 Indemnification Procedure.** Each Party will notify the other Party in writing in the event it becomes aware of a Third Party Claim for which indemnification may be sought hereunder. The Party entitled to indemnification under Section 12.1 (General Indemnification by Biogen) or 12.2 (General Indemnification by Sage) (an "**Indemnified Party**") will notify the Party potentially responsible for such indemnification (the "**Indemnifying Party**") in writing promptly upon being notified of or having knowledge of any Third Party Claim asserted or threatened against the Indemnified Party that could give rise to a right of indemnification under this Agreement; *provided* that the failure to give such notice will not relieve the Indemnifying Party of its indemnity obligation hereunder except to the extent that such failure materially prejudices the Indemnifying Party. The Indemnifying Party and the Indemnified Party will meet to discuss how to respond to any Third Party Claim. The Indemnified Party will cooperate fully with the Indemnifying Party in defense of such Third Party Claim. In any such proceeding, the Indemnified Party will have the right to retain its own counsel, but the fees and expenses of such counsel will be at the expense of the Indemnified Party unless (a) the Indemnifying Party and the Indemnified Party will have agreed to the retention of such counsel or (b) the named parties to any such proceeding (including any impleaded parties) include both the Indemnifying Party and the Indemnified Party and representation of both Parties by the same counsel would be inappropriate due to actual or potential differing interests between them. All such fees and expenses of the Indemnified Party by application of the foregoing clause (a) or (b) will be reimbursed by the Indemnifying Party as they are incurred. The Indemnifying Party will not be liable for any settlement of any proceeding effected without its written consent, but, if settled with such consent or if there is a final judgment for the Third Party plaintiff, then the Indemnifying Party agrees to indemnify the Indemnified Party from and against any Losses by reason of such settlement or judgment. The Indemnifying Party will not, without the written consent of the Indemnified Party (such consent not to be unreasonably withheld, conditioned or delayed), effect any settlement of any pending or threatened proceeding in respect of which the Indemnified Party is, or could have been, a party and indemnity could

have been sought hereunder by the Indemnified Party, unless such settlement includes an unconditional release of the Indemnified Party from all liability on claims that are the subject matter of such proceeding.

**12.4 Certain Third Party Claims Related to Licensed Products in the Profit-Share Territory.** If either Party receives notice of a Third Party Claim that is incurred from or is based on any Joint Program Activities, then such Party will inform the other Party in writing as soon as reasonably practicable, and the Parties will discuss a strategy on how to, and which Party will, defend against such Third Party Claim. Any Losses as they are incurred in connection with any such Third Party Claim, as well as any reasonable attorneys' fees and costs of litigation incurred by either Party (or any of its Indemnified Persons), in each case, that are Joint Program Damages (a) incurred by either Party (or any of its Indemnified Persons) during the Term, [\*\*], and (b) incurred by either Party (or any of its Indemnified Persons) after the Term for such Product Class, in each case ((a) and (b)), will be shared such that fifty percent (50%) thereof are borne by Sage and fifty percent (50%) thereof are borne by Biogen, and the Party (or any of its Indemnified Persons) that has incurred such Joint Program Damages will be reimbursed by the other Party such other Party's fifty percent (50%) share no later than [\*\*] after receipt of reasonable documentation evidencing such amounts.

**12.5 Limitation of Liability.** NEITHER PARTY WILL BE LIABLE FOR SPECIAL, INCIDENTAL, EXEMPLARY, CONSEQUENTIAL OR PUNITIVE DAMAGES, INCLUDING LOSS OF PROFITS OR BUSINESS INTERRUPTION (TO THE EXTENT THE SAME ARE CONSEQUENTIAL DAMAGES), HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE IN CONNECTION WITH OR ARISING OUT OF THIS AGREEMENT, THE TRANSACTIONS CONTEMPLATED HEREBY, OR THE EXERCISE OF ITS RIGHTS OR THE PERFORMANCE OF ITS OBLIGATIONS HEREUNDER, INCLUDING THE USE OF A LICENSED PRODUCT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES, EXCEPT AS A RESULT OF (A) A PARTY'S FRAUD, GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, (B) A PARTY'S BREACH OF ITS CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE 10 (CONFIDENTIALITY AND PUBLICATION), OR (C) A PARTY'S BREACH OF ITS OBLIGATIONS UNDER SECTION 11.7 (EXCLUSIVITY). NOTHING IN THIS SECTION 12.5 (LIMITATION OF LIABILITY) IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF EITHER PARTY UNDER THIS ARTICLE 12 (INDEMNIFICATION; LIMITATION OF LIABILITY; INSURANCE).

**12.6 Insurance.** Each Party will obtain and maintain insurance with a reputable, solvent insurer in an amount appropriate for its business and products of the type that are the subject of this Agreement, and for its obligations under this Agreement. Specifically, prior to (a) a Party conducting a Clinical Study of any Licensed Product, such Party will obtain product liability insurance with a limit of at least [\*\*] Dollars (\$[\*\*]) and will maintain such insurance throughout the conduct of Clinical Studies of such Licensed Product and for at least [\*\*] thereafter, and (b) the First Commercial Sale of a Licensed Product by a Party or any of its Related Parties, such Party will obtain product liability insurance with a limit of at least [\*\*] Dollars (\$[\*\*]) and will maintain such insurance for at least until [\*\*] after the last commercial sale of such Licensed Product by such Party or any of its Related Parties. Such limits to be per occurrence and in annual aggregate. It is understood that such insurance will not be construed to create a limit of either Party's liability with respect to its indemnification obligations under this Article 12 (Indemnification; Limitation of Liability; Insurance). Upon request, each Party will provide the other Party with evidence of the existence and maintenance of such insurance coverage. Notwithstanding any provision to the contrary set forth in this Agreement, Biogen may self-insure, in whole or in part, the insurance requirements described above.

### 13. INTELLECTUAL PROPERTY

### **13.1 Inventorship.**

**13.1.1** *Determination of Inventorship.* Inventorship for inventions and discoveries (including Know-How) first developed or conceived during the course of the performance of activities under this Agreement will be determined in accordance with United States patent Laws for determining inventorship.

**13.1.2** *JRA Exception.* Notwithstanding anything to the contrary in this Agreement, each Party will have the right to invoke the America Invents Act Joint Research Agreement exception codified at 35 U.S.C. § 102(c) (the “**JRA Exception**”) when exercising its rights under this Agreement only with prior written consent of the other Party (such consent not to be unreasonably withheld, conditioned or delayed) and neither Party may invoke the JRA Exception without the prior written consent of the other Party. If the Parties agree to invoke the JRA Exception through the IP Committee, the Parties will cooperate and coordinate their respective activities with such Party with respect to any filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a “joint research agreement” as defined 35 U.S.C. § 100(h).

### **13.2 Ownership.**

**13.2.1** As between the Parties, all [\*\*].

**13.2.2** Each Party will have an equal and undivided joint ownership interest in and to the Joint Collaboration Technology. Each Party may exercise its ownership rights in and to such Joint Collaboration Technology, including the right to license and sublicense or otherwise to exploit, transfer or encumber its ownership interest, without an accounting or obligation to, or consent required from, the other Party, but subject to the licenses granted under this Agreement and the other terms and conditions of this Agreement. At the reasonable written request of a Party, the other Party will grant such written consents and confirm that no such accounting is required to effect the foregoing regarding Joint Collaboration Technology.

**13.3 Disclosure of Inventions.** The Parties will promptly disclose in writing to each other any Collaboration Technology developed or conceived during the Term, but no later than [\*\*] after the applicable Party’s intellectual property department receives notice of such development or conception.

### **13.4 Prosecution and Maintenance of Patents.**

**13.4.1** *IP Committee.*

**13.4.1.1** *Composition.* The IP Committee will comprise [\*\*] of each Party, with at least [\*\*] who is an employee of each Party. Each Party will appoint its respective representatives to the IP Committee within [\*\*] after the Effective Date, and from time to time, may substitute one or more of its representatives, in its sole discretion, effective upon notice to the other Party of such change. All IP Committee representatives will have appropriate expertise, seniority, decision making authority and ongoing familiarity with the activities performed under this Agreement and each Party’s representatives collectively will have relevant expertise in intellectual property portfolio management and licensing matters. Additional representatives or consultants may from time to time, be invited to attend IP Committee meetings, subject to such representatives and consultants (or the representative’s or consultant’s employer) undertaking confidentiality and non-use obligations, whether in a written agreement or by operation of law, no less stringent than the requirements of Article10 (Confidentiality and Publication).

**13.4.1.2** *Meetings.* The IP Committee will meet as frequently as necessary to carry out its duties under Section 13.4.1.3 (IP Committee Responsibilities), but no more often than [\*\*], unless otherwise agreed by its members. The IP Committee will meet in person at locations in Massachusetts alternately selected by Sage and by Biogen or at any other location agreed by the members or, alternatively, by means of teleconference, videoconference, or other similar communications equipment. Meetings of the IP Committee will be effective only if a quorum is present, which quorum will require the presence of at least one (1) representative of each Party. Each Party will bear the expense of its respective IP Committee members' participation in IP Committee meetings.

**13.4.1.3** *IP Committee Responsibilities.* The IP Committee will have the following responsibilities:

- (a) discussing and determine whether to approve the Prosecution and Maintenance strategy of the Sage Prosecuted Patents and the Biogen Prosecuted Patents in the Territory and the Existing Partner Territory (as may be updated in accordance with this Agreement, the “**PM Strategy**” and any update thereto);
- (b) overseeing the implementation of the PM Strategy in the Territory or the Existing Partner Territory and facilitating the exchange of information between the Parties regarding the foregoing, as described in Section 13.4 (Prosecution and Maintenance of Patents);
- (c) serving as a forum for the Parties to discuss strategy for and actions to be taken with respect to any Competitive Infringement, Third Party Action or Post-Grant Proceeding, as described in Section 13.5 (Third Party Infringement, Defense and Post-Grant Proceedings);
- (d) discussing the strategy for listing patents in the Orange Book maintained by the FDA or similar or equivalent patent listing or linking source, if any, in other countries in the Territory or the Existing Partner Territory for the Licensed Products, as described in Section 13.7 (Orange Book Listings); and
- (e) determining whether to approve and otherwise providing input regarding any other matters that the Parties agree in writing will be the responsibility of the IP Committee.

**13.4.1.4** *Decision Making.* The IP Committee will endeavor to reach decisions by consensus, with each Party, through its representative members of the IP Committee, having one (1) vote. Approvals of each respective applicable IP Committee matter will require the unanimous agreement of the representatives. If the IP Committee cannot reach unanimous agreement on a matter that comes before it within [\*\*] of the meeting where such issue was raised and over which the IP Committee has oversight, then the Parties will refer such issue for resolution to the IP Heads. If a matter is referred to the IP Heads under this Section 13.4.1.4 (Decision Making), then the IP Committee will submit in writing to their respective IP Heads the respective positions of the Parties. Such IP Heads will use good faith efforts to resolve such matter promptly, which good faith efforts will include at least one (1) meeting between such IP Heads within [\*\*] after the IP Committee has submitted the Parties' respective positions on such matter to the IP Heads. If the IP Heads are unable to reach unanimous agreement on any such matter within [\*\*] (or such other period of time as is required to comply with applicable Law so as not to waive any applicable statutory rights) of the meeting between the IP Heads, then no action will be taken as to the escalated matter until a



joint decision can be made by the Parties, except that (a) with respect to any Prosecution and Maintenance matter, [\*\*] will have the final decision-making authority, (b) with respect to any enforcement, defense or Post-Grant Proceedings matter, [\*\*] will have final decision-making authority, (c) with respect to any listing of patents in the Orange Book or similar or equivalent patent listing or linking requirement, if any, in other countries in the Territory as described in Section 13.7 (Orange Book Listings), [\*\*] will have final decision-making authority, and (d) subject to the terms of this Article 13 (Intellectual Property), solely with respect to any dispute as between the Parties in the determination of inventorship, validity, scope or enforceability of any Collaboration Know-How or Collaboration Patents, [\*\*].

**13.4.1.5** *Term.* The Parties may terminate the IP Committee with respect to all Licensed Products in a Product Class upon the written agreement of the Parties.

**13.4.2** [\*\*].

**13.4.2.1** *General.* As between the Parties, [\*\*] will have (a) the first right (but not the obligation) to implement the PM Strategy approved by the IP Committee in the Prosecution and Maintenance of all [\*\*] using counsel of [\*\*] choosing (reasonably acceptable to [\*\*]) in accordance with this Section 13.4.2 ([\*\*]), and (b) the sole right (but not the obligation) to Prosecute and Maintain all [\*\*] using counsel of [\*\*] choosing in its sole discretion (such Patents in clauses (a) and (b), collectively, the “[\*\*]”). Subject to Section 13.4.4 (Patent Cost Sharing), [\*\*] will bear all Patent Costs incurred by [\*\*] for such Prosecution and Maintenance of [\*\*] will furnish to the IP Committee, via electronic mail or such other method as agreed by the Parties, copies of proposed filings and documents received from patent counsel in the course of Prosecuting and Maintaining the [\*\*], or copies of documents filed with the relevant national patent offices or other Governmental Authorities with respect to [\*\*], and such other material documents related to the Prosecution and Maintenance of the [\*\*], in sufficient time prior to filing such document or making any payment due thereunder to allow for the IP Committee to review, discuss and determine whether to approve. The IP Committee will consider in good faith timely comments and recommendations made by Sage consistent with the PM Strategy approved by the IP Committee in connection with such review.

**13.4.2.2** [\*\*] *Step-In.* In the event that [\*\*] elects not to Prosecute and Maintain (or continue to Prosecute and Maintain, including filing a Patent claiming priority to a Patent prior to its issuance) any [\*\*] will notify [\*\*] sufficiently in advance of the date on which any such [\*\*] would become abandoned, no longer available or otherwise forfeited, whereupon so as not to waive any applicable statutory rights, at the written request of [\*\*], the Parties will meet to discuss in good faith any such decision by [\*\*]. Only in the event that such election not to Prosecute and Maintain (or continue to Prosecute and Maintain) such Patent is not taken for [\*\*] (“**Strategic Prosecution Reasons**”), [\*\*] will have the right (but not the obligation), at [\*\*] sole discretion and, subject to Section 13.4.4 (Patent Costs Sharing), to assume sole responsibility for all applicable Patent Costs and to assume the Prosecution and Maintenance of such [\*\*] and continue it in accordance with the PM Strategy approved by the IP Committee in, as applicable, [\*\*] (which right will include the right to file additional Patents claiming priority to such [\*\*] will thereafter consult with [\*\*] via the IP Committee on [\*\*] strategy for the Prosecution and Maintenance of any such assumed [\*\*] will furnish to the IP Committee, via electronic mail or such other method as agreed by the Parties, copies of proposed filings and documents received from patent counsel in the course of Prosecuting and Maintaining any such assumed [\*\*], or copies of documents filed with the relevant national patent offices or other Governmental Authorities with respect to any such assumed [\*\*], and such other material documents related to the Prosecution and Maintenance of any such assumed [\*\*], in sufficient time prior to filing such document or making any payment due

thereunder to allow for the IP Committee to review, discuss and determine whether to approve. The IP Committee will consider in good faith timely comments and recommendations made by [\*\*] consistent with the PM Strategy approved by the IP Committee in connection with such review. [\*\*] will sign, or will use reasonable efforts to have signed, all legal documents as are reasonably necessary for [\*\*] to assume the Prosecution and Maintenance of any such assumed [\*\*] in, as the case may be, [\*\*]. Notwithstanding any assumption of such Prosecution and Maintenance of any such assumed [\*\*] in, as the case may be, [\*\*], [\*\*] will retain ownership of all right, title and interest in and to such assumed [\*\*] and such [\*\*] will continue to be licensed to [\*\*] under the licenses granted to [\*\*] under this Agreement to the same extent as that prior to any such assumption of such Prosecution and Maintenance.

### 13.4.3 [\*\*].

**13.4.3.1** *General.* As between the Parties, [\*\*] will have the first right (but not the obligation) to implement the PM Strategy approved by the IP Committee in the Prosecution and Maintenance of all [\*\*] using counsel of [\*\*] choosing (reasonably acceptable to [\*\*]) (such Patents in, collectively, the “[\*\*]”) in accordance with this Section 13.4.3 ([\*\*]). Subject to Section 13.4.4 (Patent Costs Sharing), [\*\*] will bear all Patent Costs incurred by [\*\*] for such Prosecution and Maintenance of the [\*\*] will furnish to the IP Committee, via electronic mail or such other method as agreed by the Parties, copies of proposed filings and documents received from patent counsel in the course of Prosecuting and Maintaining the [\*\*], or copies of documents filed with the relevant national patent offices or other Governmental Authorities with respect to the [\*\*], and such other material documents related to the Prosecution and Maintenance of the [\*\*], in sufficient time prior to filing such document or making any payment due thereunder to allow for the IP Committee to review, discuss and determine whether to approve. The IP Committee will consider in good faith timely comments and recommendations made by [\*\*] consistent with the PM Strategy approved by the IP Committee in connection with such review. [\*\*] will Prosecute and Maintain the [\*\*] in good faith and in the best interest of maximizing the overall global intellectual property rights and claims Covering the applicable Licensed Product, in each case, without regard to any other [\*\*] product or intellectual property right that is not licensed to [\*\*] under this Agreement.

**13.4.3.2** *[\*\*] Step-In.* In the event that [\*\*] elects not to Prosecute and Maintain (or continue to Prosecute and Maintain, including filing a Patent claiming priority to a Patent prior to its issuance), any [\*\*] will notify [\*\*] sufficiently in advance of the date on which any such [\*\*] would become abandoned, no longer available or otherwise forfeited so as not to waive any applicable statutory rights, whereupon, at the written request of [\*\*], the Parties will meet to discuss in good faith any such decision by [\*\*]. Only in the event that such election not to Prosecute and Maintain (or continue to Prosecute and Maintain) such Patent is not taken for Strategic Prosecution Reasons, [\*\*] will have the right (but not the obligation), at [\*\*] sole discretion and, subject to Section 13.4.4 (Patent Costs Sharing), to assume sole responsibility for all applicable Patent Costs and to assume such Prosecution and Maintenance of such [\*\*] in the name of [\*\*] and continue it in accordance with the PM Strategy approved by the IP Committee in the Territory (which right will include the right to file additional Patents claiming priority to such [\*\*] will thereafter consult with [\*\*] via the IP Committee on [\*\*] strategy for the Prosecution and Maintenance of any such assumed [\*\*] will furnish to the IP Committee, via electronic mail or such other method as agreed by the Parties, copies of proposed filings and documents received from patent counsel in the course of Prosecuting and Maintaining any such assumed [\*\*], or copies of documents filed with the relevant national patent offices or other Governmental Authorities with respect to any such assumed [\*\*], and such other material documents related to the Prosecution and Maintenance of any such assumed [\*\*], in sufficient time prior to filing such document or making any payment due thereunder to allow for the IP Committee to review, discuss and determine whether to approve.

The IP Committee will consider in good faith timely comments and recommendations made by [\*\*] consistent with the PM Strategy approved by the IP Committee in connection with such review. [\*\*] will sign, or will use reasonable efforts to have signed, all legal documents as are reasonably necessary for [\*\*] to assume the Prosecution and Maintenance of any such assumed [\*\*]. Notwithstanding any assumption of such Prosecution and Maintenance of any such assumed [\*\*] will retain ownership of all right, title and interest in and to such assumed [\*\*] and such [\*\*] will continue to be licensed to [\*\*] under the licenses granted to [\*\*] under this Agreement to the same extent as that prior to any such assumption of such Prosecution and Maintenance.

**13.4.4** *Patent Costs Sharing.* Notwithstanding any provision to the contrary in this Section 13.4 (Prosecution and Maintenance of Patents), unless and until Sage exercises an Opt-Out Right with respect to the Licensed Products in the same Product Class in accordance with Section 9.5 (Sage Opt-Out), the Patent Costs incurred by the Party controlling the Prosecution and Maintenance of any [\*\*] with respect to such Product Class will be shared by the Parties (a) as Joint Development Costs pursuant to Section 3.4.1 (Profit-Share Territory) if such Patent Covers a Licensed Product in such Product Class and such Patent Costs were incurred prior to the First Commercial Sale of the first such Licensed Product Covered by such [\*\*], as applicable, and (b) as Joint Commercialization Costs pursuant to Section 5.5.1 (Profit-Share Territory) if such Patent Covers a Licensed Product in such Product Class and such Patent Costs were incurred after the First Commercial Sale of the first such Licensed Product Covered by such [\*\*], as applicable.

**13.4.5** *Patent Miscellaneous.* Each Party hereby agrees: (a) to use reasonable efforts to make its employees, agents and consultants reasonably available to the other Party (or to the other Party's authorized attorneys, agents or representatives), to the extent reasonably necessary to enable such Party to undertake any Prosecution and Maintenance described in this Section 13.4 (Prosecution and Maintenance of Patents) and (b) to reasonably cooperate in any such Prosecution and Maintenance by the other Party.

### **13.5 Third Party Infringement, Defense and Post-Grant Proceedings.**

**13.5.1** *Notices.* Each Party will promptly report in writing to the other Party any Competitive Infringement of which such Party (or any of its Affiliates or Sublicensees) becomes aware and will provide the other Party with all available evidence of such Competitive Infringement in such Party's control; *provided, however,* that (a) for cases of Competitive Infringement under Section 13.5.2.2 (35 U.S.C. §271(e)(2) Infringement), such written notice will be given within [\*\*] after the relevant personnel at the applicable Party become aware of such Competitive Infringement with a copy sent to the IP Heads, and (b) for cases of infringement as described in Section 13.5.2.3 (Notification of Patent Certification), such written notice will be given as specified in Section 13.5.2.3 (Notification of Patent Certification). Without limiting the last sentence of the definition of "Competitive Infringement", a notice under 21 U.S.C. §355(b)(2)(A)(iv) or 355(j)(2)(A)(vii)(IV) (however those sections may be amended) or any equivalent provision under applicable Law outside of the United States with respect to any Patents that are the subject of this Agreement will be deemed to describe an act of Competitive Infringement, regardless of its content.

#### **13.5.2 *Rights to Enforce.***

**13.5.2.1** *In the Territory.* [\*\*] will have the first right (but not the obligation), at its sole discretion and sole cost and expense, through counsel of its choosing and reasonably acceptable to [\*\*], as the Defending Party to seek to abate any Competitive Infringement of a Licensed Product in the Territory by enforcing, as applicable, any [\*\*] Prosecuted Patent or [\*\*] Collaboration Patent; *provided* that, if [\*\*], the Parties will share equally all Patent Costs incurred by [\*\*] for such enforcement to abate any Competitive Infringement of a Licensed Product in the Profit-Share Territory. If practicable under the circumstances, [\*\*] will bring the Competitive

Infringement matter to the IP Committee, within a reasonable time after the IP Heads have been notified of such matter pursuant to Section 13.5.1 (Notices), for discussion pursuant to Section 13.4.1.3(c) (IP Committee Responsibilities). Thereafter, [\*\*] will notify the IP Committee of its decision as to whether it is taking any action in accordance with this Section 13.5.2.1 (In the Territory) at least [\*\*] before any time limit set forth in an applicable Law or regulation, or within [\*\*] after the relevant personnel at [\*\*] has been notified of such Competitive Infringement (or as otherwise agreed by the IP Committee), whichever is shorter. If [\*\*] decides not to take such action with respect to any [\*\*] Prosecuted Patent or [\*\*] Collaboration Patent in the Territory, then [\*\*] will so notify the IP Committee in writing, and, so long as [\*\*] election not to take any such action is not due to [\*\*] (“**Strategic Enforcement or Defense Reasons**”), following discussion of the IP Committee and consideration in good faith of any rationale provided by [\*\*] as to why it elected not to take such action, [\*\*], at its sole cost and expense, will have the right (but not the obligation) to exercise the rights set forth in Section 13.5.5.1 (Withdrawal, Cooperation and Participation) and become the Defending Party with respect to enforcing any [\*\*] Prosecuted Patent or [\*\*] Collaboration Patent, as applicable, to abate such Competitive Infringement of a Licensed Product in the Profit-Share Territory; *provided* that, if [\*\*], then the Parties will share equally all Patent Costs incurred by [\*\*] to abate any such Competitive Infringement of such Licensed Product in the Profit-Share Territory. For the avoidance of doubt, and notwithstanding anything in this Agreement to the contrary, [\*\*] will have the sole and exclusive right (but not the obligation), at [\*\*] sole discretion, to enforce any [\*\*] Background Patent against a Competitive Infringement.

**13.5.2.2** *35 U.S.C. § 271(e)(2) Infringement.* Notwithstanding anything to the contrary in this Section 13.5.2 (Rights to Enforce), for a Competitive Infringement under 35 U.S.C. § 271(e)(2), or its equivalent in a country other than the United States, [\*\*] must notify the IP Committee within [\*\*] after [\*\*] receipt of a written notice of such Competitive Infringement of [\*\*] decision as to whether to take any action with respect to such Competitive Infringement so that [\*\*] may have the right, pursuant to such Section 13.5.2.1 (In the Territory), to initiate a Proceeding if [\*\*] does not elect to initiate a Proceeding.

**13.5.2.3** *Notification of Patent Certification.* If either Party becomes aware of any allegations of alleged patent invalidity, unenforceability or non-infringement of any Patent licensed under this Agreement Covering a Licensed Product (including methods of use thereof) pursuant to a Paragraph IV Patent Certification by a Third Party filing an Abbreviated New Drug Application, or other similar patent certification by a Third Party, and any foreign equivalent thereof, for a Generic Product, then such Party will notify and provide the other Party with copies of such allegations. Such notification and copies will be provided to such other Party as soon as practicable and at least within [\*\*] after such Party receives such certification, and will be sent by email and overnight courier to the address set forth in Section 15.10 (Notices).

**13.5.3** *Defense and Post-Grant Proceedings.* [\*\*], at its sole cost and expense, will have the right (but not the obligation), as the Defending Party, at its sole discretion, (a) to defend against a declaratory judgment action or other action that is not a Post-Grant Proceedings, in each case, challenging any [\*\*] Prosecuted Patent or [\*\*] Collaboration Patent (a “**Third Party Action**”), and (b) to conduct any Post-Grant Proceedings with respect to any [\*\*] Prosecuted Patent; *provided* that, if [\*\*], then the Parties will share equally all Patent Costs incurred by [\*\*] in connection with the defense of such Third Party Action or Post-Grant Proceeding. Within [\*\*] after the relevant personnel at either Party receiving notice of a Third Party Action or becoming aware of the initiation of a Post-Grant Proceeding (or as otherwise agreed by the IP Committee), such Party will notify the other Party, and within a reasonable time to meet for a discussion thereof, the IP Committee will meet for discussion pursuant to Section 13.4.1.3(c) (IP Committee Responsibilities). Thereafter, [\*\*] will notify the IP Committee of its intent to defend such Patent or conduct any Post-Grant Proceeding under this Section 13.5.3 (Defense and Post-Grant

Proceedings), as applicable, within [\*\*] (or as otherwise agreed by the IP Committee) after such IP Committee meeting (or such shorter period of time as is required to comply with applicable Law in the Territory to not waive any statutory rights). If [\*\*] does not provide notice to the IP Committee of [\*\*] intent to defend such Patent or conduct any Post-Grant Proceeding under this Section 13.5.3 (Defense and Post-Grant Proceedings), as applicable, within [\*\*] after such IP Committee meeting (or such shorter period of time as is required to comply with applicable Law in the Territory to not waive any statutory rights), or elects not to initiate or continue any such defense or Post-Grant Proceeding (in which case it will promptly provide notice thereof to [\*\*]) then, as long as [\*\*] decision not to take any such action is not due to Strategic Enforcement or Defense Reasons, [\*\*] will, upon receiving confirmation from [\*\*] that [\*\*] has not taken any such action within the applicable period set forth in this Section 13.5.3 (Defense and Post-Grant Proceedings), have the right (but not the obligation), at its sole cost and expense, as the new Defending Party, at its sole discretion, to defend any such Patent against such a Third Party Action or conduct Post-Grant Proceedings for such Patent, as applicable, in each case of (a) and (b), as further set forth in Section 13.5.5 (Withdrawal, Cooperation and Participation); *provided* that, if [\*\*], the Parties will share equally all Patent Costs incurred by [\*\*] in connection with the defense of such Third Party Action or such Post-Grant Proceeding. For the avoidance of doubt, and notwithstanding anything in this Agreement to the contrary, [\*\*] will have the sole and exclusive right (but not the obligation), at [\*\*] sole discretion, to defend any [\*\*] Background Patent against a Third Party Action.

**13.5.4** *Cooperation Regarding Enforcement, Defense or Post-Grant Proceedings.* With respect to any Competitive Infringement action, Third Party Action or Post-Grant Proceeding identified above in Section 13.5.2 (Right to Enforce) and Section 13.5.3 (Defense and Post-Grant Proceedings) and subject to the terms and conditions of this Section 13.5.4 (Cooperation Regarding Enforcement, or Defense or Post-Grant Proceedings), the Party controlling any such Competitive Infringement action, Third Party Action or Post-Grant Proceeding (the “**Defending Party**”) will keep the other Party (the “**Non-Defending Party**”) reasonably informed of the status and progress of such enforcement, defense or Post-Grant Proceeding strategy via the IP Committee. The Defending Party will reasonably consider the Non-Defending Party’s comments on any such efforts. The Non-Defending Party will provide the Defending Party with all reasonable assistance in the enforcement or defense of the applicable Patents, as the Defending Party may request, at such Defending Party’s expense, including by signing or executing any necessary documents and consenting to it being named a party to any applicable proceedings. Where the Non-Defending Party is named a party or otherwise is joined involuntarily in any applicable proceeding, the Non-Defending Party will have the right to be represented by counsel of its choice at the Defending Party’s expense, *provided* that in all other cases the Non-Defending Party will be solely responsible for the costs and expenses of its counsel and in all instances all communications between the Non-Defending Party and the Defending Party will be subject to the principles of Section 13.9 (Common Interest).

**13.5.5** *Withdrawal, Cooperation and Participation.* With respect to any Competitive Infringement action, Third Party Action or Post-Grant Proceeding identified above, respectively, in Section 13.5.2 (Rights to Enforce) and Section 13.5.3 (Defense and Post-Grant Proceedings) and subject to the terms and conditions of this Section 13.5.5 (Withdrawal, Cooperation and Participation):

**13.5.5.1** If [\*\*] ceases to pursue or withdraws from such action, it will promptly notify [\*\*] (in sufficient time to enable [\*\*] to meet any deadlines by which any action must be taken to preserve any rights in such infringement, defensive action or Post-Grant Proceeding), then [\*\*] will have the right (but not the obligation) to substitute itself for [\*\*] in any Competitive Infringement action identified above in Section 13.5.2.2 (35 U.S.C. § 271(e)(2) Infringement) or in any Third Party Action or Post-Grant Proceeding identified above in Section 13.5.3 (Defense and Post-Grant Proceedings), in each case, involving any [\*\*] Prosecuted Patents or [\*\*] Collaboration

Patents and proceed under the terms and conditions of this [Section 13.5.5](#) (Withdrawal, Cooperation and Participation).

**13.5.5.2**            [\*\*] will cooperate with [\*\*] in controlling any such action (as may be reasonably requested by [\*\*]), including, at [\*\*] sole cost and expense, (a) providing access to relevant documents and other evidence, (b) using reasonable efforts to make [\*\*] Affiliates and its and its Affiliates' licensees and Sublicensees and all of their respective employees, subcontractors, consultants and agents available at reasonable business hours and for reasonable periods of time, but only to the extent relevant to such action, and (c) if reasonably necessary, by being joined as a party, subject to (with respect to this clause (c)) [\*\*] agreeing to indemnify [\*\*] for its involvement as a named party in such action and paying those Patent Costs incurred by [\*\*] in connection with such joinder. [\*\*], as the Defending Party in any such action, will keep [\*\*] reasonably updated via the IP Committee with respect to any such action, including providing copies of all materials documents received or filed in connection with any such action to the extent permitted by applicable Law.

**13.5.5.3**            [\*\*] will have the right to consult with [\*\*] regarding any such action for which [\*\*] is the Defending Party via the IP Committee, in each case at [\*\*] sole cost and expense. If [\*\*] elects to so be involved, [\*\*] will provide [\*\*] and its counsel with an opportunity to consult with [\*\*] and its counsel regarding the prosecution of such action (including reviewing the contents of any correspondence, legal papers or other documents related thereto). [\*\*] will take into account reasonable and timely requests and comments of [\*\*] regarding such enforcement or defense.

**13.5.6**                *Settlement.* With respect to any enforcement action, Third Party Action or Post-Grant Proceeding identified above in this [Section 13.5](#) (Third Party Infringement and Defense and Post-Grant Proceedings), the Defending Party will have the right to settle or otherwise dispose of such action (a) with the consent of the other Party, if it involved the Profit-Share Territory and (b) otherwise, on such terms and conditions as such Defending Party will determine in its sole discretion; *provided* that, in either case ((a) or (b)), notwithstanding the foregoing, no such settlement or other disposition will (i) impose any monetary restriction or obligation on or admit fault of the other Party or (ii) adversely affect the other Party's rights under this Agreement to any such Patent then being enforced or defended, in each case (i) and (ii) without the prior written consent of the other Party, not to be unreasonably withheld, conditioned or delayed).

**13.5.7**                *Other Invalidity or Unenforceability Proceedings.* If [\*\*] desires to bring an opposition, action for declaratory judgment, nullity action, interference, declaration for non-infringement, reexamination, post-grant proceedings, or other attack upon the validity, title or enforceability of a Patent Right owned or controlled by a Third Party and having one (1) or more claims that Cover a Licensed Product, or the use, sale, offer for sale or importation of a Licensed Product in the Territory, as applicable, (except insofar as such action is a counterclaim to or defense of, or accompanies a defense of a Third Party Action under [Section 13.5.3](#) (Defense and Post-Grant Proceedings), in which case the provisions of such [Section 13.5.3](#) (Defense and Post-Grant Proceedings) will govern), then [\*\*] will so notify [\*\*] and the Parties will promptly confer through the IP Committee. [\*\*] will have the initial right, but not the obligation, to bring, at its own expense and in its sole control, such action in the Territory. [\*\*] will be entitled to separate representation in such proceeding by counsel of its own choice and at its own expense, and will cooperate fully with the Party so appointed. Any awards or amounts received in bringing any such action will be first allocated to reimburse [\*\*]'s expenses in such action, and any remaining amounts will be allocated between the Parties in accordance with the principle set forth in [Section 13.5.8](#) (Allocation of Proceeds).

**13.5.8** *Allocation of Proceeds.* If either Party recovers monetary damages from any Third Party in a suit in the Territory pursuant to this [Section 13.5](#) (Third Party Infringement and Defense and Post-Grant Proceedings) or any royalties from a license agreement with a Third Party related to any alleged Competitive Infringement in the Territory, whether or not such damages or royalties result from the infringement of [\*\*] Prosecuted Patents or the [\*\*] Prosecuted Patents, then such recovery will be allocated first to the reimbursement of any expenses incurred by each Party in such litigation, action, or license, and any balance of any such recovery will be split as follows: (a) if [\*\*] brings the action, (i) treated as Net Revenues, to the extent relating to all Licensed Products in a Product Class in the Profit-Share Territory prior to [\*\*]'s exercise of an Opt-Out Right with respect to the applicable Product Class or (ii) as Net Sales, and shared with [\*\*] as royalties pursuant to [Section 9.8](#) (Licensed 217 Product and Licensed 324 Product Products Royalties), to the extent relating to all Licensed Products in a Product Class in the [\*\*] Territory or after [\*\*] has exercised an Opt-Out Right with respect to the applicable Product Class; or (b) if [\*\*] brings the action, then [\*\*]% will be retained by [\*\*] and [\*\*]% will be paid to [\*\*].

**13.6 Patent Extensions.** Subject to the rest of this [Section 13.6](#) (Patent Extensions), with respect to any election to file for patent term restoration or extension, or any of their equivalents, [\*\*] will have the sole and exclusive right to make any such decision relating to any [\*\*] Prosecuted Patents or [\*\*] Prosecuted Patents in the Territory with respect to any Licensed Product, *provided* that [\*\*] will use reasonable efforts to obtain any such patent term restoration or extension, or any of their equivalents available for the Patents subject to the enforcement rights specified in [Section 13.5.2](#) (Rights to Enforce) with respect to any Licensed Product; and further *provided, however*, that [\*\*] will not be required to use any such reasonable efforts in a manner inconsistent with any term or condition of this [Section 13.6](#) (Patent Extensions) if any such item could impair the applicable Patent (including its enforcement potential) or the ability to obtain any such patent term restoration or extension, supplemental protection certificate or any of their equivalents for any other pharmaceutical product. [\*\*] will consult with [\*\*] through the IP Committee regarding the strategy for such filings. Subject to [Section 13.4.4](#) (Patent Costs Sharing), [\*\*] will bear all Patent Costs incurred in making such filings. Upon the written request by [\*\*], [\*\*] will reasonably cooperate with the implementation of such requesting Party's decisions made in a manner consistent with this [Section 13.6](#) (Patent Extensions).

**13.7 Orange Book Listings.** [\*\*] will have lead responsibility for making any filing with respect to any [\*\*] Collaboration Patent, Joint Collaboration Patent or [\*\*] Licensed Patent in connection with the Orange Book maintained by the FDA or similar or equivalent patent listing or linking requirement, if any, in other countries in the Territory for the Licensed Products. [\*\*] will consult with [\*\*] through the IP Committee regarding the strategy for such filings. If the Parties disagree on the appropriate strategy with respect to any such filings, the disagreement will be resolved by the IP Committee, subject to [Section 13.4.1.4](#) (Decision Making). [\*\*] will provide reasonable assistance to [\*\*] in connection with any such filing.

**13.8 Third Party Rights.** Notwithstanding the foregoing provisions of this [Article 13](#) (Intellectual Property), each Party's rights and obligations with respect to any Patent under this [Article 13](#) (Intellectual Property) will be subject to the Third Party rights and obligations (including under any in-license of a Patent applicable to such Party's licensed intellectual property rights hereunder) set forth in [Schedule 13.8](#) (Third Party Rights).

**13.9 Common Interest.** All information exchanged between the Parties regarding the Prosecution and Maintenance, and enforcement and defense, of Patents under this [Article 13](#) (Intellectual Property) will be deemed Confidential Information of the disclosing Party. In addition, the Parties acknowledge and agree that, with regard to such Prosecution and Maintenance, and enforcement and defense, the interests of the Parties as collaborators and licensor and licensee are to obtain the strongest patent protection possible, and as such, are aligned and are legal in nature. The Parties agree and

acknowledge that they have not waived, and nothing in this Agreement constitutes a waiver of, any legal privilege concerning the Patents under this [Article 13](#) (Intellectual Property), including privilege under the common interest doctrine and similar or related doctrines. Notwithstanding anything to the contrary contained herein, to the extent a Party has a good faith belief that any information required to be disclosed by such Party to the other Party under this [Article 13](#) (Intellectual Property) is protected by attorney-client privilege or any other applicable legal privilege or immunity, such Party will not be required to disclose such information and the Parties will in good faith cooperate to agree upon a procedure (including entering into a specific common interest agreement, disclosing such information on a “for counsel eyes only” basis or similar procedure) under which such information may be disclosed without waiving or breaching such privilege or immunity.

**13.10 Trademarks.** In the Profit-Share Territory, (a) the JCC will recommend to the JSC to determine whether to approve a designated Commercialization Lead Party to be responsible for implementing the LP U.S. TM Strategy for the registration, maintenance, enforcement and defense of the LP U.S. Trademark for a Licensed Product, which Party will own all applications for registration and registrations for such LP U.S. Trademark, and (b) any and all Trademark Costs for the LP U.S. Trademarks incurred in accordance with the applicable Joint Commercialization Plan and Joint Commercialization Budget will be deemed Joint Commercialization Costs. In the Biogen Territory, Biogen will be responsible for the registration, maintenance, enforcement and defense of, and will own all applications for registration and registrations for, all Trademarks for use in connection with the Licensed Products in the Biogen Territory, and will be solely responsible for all Trademark Costs incurred for such activities.

## 14. TERM AND TERMINATION

**14.1 Term.** This Agreement will be effective as of the Effective Date and, unless terminated earlier pursuant to this [Article 14](#) (Term and Termination), will continue on a Licensed Product-by-Licensed Product and country-by-country basis until the date on which: (a) in any country in the Biogen Territory, the Royalty Term has expired for all Licensed Products in a Product Class in such country, and (b) for the Profit-Share Territory, the Parties agree to permanently cease to Commercialize all Licensed Products in a Product Class in the Profit-Share Territory (the “**Term**”). Upon the expiration of this Agreement for all Licensed Products in a Product Class in a country, the licenses granted from Sage to Biogen under this Agreement with respect to such Licensed Products in such Product Class in such country will become fully-paid, irrevocable, and perpetual.

**14.2 Termination Prior to Effective Date.** On the Effective Date, Sage will provide to Biogen updated versions of any schedules required to be provided under [Section 11.2](#) (Representations and Warranties of Sage of the Execution Date and the Effective Date) as a result of Sage making anew as of the Effective Date the representations and warranties of [Section 11.2](#) (Representations and Warranties of Sage of the Execution Date and the Effective Date). If any of the representations and warranties set forth in [Section \[\\*\\*\]](#), or [Section \[\\*\\*\]](#) (Representations and Warranties of Sage as of Execution Date and Effective Date) do not remain true and correct as of the Effective Date to the same extent as of the Execution Date, then Biogen may terminate this Agreement in its entirety with respect to all Product Classes upon written notice to Sage [\*\*].

**14.3 Termination by Biogen for Convenience.** At any time during the Term, Biogen may terminate this Agreement (a) in its entirety or (b) on a Product Class-by-Product Class basis for the United States, each Major European Country, or for a Product Class in its entirety as to the entire Territory, in each case ((a) and (b)), for any reason or no reason upon one hundred and fifty (150) days’ prior written notice to Sage.

### **14.4 Termination for Material Breach.**



**14.4.1.1** Subject to Section 14.4.2 (Disputed Breach), Sage will have the right to terminate this Agreement upon delivery of written notice to Biogen in the event of any material breach by Biogen of this Agreement, solely with respect to the Product Class(es) and Region(s) to which such material breach relates, *provided* that such termination will not be effective if such breach has been cured within [\*\*] after written notice thereof is given by Sage to Biogen specifying the nature of the alleged breach (or, if such default cannot be cured within such [\*\*] period, within [\*\*] after such notice if Biogen commences actions to cure such default within such [\*\*] period and thereafter diligently continues such actions, but fails to cure the default by the end of such [\*\*]). Notwithstanding any provision to the contrary set forth in this Agreement, to the extent a material breach involves the failure to make a payment when due, such breach must be cured within [\*\*] after written notice thereof is given by Sage to Biogen.

**14.4.1.2** Subject to Section 14.4.2 (Disputed Breach), Biogen will have the right to terminate this Agreement upon delivery of written notice to Sage in the event of any material breach by Sage of this Agreement, solely with respect to the Product Class(es) and Region(s) to which such material breach relates, *provided* that such termination will not be effective if such breach has been cured within [\*\*] after written notice thereof is given by Biogen to Sage specifying the nature of the alleged breach (or, if such default cannot be cured within such [\*\*] period, within [\*\*] after such notice if Sage commences actions to cure such default within such [\*\*] period and thereafter diligently continues such actions, but fails to cure the default by the end of such [\*\*]). Notwithstanding any provision to the contrary set forth in this Agreement, to the extent a material breach involves the failure to make a payment when due, such breach must be cured within [\*\*] after written notice thereof is given by Biogen to Sage.

**14.4.2** *Disputed Breach.* If the alleged breaching Party disputes in good faith the existence of a breach specified in a notice provided by the other Party in accordance with Section 14.4.1 (Material Breach) and such alleged breaching Party provides the other Party notice of such dispute within the applicable [\*\*] or [\*\*] cure period, then (a) the non-breaching Party will not have the right to terminate this Agreement under Section 14.4.1 (Material Breach) and (b) the applicable cure period set forth in Section 14.4.1 (Material Breach) will be tolled during the pendency of the dispute resolution process set forth in Section 15.3 (Dispute Resolution), in each case ((a) and (b)), unless and until the dispute resolution process set forth in Section 15.3 (Dispute Resolution) has been completed (including the tolling and cure periods set forth therein), and in any event the terms of Section 15.3.7 (Tolling) will apply.

**14.5** **Termination for Insolvency.** To the extent permitted by applicable Law, either Party may terminate this Agreement upon the filing or institution of bankruptcy, reorganization, liquidation, or receivership proceedings, upon the appointment of a receiver or trustee over all or substantially all property, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party; *provided, however*, that in the case of any involuntary bankruptcy proceeding such right to terminate will only become effective if the Party consents to the involuntary bankruptcy or such proceeding is not dismissed within [\*\*] after the filing thereof.

**14.5.1** All rights and licenses now or hereafter granted by one Party to the other Party under or pursuant to this Agreement are, for all purposes of Section 365(n) of Title 11 of the United States Code, as amended or analogous provisions of applicable Law outside the United States (the “**Bankruptcy Code**”), licenses of rights to “intellectual property” as defined in the Bankruptcy Code. Upon the filing or institution of bankruptcy, reorganization, liquidation, or receivership proceedings, upon the appointment of a receiver or trustee over all or substantially all property, or upon an assignment of a substantial portion of the assets for the benefit of creditors by a Party, such Party agrees that the other Party, as licensee of such

rights under this Agreement, will retain and may fully exercise all of its rights and elections under the Bankruptcy Code. Subject to Section 365 of the Bankruptcy Code, each Party will, during the Term, create and maintain current copies or, if not amenable to copying, other appropriate embodiments, to the extent feasible, of all intellectual property rights licensed under this Agreement. Each Party acknowledges and agrees that “embodiments” of intellectual property rights within the meaning of Section 365(n) include laboratory notebooks, cell lines, product samples, and inventory, research studies and data, all Regulatory Approvals (and all applications for Regulatory Approval) and rights of reference therein, in each case, to the extent licensed by a Party to the other Party hereunder, as well as the Sage Licensed Technology and the Biogen Licensed Technology (as the case may be), and all information related to the Sage Licensed Technology and the Biogen Licensed Technology (as the case may be). If (a) a case under the Bankruptcy Code is commenced by or against the debtor Party, (b) this Agreement is rejected as provided in the Bankruptcy Code and (c) the non-debtor Party elects to retain its rights hereunder as provided in Section 365(n) of the Bankruptcy Code and upon written request of the non-debtor Party, then:

**14.5.1.1** the non-debtor Party will be authorized to retain and exercise its rights under this Agreement (including a right to enforce any exclusivity provision contained herein) to intellectual property rights (including all embodiments thereof) licensed hereunder and held by the debtor Party as such rights existed immediately before the commencement of the case referenced in clause (a) of Section 14.5 (Termination for Insolvency) above, subject to the provisions of Section 365(n) of the Bankruptcy Code related to, among other things, payment of the royalties and waiver of rights to setoff and any claim allowable under Section 503(b) of the Bankruptcy Code related to the performance of this Agreement, but neither such provision nor such performance by the non-debtor Party will release the debtor Party from liability resulting from rejection of the license or the failure to perform such obligations

**14.5.1.2** to the extent provided herein, the debtor Party will provide to the non-debtor Party any intellectual property (including any applicable embodiment) held by the debtor Party; and

**14.5.1.3** the debtor Party will not interfere with the non-debtor Party’s rights under this Agreement, or any agreement supplemental hereto, with respect to such intellectual property rights (including such embodiments), including any right to obtain such intellectual property rights (or such embodiments) from another entity, to the extent provided in Section 365(n) of the Bankruptcy Code.

**14.6 Effect of Termination by Sage for Cause or for Biogen’s Insolvency, or by Biogen for Convenience.** Upon termination of this Agreement by Sage pursuant to Section 14.4.1.1 (Material Breach) or Section 14.5 (Termination for Insolvency) or by Biogen pursuant to Section 14.3 (Termination by Biogen for Convenience):

**14.6.1** *Termination of Licenses.* If this Agreement is terminated in its entirety, then all licenses granted under Article 8 (Licenses) granted under this Agreement with respect to all Licensed 217 Products and all Licensed 324 Products will terminate. If this Agreement is terminated in part with respect to the Terminated Products or the Terminated Territory, then all licenses granted by Sage to Biogen under Section 8.1.1 (License Grant to Biogen; Sage Retained Rights) will terminate solely with respect to the Terminated Products and the Terminated Territory, as applicable, and all licenses granted by Biogen to Sage under Section 8.1.2 (License Grant to Sage; Biogen Retained Rights) will terminate solely with respect to the Terminated Products and the Terminated Territory, as applicable.

**14.6.2** *Reversion License.* Effective upon either (a) the date of termination of this Agreement in case of termination by Sage pursuant to Section 14.4.1.1 (Material Breach) or Section 14.5

(Termination for Insolvency) or termination of this Agreement in its entirety by Biogen pursuant to Section 14.3 (Termination by Biogen for Convenience) or (b) the date of expiration of the specified notice period in Biogen's notice of termination of this Agreement *in part* pursuant to Section 14.3 (Termination by Biogen for Convenience), subject to the terms of this Section 14.6.2 (Reversion License), Biogen, on behalf of itself and its Affiliates, hereby grants (without any further subsequent action required on the part of Sage) to Sage and its Affiliates, an irrevocable, perpetual license for the Terminated Products in the Terminated Territory, with the right to grant sublicenses through multiple tiers, under the Reversion Technology [\*\*] (the "**Reversion License**"), where the Reversion License will be [\*\*]. If any Reversion Technology is in-licensed by Biogen or any of its Related Parties, then Biogen will promptly inform Sage of any payment obligations and any other obligations applicable to Sage under such Third Party agreements and, unless Sage elects to decline receiving a sublicense under such in-licensed Reversion technology as part of the Reversion License, then (i) in consideration therefor, Sage will pay to Biogen amounts equal to any payments that Biogen owes to any Third Party with respect to such in-licensed Reversion Technology solely with respect to the Terminated Product for the Terminated Territory, with all payments made in accordance with Section 9.10 (Other Amounts Payable) and Section 9.11 (Payment Terms) *mutatis mutandis*, and (ii) Sage's rights under the Reversion License will be subject to the applicable terms of the applicable Third Party agreement of which Sage has been made aware.

**14.6.3** *Wind Down Costs.* In the event of termination of this Agreement by Sage pursuant to Section 14.4.1.1 (Material Breach) or Section 14.5 (Termination for Insolvency) or termination of this Agreement by Biogen pursuant to Section 14.3 (Termination by Biogen for Convenience), each Party will pay for [\*\*], for (i) [\*\*], or (ii) [\*\*], and (b) Biogen will pay for the costs and expenses for all Clinical Studies conducted by Biogen in support of obtaining Regulatory Approval for Commercialization in the Biogen Territory that are ongoing prior to the date of the written notice from one Party to the other Party under Section 14.4.1.1 (Material Breach), Section 14.5 (Termination for Insolvency) or Section 14.3 (Termination by Biogen for Convenience), as applicable, for (i) all Licensed 217 Products and all Licensed 324 Products, if this Agreement is terminated in its entirety, or (ii) a Region of the Biogen Territory, if this Agreement is terminated in part with respect to such Region of the Biogen Territory, in each case ((a) and (b)), for a period of [\*\*] after the effective date of termination of this Agreement (the "**Termination Wind-Down Period**").

**14.6.4** *Regulatory Materials; Commercial Materials.* Biogen, on behalf of itself and its Affiliates, at its cost, will (a) assign to Sage or Sage's designee possession and ownership of all Regulatory Materials, Pricing and Reimbursement Approvals and material correspondence and conversation logs solely relating to the applicable Terminated Products in the Terminated Territory, in each case, in Biogen's Control, and (b) transfer to Sage or Sage's designee copies of all data, reports, records, materials and information, including customer lists and other sales and marketing information in Biogen's Control to the extent that such data, reports, records, materials or other information solely related to the applicable Terminated Products in the Terminated Territory, including all non-clinical and clinical data relating to the applicable Terminated Products, and all adverse event data solely related to the applicable Terminated Products in Biogen's Control, and (c) transfer to Sage all records and materials in Biogen's Control containing Confidential Information of Sage solely relating to the applicable Terminated Products in the Terminated Territory. In addition, effective upon the effective date of termination, Biogen, on behalf of itself and its Affiliates, will appoint Sage as Biogen's or Biogen's Related Parties' agent for all matters involving Regulatory Authorities in the Terminated Territory solely relating to the applicable Terminated Products until all Regulatory Materials, Pricing and Reimbursement Approvals and other governmental or Regulatory Approvals relating to the Development, Manufacture, performance of Medical Affairs Activities with respect to or Commercialization of the Terminated Products in the Terminated Territory have been assigned to Sage or its designee. In the event of failure to obtain such assignment, effective upon the effective date of termination, Biogen, on behalf of itself and its Affiliates, hereby consents and grants to Sage the right to access and reference (without any further action required on the part of Biogen, whose

authorization to file this consent with any Regulatory Authority of the Terminated Territory is hereby granted effective as of the date of termination) any such item with respect to the applicable Terminated Products in the Terminated Territory.

**14.6.5** *Sell-Off and Appointment as Distributor.* If the effective date of termination of this Agreement in its entirety or of this Agreement in part, as the case may be, is after the First Commercial Sale in the applicable Terminated Territory of the applicable Terminated Products, then, to the extent permitted by applicable Law, effective upon such date of such termination, Biogen, its Affiliates and its Sublicensees will have the right to sell any inventory of such Terminated Products intended for Commercialization in the Terminated Territory existing as of such date of termination in accordance with the terms and conditions of this Agreement in such Terminated Territory by or under the authority of Biogen as of the notice date of the applicable termination, for up to (a) [\*\*] after the effective date of the applicable termination, in the case that Sage has obtained all Regulatory Approvals required to sell such Terminated Products as of the notice date of the applicable termination or (b) [\*\*] after the effective date of the applicable termination or such longer time as may be agreed by the Parties, in the case that Sage has not obtained all Regulatory Approvals required to sell such Terminated Products as of the notice date of the applicable termination (either of ((a) or (b)), the “**Commercialization Wind-Down Period**”). Any Terminated Product sold or disposed of by Biogen, its Affiliates or its Sublicensees in the Terminated Territory during the Commercialization Wind-Down Period will be subject to applicable payment obligations under Article 9 (Payments). Within [\*\*] after the end of the Commercialization Wind-Down Period, Biogen will notify Sage of any quantity of Terminated Product for the Terminated Territory remaining in Biogen’s inventory and, subject to the terms of Section 14.6.6 (Continuation of Supply), and Sage may purchase, in its discretion, any such quantities of the Terminated Product from Biogen at a transfer price equal to (i) [\*\*]. After the Commercialization Wind-Down Period for a Terminated Product, Biogen or its Related Parties will appoint Sage as exclusive distributor of such Terminated Product in the Territory and grant Sage the right to appoint sub-distributors, until such time as all Regulatory Approvals for the applicable Terminated Product in the Territory have been transferred to Sage or its designee; *provided* that, Biogen will not be required to appoint Sage as its distributor of the applicable Terminated Products as contemplated by this Section 14.6.5 (Sell-Off and Appointment as Distributor) if the terms of any Third Party agreements of Biogen or any of its Related Parties necessary for the Development, Manufacture or Commercialization of the applicable Terminated Products (A) [\*\*] or (B) [\*\*]; *further provided* that if no such appointment is possible, then [\*\*]. Without limiting the foregoing, if such termination occurs after the First Commercial Sale of a Terminated Product then, during the Commercialization Wind-Down Period for such Terminated Product, the Parties will use reasonable efforts to transition all Commercialization activities to Sage as Sage may reasonably request.

**14.6.6** *Continuation of Supply.* Upon Sage’s request, if (a) the effective date of termination of this Agreement in its entirety or of this Agreement in part, as the case may be, is after the First Commercial Sale of the applicable Terminated Products in any country of the Terminated Territory, (b) as of the effective date of such termination, Biogen or its Related Parties are Manufacturing finished product with respect to the applicable Terminated Products for Commercialization thereof in the Terminated Territory, and (c) as of the effective date of such termination, neither Sage nor any of its Related Parties has obtained all necessary Regulatory Approvals to Manufacture the applicable Terminated Products and procured or developed its own source of finished product supply with respect to the applicable Terminated Products for Commercialization thereof in the Terminated Territory, then, at Sage’s option and at Sage’s sole cost and expense, Biogen or its Related Parties will supply to Sage such finished product with respect to the applicable Terminated Products for Commercialization in the Territory at a price equal to (i) [\*\*] following the applicable effective date of termination of this Agreement in its entirety or in part and (ii) [\*\*] following the applicable effective date of termination of this Agreement in its entirety or in part.

**14.6.7** *Third Party Agreements.* If Sage so requests in writing, and to the extent permitted under Biogen's obligations to Third Parties on the effective date of termination of this Agreement in its entirety or of this Agreement in part, as the case may be, effective as of the effective date of such termination, Biogen will assign to Sage, and Sage will assume, [\*\*]; provided that, if the assignment of any such Third Party agreement [\*\*], such assignment of such Third Party agreement will [\*\*].

**14.6.8** *Sublicense Survival.* Sage will, [\*\*] (each, a "New License Agreement"). Notwithstanding any provision to the contrary set forth in this Agreement, Sage will [\*\*]

**14.6.9** *Biogen Trademarks.* If as of the effective date of termination of this Agreement in its entirety or of this Agreement in part, as the case may be, (a) Biogen owns any Trademarks that are used exclusively for the applicable Terminated Products in the Terminated Territory and (b) such Trademarks have been approved by the Regulatory Authority in a country of the Terminated Territory for use with the applicable Terminated Products (such Trademarks, the "Reversion Trademarks"), then, at Sage's written request, promptly following the effective date of such termination, Biogen, on behalf of itself and its Affiliates, will transfer and assign to Sage all of Biogen's and its Affiliates' rights, title and interest in and to such Reversion Trademarks for the applicable country of the Terminated Territory, pursuant to an agreement that the Parties will negotiate and enter into after such effective date of termination, which agreement will contain, to the extent applicable, quality control and indemnification obligations customary of such agreements applying to Sage's use of such transferred Reversion Trademarks(s) following such assignment or license, as applicable.

**14.6.10** *Exclusivity.* In any event of termination of this Agreement, each Party's obligations under Section 11.7.1.1 (Exclusivity) will terminate with respect to (a) 217 Competing Products, if the Product Class with respect to which this Agreement is terminated is the Licensed 217 Products, or (b) 324 Competing Products, if the Product Class with respect to which this Agreement is terminated is the Licensed 324 Products, or (c) a Product Class for the Profit-Share Territory, if the Agreement is terminated for such Product Class for the Profit-Share Territory or a Region.

**14.6.11** *Return of Confidential Information.* Except in the case of Sage for any Confidential Information that is the subject of its Reversion License, each Party, at its cost, will promptly return to the other Party (or as directed by such other Party destroy and certify to such other Party in writing as to such destruction) all of such other Party's Confidential Information that relates to the Terminated Products for the Terminated Territory and that was provided by or on behalf of such other Party hereunder that is in the possession or control of such Party (or any of its Affiliates, Sublicensees or subcontractors), except that such Party will have the right to retain copies of intangible Confidential Information of such other Party for legal purposes in accordance with such Party's internal compliance policies. Notwithstanding the return or destruction of any Confidential Information, the Parties will continue to be bound by their confidentiality obligations under this Agreement.

**14.6.12** *IP Files Transfer.* With respect to any Biogen Collaboration Patents that claim solely the Terminated Products in the Terminated Territory and under which Sage is granted an exclusive license pursuant to Section 14.6.2 (Reversion License), at Sage's cost and expense, Biogen will transfer to Sage or its designee copies of filings, applications and correspondence received or generated by Biogen in the course of Prosecuting and Maintaining such Biogen Collaboration Patents. With respect to any Sage Prosecuted Patents for which Biogen has exercised its step-in rights under Section 13.4.3.2 (Biogen Step-In) or in respect of which Biogen has engaged in the enforcement thereof or defense or Post-Grant Proceedings therefor under, respectively, Section 13.5.2 (Right to Enforce) and Section 13.5.3 (Defense and Post-Grant Proceedings), at Sage's cost and expense, Biogen will transfer to Sage or its designee copies of filings, applications, correspondence and other related records received or generated by Biogen in the course of exercising such activities.

**14.6.13** *Dissolution of Committees.* If this Agreement is terminated in its entirety, all Committees will be dissolved as of the effective date of such termination, *provided* that, for any surviving provisions requiring action or decision by any of the Committees or an Executive Officer, each Party will appoint representatives to act as its Committee members or Executive Officer, as applicable. If this Agreement is terminated in part, then the subject-matter responsibility of the respective Committees will no longer extend to the Terminated Products.

**14.6.14** *Termination of Rights and Obligations.* Except as set forth in this Section 14.6 (Effect of Termination by Sage for Cause or for Biogen's Insolvency, or by Biogen for Convenience) and Section 14.8 (Effect of Expiration or Termination; Survival), all rights and obligations of the Parties under this Agreement will terminate as of the applicable effective date of any termination of this Agreement in its entirety.

**14.6.15** *Further Assurances.* Each Party will execute all reasonable documents and take all such further actions as may be reasonably requested by the other Party, at such other Party's cost, in order to give effect to the foregoing clauses.

**14.7** **Biogen Right of Termination for Cause or for Sage's Insolvency.** If Biogen has the right to terminate this Agreement pursuant to Section 14.4.1.2 (Material Breach) or Section 14.5 (Termination for Insolvency), then Biogen will have the option to either: (a) terminate this Agreement with respect to the Product Class(es) and Region(s) to which such material breach relates or in its entirety, or (b) [\*\*]. Biogen's notice to Sage, under Section 14.4.1.2 (Material Breach) or Section 14.5 (Termination for Insolvency), as applicable, will specify which of the foregoing options Biogen has elected.

**14.7.1** *Reversion of Rights to Sage.* The provisions of Section 14.6 (Effect of Termination by Sage for Cause or for Biogen's Insolvency, or by Biogen for Convenience) covering a termination of this Agreement in its entirety will apply *mutatis mutandis* as of the effective date of such termination, except that in the event Biogen terminates this Agreement pursuant to Section 14.4.1.2 (Material Breach) or Section 14.4 (Termination for Insolvency):

**14.7.1.1** With respect to the Reversion License, [\*\*]: (a) [\*\*], (b) [\*\*]; and

**14.7.1.2** Sage will reimburse Biogen for the undisputed portion of all reasonable and documented costs and expenses incurred by Biogen in the performance of any of Biogen's obligations under Section 14.6 (Effect of Termination by Sage for Cause or for Biogen's Insolvency, or by Biogen for Convenience) no later than [\*\*] after receiving an applicable invoice from Biogen for the same.

**14.7.2** [\*\*]. In the event [\*\*]

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**14.7.2.5** *Further Assurances.* Each Party will execute all reasonable documents and take all such further actions as may be reasonably requested by the other Party, at such other Party's cost, in order to give effect to the foregoing clauses.

**14.8** **Effect of Expiration or Termination; Survival.**

**14.8.1** Expiration or termination of this Agreement for any reason will not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination

or expiration, nor preclude either Party from pursuing all rights and remedies it may have hereunder or at Law or in equity, with respect to any breach of this Agreement.

**14.8.2** In addition to the termination consequences set forth in Section 14.6 (Effect of Termination by Sage for Cause or for Biogen's Insolvency, or by Biogen for Convenience) and Section 14.7 (Biogen Right of Termination for Cause or for Sage's Insolvency) (and any Sections referenced therein), the following provisions will survive expiration or termination of this Agreement in its entirety for any reason: Article 1 (Definitions), Section 3.7 (Joint Program Activities Records) (to the extent consistent with the applicable Party's record retention policies), Section 6.9 (Recalls, Market Withdrawals or Corrective Actions), Section 6.11 (Priority Review Voucher), Section 7.8.1 (Manufacturing Technology Transfer) (solely in case of termination and solely with respect to amounts accrued prior to termination but not paid and the cost allocation provisions therein), Section 8.5 (No Other Rights) (solely in case of termination), Article 9 (Payments) (other than Section 9.4 (Finance Working Group) and Section 9.5 (Sage Opt-Out)) (solely with respect to amounts accrued prior to termination but not paid, and the reporting, information procedures and audits associated therewith), Article 10 (Confidentiality and Publications), Article 12 (Indemnification, Limitation of Liability, Insurance), Section 13.1 (Inventorship), Section 13.2 (Ownership), Section 13.4.3 (\*\*\*) (solely with respect to the Joint Collaboration Patents), Section 13.4.4 (Patent Costs Sharing) (solely with respect to the Joint Collaboration Patents and for the Parties to continue sharing 50:50 the Patent Costs incurred for their Prosecution and Maintenance of the Joint Collaboration Patents), Section 13.4.5 (Patent Miscellaneous) (solely with respect to the Joint Collaboration Patents), Section 13.9 (Common Interest), Section 14.1 (Term) (solely in case of expiration), Section 14.8 (Effect of Expiration or Termination, Survival), and Article 15 (Miscellaneous).

## 15. MISCELLANEOUS

### 15.1 Assignment.

**15.1.1** *General.* Except as provided in this Section 15.1 (Assignment), this Agreement may not be assigned or otherwise transferred, nor may any right or obligation hereunder be assigned or transferred, by either Party without the prior written consent of the other Party. Notwithstanding the foregoing, (a) either Party may, without the other Party's prior written consent, (i) assign this Agreement and its rights and obligations hereunder in whole or in part to an Affiliate, (ii) assign this Agreement and its rights and obligations hereunder in whole to a party that acquires, by merger, sale of assets, reorganization or otherwise, all or substantially all of the business of such Party, and (b) subject to Section 9.11.5.3 (Tax Actions), Biogen may[, \*\*], *provided* that Biogen may not [\*\*]. Any permitted successor or assignee of any rights or obligation under this Agreement must expressly assume performance thereof. Notwithstanding, the assigning Party will remain responsible for the performance by its assignee of any obligation hereunder so assigned. Any purported assignment in violation of this Section 15.1 (Assignment) will be void.

**15.1.2** *Securitization.* Notwithstanding anything to the contrary in Section 15.1.1 (General) or elsewhere in this Agreement (but subject to the indemnification obligations under Section 9.11.5.3 (Tax Actions)), Sage may assign to a Third Party its right to receive the milestone payments under Sections 9.6 (Licensed Products Regulatory/Commercial Milestone Payments) and 9.7 (Licensed Products Sales Milestone Payments) and the royalty payments under Section 9.8 (Licensed Products Royalties) (such assignment, a "**Securitization Transaction**"). In connection with a contemplated Securitization Transaction, Sage may disclose to such Third Party [\*\*] (*provided* that such Third Party is under obligations of confidentiality and non-use with respect to Confidential Information included in [\*\*] that are no less stringent than the terms of Article 10 (Confidentiality and Publication) (but of duration customary in confidentiality agreements entered into for a similar purpose)), and to allow such Third Party to exercise its rights with respect to such Securitization Transaction. After the closing of any such Securitization

Transaction with a Third Party, Sage may disclose to such Third Party [\*\*], to the extent reasonably necessary to enable such Third Party to exercise its rights with respect to such Securitization Transaction. As part of any consummated Securitization Transaction, subject to the terms of this [Section 15.1.2](#) (Securitization), Sage may assign, [\*\*], its right to receive the royalty reports and to conduct audits under, respectively, [Section 9.11.2](#) (Reports and Royalty Payments) and [Section 9.11.3](#) (Records and Audits) to the counterparty in such Securitization Transaction, and to allow such counterparty to exercise its rights under such Sections.

**15.2 Governing Law.** The Agreement will be construed and the respective rights of the Parties determined in accordance with the substantive Laws of the Commonwealth of Massachusetts, notwithstanding any provisions of the Laws of the Commonwealth of Massachusetts or any other Law governing conflicts of laws to the contrary.

### **15.3 Dispute Resolution.**

**15.3.1 Disputes.** Except as otherwise expressly set forth in this Agreement, including [Section 2.7](#) (Resolution of Committee Disputes), [Section 8.3.2.4](#) (New Technology Disputes) and [Section 13.4.1.4](#) (Decision Making), disputes of any nature arising under, relating to, or in connection with this Agreement (“**Disputes**”) will be resolved pursuant to this [Section 15.3](#) (Dispute Resolution). For the avoid of doubt, disputes of any nature arising under, relating to, or in connection with the SPA will be subject to resolution in accordance with the dispute resolution provisions thereunder.

**15.3.2 Dispute Escalation.** In the event of a Dispute between the Parties, the Parties will first attempt to resolve such Dispute by negotiation and consultation between themselves. In the event that such Dispute is not resolved on an informal basis within [\*\*] from receipt of the written notice of a Dispute, any Party may, by written notice to the other, have such Dispute referred to the Executive Officers (or their designee, which designee is required to have decision-making authority on behalf of such Party), who will attempt to resolve such Dispute by negotiation and consultation for a [\*\*] period following receipt of such written notice. Any final decision agreed by the Executive Officers will be conclusive and binding on the Parties under the then existing circumstances, *provided* that no such decision shall modify or amend the terms or conditions of this Agreement.

**15.3.3 General.** Except as set forth in [Section 2.7](#) (Resolution of Committee Disputes), [Section 8.3.2.4](#) (New Technology Disputes), [Section 9.11.3.2](#) (Audit Disputes) or [Section 13.4.1.4](#) (Decision Making), or [Section 15.3.5](#) (Expert Arbitration), or as otherwise expressly set forth in this Agreement, in the event the Parties have not resolved such Dispute within [\*\*], either Party may at any time after such [\*\*] period elect to initiate a proceeding pursuant to the procedures set forth in [Section 15.3.4](#) (Jurisdiction) for purposes of having the Dispute settled.

**15.3.4 Jurisdiction.** Each of the Parties (a) hereby submits to the jurisdiction of the United States District Court for the District of Massachusetts or any Massachusetts court sitting in Boston so long as one of such courts will have subject matter jurisdiction over such claim, in any proceeding arising out of or relating to this Agreement and (b) agrees not to commence any suit, action or proceeding relating thereto except in such court, and waives, to the fullest extent permitted by applicable Law, the right to move or dismiss or transfer any action brought in such court on the basis of any objection to personal jurisdiction, venue or inconvenient jurisdiction. Any rights to trial by jury with respect to any suit, action, proceeding or claim (whether based upon contract, tort or otherwise), directly or indirectly, arising out of or relating to this Agreement hereunder are expressly and irrevocably waived by each of the Parties.



**15.3.5** *Expert Arbitration.* Any dispute expressly stated in this Agreement to be resolved pursuant to this Section 15.3.5 (Expert Arbitration) will take place pursuant to the following procedures.

**15.3.5.1** The expert arbitration will be overseen by and conducted as a “baseball” form of binding arbitration conducted by a panel of three (3) arbitrators (“**Panel**”). No later than [\*\*] after the initiation of arbitration, each Party will appoint one (1) arbitrator and, no later than [\*\*] after confirmation of the two (2) Party-appointed arbitrators, the third (3<sup>rd</sup>) arbitrator will be selected by the two (2) Party-appointed arbitrators and will act as the chair. The Parties may confer with their respective Party-appointed arbitrators regarding the appointment of the chair. Each arbitrator comprising the Panel will have at least [\*\*] of experience in the negotiation of biotechnology and pharmaceutical license and collaboration agreements. At the election of any member of the Panel, the Panel may engage one or more independent experts with experience in the subject matter of the Dispute to advise the Panel, but final decision-making authority will remain with the panel.

**15.3.5.2** No later than [\*\*] after the constitution of the Panel, each Party will submit to both the Panel and the other Party a detailed written proposal setting forth its proposed resolution of the Dispute. The Parties will also provide to the Panel a copy of this Agreement, as may be amended at such time.

**15.3.5.3** No later than [\*\*] after the delivery of the Parties’ detailed written proposals to the Panel, each Party will submit to both the Panel and the other Party a legal brief (and any exhibits) explaining and supporting the Party’s detailed written proposal, which legal brief shall be no more than [\*\*].

**15.3.5.4** There will be no discovery and there will be no hearing, although such arbitration proceeding will be deemed to have its seat in Boston, Massachusetts, and all arbitration proceedings will be conducted in the English language.

**15.3.5.5** No later than [\*\*] after the submission of the Parties’ legal briefs, the Panel will select one of the two detailed written proposals (without modification) provided by the Parties that the Panel believes is most consistent with the intention underlying and agreed principles set forth in this Agreement. The decision of the Panel will be final and unappealable. The detailed written proposal selected by the Panel will automatically be binding on the Parties.

**15.3.5.6** The Panel must select one of the two detailed written proposals and may not combine elements of both detailed written proposals or take any other action.

**15.3.5.7** Each Party shall bear its own attorneys’ fees, costs and disbursements arising out of the arbitration, and shall pay an equal share of the fees and costs of the Panel.

**15.3.6** *Injunctive Relief.* Notwithstanding the dispute resolution procedures set forth in this Section 15.3 (Dispute Resolution), in the event of an actual or threatened breach of this Agreement, the aggrieved Party may seek equitable relief (including restraining orders, specific performance or other injunctive relief), without first submitting to any dispute resolution procedures hereunder. Any claim for such equitable relief will be submitted to the United States District Court for the District of Massachusetts or any Massachusetts court sitting in Boston so long as one of such courts will have subject matter jurisdiction over such claim, and each Party hereby irrevocably consents to the exclusive jurisdiction of such courts (and of the appropriate appellate courts therefrom) in any proceeding with respect to any such claim and irrevocably waives, to the fullest extent permitted by Law, any objection that it may now or

hereafter have to the laying of the venue of any such proceeding in any such court or that any such proceeding brought in any such court has been brought in an inconvenient forum. Process in any such proceeding may be served on either Party anywhere in the world, whether within or without the jurisdiction of any such court. Without limiting the foregoing, each Party agrees that service of process on such Party in accordance with Section 15.10 (Notices) will be deemed effective service of process on such Party. Each of the Parties hereby irrevocably waives any and all right to trial by jury in any such proceeding.

**15.3.7** *Tolling.* The Parties agree that all applicable statutes of limitation and time-based defenses (such as estoppel and laches), as well as all time periods in which a Party must exercise rights or perform obligations hereunder, will be tolled once the dispute resolution procedures set forth in this Section 15.3 (Dispute Resolution) have been initiated and for so long as they are pending, and the Parties will cooperate in taking all actions reasonably necessary to achieve such a result. In addition, during the pendency of any Dispute under this Agreement initiated before the end of any applicable cure period, including under Section 14.4 (Termination for Material Breach) or Section 14.5 (Termination for Insolvency), (a) this Agreement will remain in full force and effect, (b) the provisions of this Agreement relating to termination for material breach with respect to such Dispute will not be effective, (c) the time periods for cure under Section 14.4 (Termination for Material Breach) or Section 14.5 (Termination for Insolvency) as to any termination notice given prior to the initiation of the applicable dispute resolution procedure will be tolled, (d) any time periods to exercise rights or perform obligations will be tolled; and (e) neither Party will issue a notice of termination pursuant to this Agreement based on the subject matter of the Dispute until such Dispute has been resolved in accordance with the applicable dispute resolution procedure, the outcome of such dispute resolution procedure confirmed the material breach and the existence of the facts claimed by a Party to be the basis for the asserted material breach and all previously tolled cure periods have run; *provided* that if such breach can be cured by (i) the payment of money, the defaulting Party will have an additional **[\*\*]** within its receipt of the applicable dispute resolution decision, if necessary in addition to the remainder of any applicable previously tolled cure period, to pay such amount or (ii) the taking of specific remedial actions, the defaulting Party will have a reasonably necessary period to diligently undertake and complete such remedial actions within such reasonably necessary period or any specific timeframe established by the applicable dispute resolution decision, as necessary in addition to the remainder of any applicable previously told cure period, before any such notice of termination can be issued.

**15.4** **Entire Agreement; Amendments.** This Agreement, together with the SPA, the Supply Agreement and the Pharmacovigilance Agreement, contains the entire understanding of the Parties with respect to the subject matter hereof, and supersedes all previous arrangements with respect to the subject matter hereof, whether written or oral, including, effective as of the Execution Date. This Agreement may be amended, or any term or condition hereof modified, only by a written instrument duly-executed by authorized representatives of both Parties. Any term or condition of this Agreement may be waived if, but only if, such waiver is in writing and signed by an authorized representative of the Party against whom the waiver is to be effective. The Schedules attached hereto may be amended, or any term or conditions hereof modified, only by a written instrument duly-executed by authorized representatives of both Parties.

**15.5** **Severability.** If any provision hereof should be held invalid, illegal or unenforceable in any respect in any jurisdiction, then the Parties will substitute valid provisions for such invalid, illegal or unenforceable provisions as may be agreed by the Parties, which valid provisions in their economic effect are sufficiently similar to the invalid, illegal or unenforceable provisions that it can be reasonably assumed that the Parties would have entered into this Agreement with such valid provisions. In case such valid provisions cannot be agreed upon by the Parties, the invalid, illegal or unenforceable nature of one or several provisions of this Agreement will not affect the validity of this Agreement as a whole, unless the invalid, illegal or unenforceable provisions are of such essential importance to this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without the invalid, illegal or unenforceable provisions.

**15.6 Headings.** The captions to the Sections hereof are not a part of this Agreement, but are merely for convenience to assist in locating and reading the several Sections hereof.

**15.7 Waiver of Rule of Construction.** Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement. Accordingly, the rule of construction that any ambiguity in this Agreement will be construed against the drafting Party will not apply.

**15.8 Interpretation.** Except where the context expressly requires otherwise, (a) the use of any gender herein will be deemed to encompass references to either or both genders, and the use of the singular will be deemed to include the plural (and vice versa); (b) the words “include”, “includes” and “including” will be deemed to be followed by the phrase “without limitation” and will not be interpreted to limit the provision to which it relates; (c) the word “shall” will be construed to have the same meaning and effect as the word “will”; (d) any definition of or reference to any agreement, instrument or other document herein will be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein); (e) any reference herein to any Person will be construed to include the Person’s successors and assigns; (f) the words “herein”, “hereof” and “hereunder”, and words of similar import, will be construed to refer to this Agreement in each of their entirety, as the context requires, and not to any particular provision hereof; (g) all references herein to Sections or Schedules will be construed to refer to Sections or Schedules of this Agreement, and references to this Agreement include all Schedules hereto and any capitalized terms used but not defined in any Schedules will have their respective meanings as defined in this Agreement; (h) the word “notice” means notice in writing (whether or not specifically stated) and will include notices, consents, approvals and other written communications contemplated under this Agreement; (i) provisions that require that a Party, the Parties or any committee hereunder “agree,” “consent” or “approve” or the like will require that such agreement, consent or approval be specific and in writing, whether by written agreement, letter, approved minutes or otherwise (but excluding e-mail and instant messaging); (j) references to any specific Law, or article, section or other division thereof, will be deemed to include the then-current amendments thereto or any replacement or successor Law thereof; and (k) the term “or” will be interpreted in the inclusive sense commonly associated with the term “and/or.”

**15.9 No Implied Waivers; Rights Cumulative.** No failure on the part of Sage or Biogen to exercise, and no delay in exercising, any right, power, remedy or privilege under this Agreement, or provided by statute or at Law or in equity or otherwise, will impair, prejudice or constitute a waiver of any such right, power, remedy or privilege or be construed as a waiver of any breach of this Agreement or as an acquiescence therein, nor will any single or partial exercise of any such right, power, remedy or privilege preclude any other or further exercise thereof or the exercise of any other right, power, remedy or privilege.

**15.10 Notices.** All notices that are required or permitted hereunder will be in writing and sufficient if delivered (a) personally, (b) sent by reliable electronic transmission (with complete transmission confirmed and confirmed by a hard copy delivered as soon as practicable thereafter by the method described in clauses (c) or (d)), (c) sent by nationally-recognized overnight courier, or (d) sent by registered or certified mail, postage prepaid, return receipt requested, addressed as follows:

If to Sage, to: Sage Therapeutics, Inc.  
215 First Street  
Cambridge, MA 02142  
Attention: Chief Operating Officer  
(with copy to) General Counsel  
Email:[\*\*] and [\*\*]

With a copy to (which will not constitute notice): Gibson Dunn & Crutcher LLP  
555 Mission Street  
San Francisco, CA 94105-0921  
Attention: Karen A. Spindler  
Email: KSpindler@gibsondunn.com

If to Biogen, to: Biogen MA Inc.  
225 Binney Street  
Cambridge, MA 02142  
Attention: Chief Legal Officer  
Email: [\*\*]

With a copy to (which will not constitute notice): Ropes & Gray LLP  
Prudential Tower  
800 Boylston Street  
Boston, MA 02199-3600  
Attention: Hannah Freeman  
Email: [\*\*]

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such notice will be deemed to have been given: (a) when delivered if personally delivered on a Business Day (or if delivered or sent on a non-Business Day, then on the next Business Day); (b) as of the date transmitted by electronic transmission (with complete transmission confirmed); (c) on the Business Day of receipt if sent by overnight courier or facsimile; or (d) on the Business Day of receipt if sent by mail. Any notice delivered by electronic transmission will be confirmed by a hard copy delivered as soon as practicable thereafter by the method described in clauses (c) or (d) above.

**15.11 Compliance with Export Regulations.** Neither Party will export any technology licensed to it by the other Party under this Agreement except in compliance with U.S. export Laws and regulations.

**15.12 Force Majeure.** Neither Party will be held liable to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in achieving any objective, satisfying any condition, or performing any obligation under this Agreement to the extent that such failure or delay is caused by or results from acts or events beyond the reasonable control of such Party, including acts of God, embargoes, war, acts of war (whether war be declared or not), terrorism, insurrections, riots, civil commotions, strikes, lockouts, or other labor disturbances (other than strikes, lockouts, or labor disturbances involving a Party's own employees), government actions, fire, earthquakes, floods, epidemics, pandemics, the spread of infectious diseases, and quarantines ("Force Majeure") beyond such Party's reasonable control and renders the performance impossible or illegal. The Parties agree the effects of the

COVID-19 pandemic that is ongoing as of the Execution Date may be invoked as a Force Majeure for the purposes of this Agreement even though the pandemic is ongoing to the extent those effects are not be reasonably foreseeable by the Parties as of the Execution Date. The affected Party will notify the other Party in writing of any Force Majeure event that may affect its performance under this Agreement as soon as reasonably practical, will provide a good faith estimate of the period for which its failure or delay in performance under this Agreement is expected to continue based on currently available information, and will undertake reasonable efforts necessary to mitigate and overcome such Force Majeure event and resume normal performance of its obligations hereunder as soon as a reasonably practicable under the circumstances. If the Force Majeure event continues, then the affected Party will update such notice to the other Party on a weekly basis, or more frequently if requested by the other Party, to provide updated summaries of its mitigation efforts and its estimates of when normal performance under the Agreement will be able to resume.

**15.13 Relationship of the Parties.** This Agreement will not constitute a partnership for any applicable Tax purposes, except as determined under Schedule 15.21 (Tax Partnership Agreement Terms). For the avoidance of doubt, the joint Commercialization will not be considered a partnership or a joint venture for purposes of VAT (in non-United States jurisdictions) unless specifically agreed between the Parties, and no Party will take any action so as to create a VAT establishment for any joint Commercialization activities in any non-United States jurisdiction in the Profit-Share Territory. Except to the extent expressly stated in this Agreement, neither Sage, on the one hand, nor Biogen, on the other hand, will have the authority to make any statements, representations or commitments of any kind, or to take any action, that will be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party will be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such Party.

**15.14 Performance by BIMA and BIG.** BIG unconditionally guarantees to Sage performance of BIMA's obligations under this Agreement (including all agreements, commitments to perform activities or incur expenditures, undertakings, licenses and payment obligations, now or hereafter entered into pursuant to this Agreement) ("**Guaranteed Obligations**"), and BIMA unconditionally guarantees to Sage performance of BIG's Guaranteed Obligations. Each of BIG and BIMA agrees that the validity of their respective guaranties in this Section 15.14 (Performance by BIMA and BIG) and their respective obligations hereunder will not be terminated, affected, diminished or impaired by reason of the assertion or the failure to assert by Sage against BIMA or BIG any of the rights or remedies reserved to Sage pursuant to the provisions of this Agreement or otherwise or any other remedy or right which such Sage may have at law or in equity or otherwise. The foregoing guarantee will be continuing until all Guaranteed Obligations now existing or hereafter arising have been discharged in full, and shall be and continue to be fully effective notwithstanding any amendment to this Agreement or any of the Guaranteed Obligations (but subject to any changes to the Guaranteed Obligations resulting therefrom). To the extent Sage grants to BIG (a) any waiver of any default by BIMA of the Guaranteed Obligations, (b) any extension of time of performance by BIMA of the Guaranteed Obligations, or (c) any release of BIMA from the performance of the Guaranteed Obligations, Sage will have and be deemed to have also granted the same to BIG hereunder. To the extent Sage grants to BIMA (i) any waiver of any default by BIG of its Guaranteed Obligations, (ii) any extension of time of performance by BIG of its Guaranteed Obligations or (iii) any release of BIG from the performance of its Guaranteed Obligations, Sage will have and be deemed to have also granted the same to BIMA hereunder. The obligations of BIG and BIMA under this Section 15.14 (Performance by BIMA and BIG) will not be subject to any counterclaim, setoff, deduction or defense based on any claim that such guaranteeing party may have against the guaranteed party, or any other person or entity, and will remain in full force and effect without regard to, and will not be released, suspended, abated, deferred, reduced, limited, discharged, terminated or otherwise impaired or adversely affected by any circumstance or occurrence whatsoever, other than full performance of the respective Guaranteed Obligations.

**15.15 Coordination between BIMA and BIG.** It is understood and agreed that any performance due to Biogen by Sage under this Agreement will be deemed rendered to Biogen to the extent such performance by Sage is rendered to either BIMA or BIG, and BIMA and BIG may only look to the other for any share or benefit from Sage's obligations under this Agreement. It is further agreed that BIMA and BIG will not act separately under this Agreement, and with respect to the exercise of the rights of Sage or Biogen under this Agreement, BIMA will be deemed to have the authority to bind both itself and BIG and BIG will be deemed to have the authority to bind both itself and BIMA. BIMA and BIG will be jointly liable for their obligations under this Agreement, and it is understood and agreed that for purposes of Section 14.4 (Termination for Material Breach), an uncured breach by either BIMA or BIG will be deemed a breach by both BIMA and BIG. Without limiting the foregoing, any notice to or from Biogen and any consent, approval, agreement, actions or inactions of Biogen under this Agreement will be deemed notices to or from both BIMA and BIG and consent, approval, agreement, actions or inactions by both BIMA and BIG under this Agreement.

**15.16 Expenses.** Except as otherwise provided herein, all fees, costs and expenses (including any legal, accounting and banking fees) incurred in connection with the preparation, negotiation, execution and delivery of this Agreement and to consummate the transactions contemplated hereby will be paid by the Party hereto incurring such fees, costs and expenses.

**15.17 Counterparts.** The Agreement may be executed in two or more counterparts, including by facsimile or PDF signature pages, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

**15.18 Performance by Affiliates.** Each Party acknowledges and accepts that the other Party may exercise its rights and perform its obligations (including granting or continuing licenses and other rights) under this Agreement either directly or through one or more of its Affiliates. A Party's Affiliates will have the benefit of all rights (including all licenses and other rights) of such Party under this Agreement, but not be subject to such Party's obligation, unless expressly provided herein, or in the case of a permitted assignment, in accordance with Section 15.1 (Assignment). Accordingly, in this Agreement "Biogen" will be interpreted to mean "Biogen or its Affiliates" and "Sage" will be interpreted to mean "Sage or its Affiliates" where necessary to give each Party's Affiliates the benefit of the rights provided to such Party in this Agreement and the ability to perform its obligations (including granting or continuing licenses and other rights) under this Agreement; *provided, however*, that in any event each Party will remain responsible for the acts and omissions, including financial liabilities, of its Affiliates.

**15.19 Binding Effect; No Third Party Beneficiaries.** As of the Execution Date, this Agreement will be binding upon and inure to the benefit of the Parties and their respective permitted successors and permitted assigns. Except as expressly set forth in this Agreement, no Person other than the Parties and their respective Affiliates and permitted assignees hereunder will be deemed an intended beneficiary hereunder or have any right to enforce any obligation of this Agreement.

**15.20 Further Assurances.** The Parties agree to reasonably cooperate with each other in connection with any actions required to be taken in furtherance of their respective obligations under this Agreement, including (a) furnishing to each other such further information; (b) executing and delivering to each other such other documents; and (c) doing such other acts and things (including working collaboratively to correct any clerical, typographical, or other similar errors in this Agreement), all as the other Party may reasonably request for the purpose of carrying out the intent of this Agreement.

## **15.21 Tax Matters.**

### **15.21.1** *Tax Treatment.*

**15.21.1.1** The Parties agree to treat the transactions contemplated by this Agreement related to the Profit-Share Territory as a partnership for United States federal and state income Tax purposes between Sage and BIMA (the “**Tax Partnership**”), with Sage and BIMA as partners of the Tax Partnership only upon receipt of Regulatory Approval by the FDA with respect to a Licensed Product to be sold in the Profit-Share Territory; *provided, however*, that no Tax Partnership will be treated as being formed if (a) prior to the receipt of such Regulatory Approval by the FDA, Sage exercises its Opt-Out Right with respect to such Licensed Product or (ii) Biogen reasonably determines based on the advice of a nationally recognized tax advisor that the Parties are not required to treat the transactions contemplated by this Agreement as a partnership for U.S. Federal income tax purposes. The Parties shall file all Tax returns consistent with such Tax treatment. The Parties will work together in good faith to execute a written tax partnership agreement for the Tax Partnership between BIMA and Sage that will incorporate the principles of Schedule 15.21 (Tax Partnership Agreement Terms).

**15.21.1.2** Unless Biogen notifies Sage in writing that Biogen has determined that Biogen and Sage will not follow the tax treatment set forth in this Section 15.21.1.2 (Tax Treatment), then the Parties agree to treat the transactions contemplated by this Agreement related to the Biogen Territory, including the payment by BIG pursuant to Section 9.11.6.2 (Payment Allocation), as not being a partnership between any of the Parties for any Tax purposes. The Parties agree that BIG shall not be a partner of the Tax Partnership and that the transactions contemplated by this Agreement related to the Biogen Territory shall be treated as occurring outside of, and separate from, the Tax Partnership. The Parties shall file all Tax returns consistent with such Tax treatment.

**15.22 HSR Act.** Notwithstanding any provision to the contrary in this Agreement, the following provisions of this Agreement will be in full force and effect as of the Execution Date: Article 1 (Definitions), Article 11 (Representations, Warranties and Covenants), Section 14.2 (Termination Prior to Effective Date) and Article 15 (Miscellaneous). The Confidentiality Agreement between Sage and Biogen, dated as of [\*\*], as amended on [\*\*], will continue to be effective and, if the Effective Date occurs, shall terminate on the Effective Date and all information disclosed or exchanged under such agreement will be treated as Confidential Information disclosed under this Agreement. Neither Party shall have the right to terminate this Agreement during any HSR clearance period, unless (a) in the event that the SPA is validly terminated pursuant to Section 9.1 of the SPA prior to Closing as defined in the SPA occurring thereunder, in which case this Agreement will terminate concurrently with the termination of the SPA or (b) Section 14.2 (Termination Prior to Effective Date) applies, and, in each case ((a) or (b)), notwithstanding any provisions that are stated to survive under Section 14.8.2 (Effect of Expiration or Termination; Survival) all provisions of this Agreement will terminate and be of no force or effect whatsoever.

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IN WITNESS WHEREOF, the Parties have executed this Agreement as of the Effective Date.

**Sage Therapeutics, Inc.**

BY: /s/ Jeff Jonas, M.D.  
NAME: Jeff Jonas, M.D.  
TITLE: Chief Executive Officer

**Biogen MA Inc.**

BY: /s/ Michel Vounatsos  
NAME: Michel Vounatsos  
TITLE: Chief Executive Officer

**Biogen International, GmbH**

BY: /s/ Fred Lawson  
NAME: Fred Lawson  
TITLE: Director

*[Signature Page to Collaboration and License Agreement]*

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## SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Severance and Change in Control Agreement (this “Agreement”) is made as of September 13, 2021 by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Christopher Benecchi (the “Executive”) and shall become effective on the date of hire with the Company.

1. **Purpose.** The Company considers it essential to the best interests of its stockholders to promote and preserve the continuous employment of key management personnel. The Board of Directors of the Company (the “Board”) recognizes that, as is the case with many corporations, the possibility of a Change in Control (as defined in Section 2 hereof) exists and that such possibility, and the uncertainty and questions that it may raise among management, may result in the departure or distraction of key management personnel to the detriment of the Company and its stockholders. Therefore, the Board has determined that appropriate steps should be taken to reinforce and encourage the continued attention and dedication of members of the Company’s key management, including the Executive, to their assigned duties without distraction, including in the face of potentially disturbing circumstances arising from the possibility of a Change in Control. Nothing in this Agreement shall be construed to affect the at-will nature of the employment relationship, the Executive shall not have any right to be retained in the employ of the Company.

2. **Change in Control.** A “Change in Control” shall be deemed to have occurred upon the occurrence of any one of the following events: (a) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (b) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (c) the sale of all of the stock of the Company to an unrelated person, entity or group thereof acting in concert, or (d) any other transaction in which the owners of the Company’s outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

### 3. **Terminating Event.**

A “Terminating Event” shall mean any of the events provided in this Section 3:

(a) Termination by the Company. Termination by the Company of the employment of the Executive with the Company for any reason other than for Cause, death or Disability. For purposes of this Agreement, “Cause” shall mean, as determined by the Company in good faith:

(i) the indictment the Executive of any felony, any crime involving the Company, or any crime involving fraud, moral turpitude or dishonesty;

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(ii) any unauthorized use or disclosure of the Company's proprietary information which has an adverse effect on the Company's business or reputation. As used in this paragraph, "Proprietary Information" means any information in whatever form, tangible or intangible, related to the business of the Company unless the information is publicly available in hard copy or electronic format, through lawful means;

(iii) any intentional misconduct or gross negligence on the Executive's part which has a materially adverse effect on the Company's business or reputation; or

(iv) the Executive's repeated and willful failure to perform the duties, functions and responsibilities of the Executive's position after a written warning from the Company.

A Terminating Event shall not be deemed to have occurred pursuant to this Section 3(a) solely as a result of the Executive becoming an employee of any direct or indirect successor to the business or assets of the Company, rather than continuing as an employee of the Company following a Change in Control. For purposes hereof, the Executive will be considered "Disabled" if, as a result of the Executive's incapacity due to physical or mental illness, the Executive shall have been absent from his duties to the Company on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

(b) Termination by the Executive for Good Reason. Termination by the Executive of the Executive's employment with the Company for Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following, the occurrence of any of the following events:

(i) a material diminution in the Executive's responsibilities, authority or duties;

(ii) a material diminution in the Executive's base salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all senior management employees of the Company;

(iii) a material change, defined as miles or more, in the geographic location at which the Executive is required to provide services to the Company, not including business travel and short-term assignments; or

(iv) a material breach of this Agreement by the Company.

"Good Reason Process" shall mean that (i) the Executive reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive provides a Notice of Termination to the Company within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

4. **Change in Control Payment.** In the event a Terminating Event occurs on or within the 12 months immediately after a Change in Control (such 12-month period, the "Change in Control

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Period”), subject to the Executive signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities, confidentiality, return of property and non-disparagement, in the form attached hereto as Attachment A (the “Separation Agreement and Release”) and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination or end of the Cure Period , the following shall occur

(a) the Company shall pay to the Executive an amount equal to the sum of (i) 9 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event (or the Executive’s annual base salary in effect immediately prior to the Change in Control, if higher), and (ii) a pro rata portion of the Executive’s target bonus for the fiscal year in which the termination of employment occurs, determined by multiplying the target bonus by a fraction, the numerator of which shall be the number of days during the fiscal year in which the Executive was employed by the Company and the denominator of which shall be 365;

(b) if the Executive was participating in the Company’s group health plan immediately prior to the Date of Termination and elects COBRA health continuation , then the Company shall pay to the Executive a lump sum payment, in an amount equal to 12 times the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company;

(c) notwithstanding anything to the contrary in any applicable option agreement or stock-based award agreement, all stock options and other stock-based awards with time-based vesting held by the Executive shall immediately accelerate and become fully exercisable and nonforfeitable as of the Executive’s Date of Termination conditioned upon the Separation Agreement and Release becoming irrevocable; and

(d) the amounts payable under this Section 4 shall be paid out in a lump sum commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the amounts shall be paid in the second calendar year by the last day of such 60-day period. All other wages earned, including, but not limited to, accrued vacation, to the Date of Termination shall be paid on the Date of Termination.

5. **Severance Outside the Change in Control Period**. In the event a Terminating Event occurs at any time other than during the Change in Control Period, subject to the Executive signing the Separation Agreement and Release and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination, the following shall occur:

(a) the Company shall pay to the Executive an amount equal to 12 months times the Executive’s annual base salary in effect immediately prior to the Terminating Event;

(b) if the Executive was participating in the Company’s group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a monthly cash payment for 12 months in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company; and

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(c) the amounts payable under this Section 5 shall be paid out in substantially equal installments in accordance with the Company's payroll practice over 12 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the Severance Amount shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

#### **6. Additional Limitation.**

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the "Compensatory Payments"), would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), (or any successor provision), then the Compensatory Payments shall be reduced so that the sum of all of the Compensatory Payments shall be \$1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code (or any successor provision); provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Compensatory Payments were not subject to such reduction. In such event, the Compensatory Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Compensatory Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (i) cash payments not subject to Section 409A of the Code; (ii) cash payments subject to Section 409A of the Code; (iii) equity-based payments and acceleration; and (iv) non-cash forms of benefits; provided that in the case of all the foregoing Compensatory Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 6, the "After Tax Amount" means the amount of the Compensatory Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive's receipt of the Compensatory Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Compensatory Payments shall be made pursuant to Section 6(a) shall be made by an accounting firm selected by the Company (the "Accounting Firm"), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

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## 7. Section 409A.

(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's "separation from service" within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death.

(b) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(c) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(d) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. **Term.** This Agreement shall take effect on the date first set forth above and shall terminate upon the earlier of (a) the termination of the Executive's employment with the Company for any reason other than the occurrence of a Terminating Event, or (b) the date all amounts have been paid to the Executive upon a Terminating Event pursuant to Section 4 or Section 5 hereof.

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9. **Withholding.** All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

10. **Notice and Date of Termination.**

(a) Notice of Termination. After a Change in Control and during the term of this Agreement, any purported termination of the Executive's employment (other than by reason of death) shall be communicated by written Notice of Termination from one party hereto to the other party hereto in accordance with this Section 10. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) Date of Termination. "Date of Termination" shall mean: (i) if the Executive's employment is terminated by his death, the date of his death; (ii) if the Executive's employment is terminated on account of Executive's Disability or by the Company for Cause, the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause the date on which a Notice of Termination is given; (iv) if the Executive's employment is terminated by the Executive without Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

11. **No Mitigation.** The Company agrees that, if the Executive's employment by the Company is terminated during the term of this Agreement, the Executive is not required to seek other employment or to attempt in any way to reduce any amounts payable to the Executive by the Company pursuant to Section 4 or Section 5 hereof. Further, the amount of any payment provided for in this Agreement shall not be reduced by any compensation earned by the Executive as the result of employment by another employer.

12. **Consent to Jurisdiction.** The parties hereby consent to the jurisdiction of the Superior Court or the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

13. **Integration.** This Agreement constitutes the entire agreement between the parties with respect to severance pay, benefits and accelerated vesting in connection with any termination of employment, to the extent inconsistent with any prior agreements supersedes the inconsistent provisions of such prior agreements between the parties concerning such subject matter, including without limitation any provisions of any offer letter or employment agreement relating to severance pay or benefits in connection with the ending of Executive's employment relationship with the Company. In the interest of clarity, any agreement relating to confidentiality, noncompetition, nonsolicitation or assignment of inventions shall not be affected by the Agreement.

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14. **Successor to the Executive.** This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after a Terminating Event but prior to the completion by the Company of all payments due him under this Agreement, the Company shall continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

15. **Enforceability.** If any portion or provision of this Agreement (including, without limitation, any portion or provision of any Section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

16. **Waiver.** No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

17. **Notices.** Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company, or to the Company at its main office, attention of the Board of Directors.

18. **Amendment.** This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

19. **Effect on Other Plans and Agreements.** An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 6 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such agreement and this Agreement, the terms of this Agreement shall govern and Executive may receive payment under this Agreement only and not both. Further, Section 4 and Section 5 of this Agreement are mutually exclusive and in no event shall Executive be entitled to payments or benefits pursuant to Section 4 and Section 5 of this Agreement.

20. **Governing Law.** This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

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21. **Successor to Company**. The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

22. **Gender Neutral**. Wherever used herein, a pronoun in the masculine gender shall be considered as including the feminine gender unless the context clearly indicates otherwise.

23. **Counterparts**. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

[Remainder of Page Intentionally Left Blank]

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**IN WITNESS WHEREOF**, the parties have executed this Agreement effective on the date and year first above written.

**SAGE THERAPEUTICS, INC.**

By: /s/ Barry Greene

Name: Barry Greene

Title: Chief Executive Officer

/s/ Christopher Benecchi

Employee Name: Christopher Benecchi

[Signature Page to Severance and Change in Control Agreement]

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## AMENDMENT TO SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Amendment to Severance and Change in Control Agreement (this “Amendment”) is made as of February 15, 2023 (the “Amendment Effective Date”) by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Christopher Benecchi (the “Executive”).

**WHEREAS**, the Company and the Executive previously entered into a certain Severance and Change in Control Agreement dated as of September 13, 2021 (the “Agreement”); and

**WHEREAS**, the Agreement contains a scrivener’s error and the parties desire to amend the terms of the Agreement to clarify the intent of the parties.

**NOW THEREFORE**, for good and valuable mutual consideration, including, but not limited to, your continued employment and access to Company confidential information, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree to amend the Agreement as follows:

1. Section 5(a) of the Agreement is hereby deleted in its entirety and replaced with the following:

“(a) the Company shall pay to the Executive an amount equal to 12 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event;”

2. All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. Except as set forth in this Amendment the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this Amendment, the terms of this Amendment will prevail.
3. This Amendment may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original, but such counterparts shall together constitute one and the same document.

**IN WITNESS WHEREOF**, the parties have executed this Amendment as of the Amendment Effective Date.

**CHRISTOPHER BENECCHI**

**By:** /s/ Christopher Benecchi  
duly authorized

**Print Name:** Christopher Benecchi

**Title:** Chief Business Officer

**SAGE THERAPEUTICS, INC.**

**By:** /s/ Barry Greene  
duly authorized

**Print Name:** Barry Greene

**Title:** Chief Executive Officer

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October 13, 2022

Laura M. Gault, M.D., Ph.D.

Dear Laura:

At Sage, our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. Our success results from our people creating therapeutics with benefits for patients coupled with our drive to excel in all areas of our business together.

On behalf of Sage Therapeutics, (the "Company" or "Sage"), I am pleased to extend an offer of employment to you. You have made an outstanding impression, and we welcome you to join our team and our quest to make a difference for patients. The purpose of this letter is to summarize the terms of your employment with the Company.

**Position**

Chief Medical Officer, Reporting to Barry Greene, Chief Executive Officer.

This position is a key factor in Sage's continued success, and we are confident that it will be an exciting opportunity for you as well. In considering this role, we ask that you agree to devote your full business time, best efforts, skill, knowledge, attention, and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company.

**Compensation**

Your base rate of compensation will be \$21,875.00 bi-monthly (annualized rate of \$525,000.00), less all applicable federal, state, and local taxes and withholdings, to be paid in installments in accordance with the Company's standard payroll practices. Such base salary may be adjusted from time to time in accordance with normal business practices and at the sole discretion of the Company.

In addition, you will be eligible to participate in the Sage Bonus Plan at an annual target of 40% your base salary, which will be prorated based upon your date of hire. Eligible employees starting on or before November 1 in the current plan year are eligible to participate in the plan. This discretionary bonus will be based on the Company's assessment and attainment of corporate and individual goals.

Subject to the approval of the Company's Board of Directors (the "Board") or designee and in connection with the commencement of your employment, you will be granted an equity award that includes a stock option grant (the "Option") and a performance share unit ("PSU") grant. The Option grant will be to purchase 64,410 shares of the Company's common stock, and the

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PSU grant will be for 52,545 units. The Option and PSUs will be granted on the first business day of the month following the commencement of your employment.

The exercise price of the Option will be equal to the fair market value of the Company's common stock on the date of grant. The Option will vest as follows: the Option will become exercisable as to 25% of the shares on the first anniversary of the Vesting Commencement Date, as defined below; and thereafter, shall become exercisable as to the remaining 75% of the shares in 36 equal monthly installments following the first anniversary of the Vesting Commencement Date until fully vested. The Vesting Commencement Date is your date of hire with the Company.

The PSUs will vest upon the achievement of certain performance goals of the Company. The goals and associated vesting are determined annually by the Board and are reflected in the grant agreement that will be provided to you. On any PSU vesting date, the tax liability will automatically be settled through net settlement of shares, and you will be issued the remaining vested shares.

Vesting of both the Option and PSUs assumes continued employment with Sage on the relevant vesting date(s). The Option and PSU grants will be subject to the terms and conditions of the Company's then-current shareholder-approved equity plan and its standard form of equity agreements.

### ***Sign On Bonus***

The Company will provide you with a sign-on bonus of \$200,000.00, to be paid on your first pay cycle, which will be subject to customary deductions and withholdings as required by law. If you should voluntarily terminate your employment with Sage within the first 12 months of receiving the sign-on bonus, you agree to return the net amount of the payment within 30 days of your departure date. If you should voluntarily terminate your employment with Sage within 13-24 months of receiving the sign-on bonus, you agree to return to the Company 50% of the net amount of the sign-on bonus within 30 days of your departure date.

The Company will provide you with a second sign-on bonus of \$175,000.00, to be paid on the first pay cycle following your one-year anniversary of employment, which will be subject to customary deductions and withholdings as required by law. If you should voluntarily terminate your employment with Sage within the first 12 months of receiving the sign-on bonus, you agree to return the net amount of the payment within 30 days of your departure date. If you should voluntarily terminate your employment with Sage within 13-24 months of receiving the sign-on bonus, you agree to return to the Company 50% of the net amount of the sign-on bonus within 30 days of your departure date.

### ***Benefits***

Because we care about the well-being of our employees, we are pleased to provide you with a comprehensive benefits and wellness package. This is meant to assist you in staying healthy,

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planning for the future, and developing your career. Our benefits currently include medical, dental, vision, vacation, wellness benefit, flexible-spending accounts, 401k, and much more. Additional information about these benefits is outlined in the enclosed summary.

***Eligibility for Employment***

For purposes of federal immigration law, you will be required to provide the Company documentary evidence that you are eligible for employment in the United States and evidence of your identity. This requirement applies to U.S. citizens, as well as foreign nationals. Such documentation must be provided to the Company within three (3) business days of your date of hire. Please bring the appropriate documents with you on your first day of employment.

***Employee Agreement***

As a condition of your employment, you will be required to execute the “Agreement Concerning Loyalty, Confidential Business Information, Inventions and Post-Employment Activity” (the “Employee Agreement”).

***Employment Relationship***

You acknowledge that this letter does not constitute a contract of employment for any particular period of time and does not affect the at-will nature of the employment relationship with the Company. Either you or Sage has the right to terminate your employment at any time, with or without cause, and with or without notice.

***Prior Obligations***

By signing this letter, you represent that you are not bound by any employment contract, restrictive covenant, or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter. Please note that this offer letter is your formal offer of employment and supersedes any and all prior or contemporaneous agreements, discussions, and understandings, whether written or oral, relating to the subject matter of this letter or your employment with the Company.

To accept this offer of employment, please sign this letter in the space provided below and return it to me along with the signed Employee Agreement. This offer will remain open for two business days from the date of this letter. This offer of employment is contingent on a satisfactory background check, satisfactory reference checks and your ability to provide documentation that you are fully vaccinated against COVID-19 or, if not, you are legally entitled to an accommodation due to a medical condition or a sincerely held religious belief. Requests for accommodation will be considered on a case-by-case basis, and Sage will consider, among other things, whether the proposed accommodation would create an undue hardship.

We are very enthusiastic about having you join our team! We believe you will make a critical contribution to our success and believe that the opportunities presented will allow you significant personal and professional growth. We hope that you will find Sage a rewarding

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experience as we fearlessly lead the way to create a world with better brain health. If you have any questions, please do not hesitate to call anytime.

/s/ Laura Gault \_\_\_\_\_

SIGNATURE

10/18/2022 \_\_\_\_\_

DATE

Very truly yours,  
**Sage Therapeutics**

/s/ Lee Guidetti  
By: Lee Guidetti  
Vice President, Talent Acquisition

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## SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Severance and Change in Control Agreement (this “Agreement”) is made as of 10/18/2022 by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Laura Gault (the “Executive”) and shall become effective on the date of hire with the Company.

1. **Purpose.** The Company considers it essential to the best interests of its stockholders to promote and preserve the continuous employment of key management personnel. The Board of Directors of the Company (the “Board”) recognizes that, as is the case with many corporations, the possibility of a Change in Control (as defined in Section 2 here of) exists and that such possibility, and the uncertainty and questions that it may raise among management, may result in the departure or distraction of key management personnel to the detriment of the Company and its stockholders. Therefore, the Board has determined that appropriate steps should be taken to reinforce and encourage the continued attention and dedication of members of the Company’s key management, including the Executive, to their assigned duties without distraction, including in the face of potentially disturbing circumstances arising from the possibility of a Change in Control. Nothing in this Agreement shall be construed to affect the at-will nature of the employment relationship, the Executive shall not have any right to be retained in the employ of the Company.

2. **Change in Control.** A “Change in Control” shall be deemed to have occurred upon the occurrence of any one of the following events: (a) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (b) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (c) the sale of all of the stock of the Company to an unrelated person, entity or group thereof acting in concert, or (d) any other transaction in which the owners of the Company’s outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

### 3. **Terminating Event.**

A “Terminating Event” shall mean any of the events provided in this Section 3:

(a) Termination by the Company. Termination by the Company of the employment of the Executive with the Company for any reason other than for Cause, death or Disability. For purposes of this Agreement, “Cause” shall mean, as determined by the Company in good faith:

(i) the indictment the Executive of any felony, any crime involving the Company, or any crime involving fraud, moral turpitude or dishonesty;

(ii) any unauthorized use or disclosure of the Company’s proprietary information which has an adverse effect on the Company’s business or reputation. As used in this paragraph, “Proprietary

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Information" means any information in whatever form, tangible or intangible, related to the business of the Company unless the information is publicly available in hard copy or electronic format, through lawful means;

(iii) any intentional misconduct or gross negligence on the Executive's part which has a materially adverse effect on the Company's business or reputation; or

(iv) the Executive's repeated and willful failure to perform the duties, functions and responsibilities of the Executive's position after a written warning from the Company.

A Terminating Event shall not be deemed to have occurred pursuant to this Section 3(a) solely as a result of the Executive becoming an employee of any direct or indirect successor to the business or assets of the Company, rather than continuing as an employee of the Company following a Change in Control. For purposes hereof, the Executive will be considered "Disabled" if, as a result of the Executive's incapacity due to physical or mental illness, the Executive shall have been absent from his duties to the Company on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

(b) Termination by the Executive for Good Reason. Termination by the Executive of the Executive's employment with the Company for Good Reason. For purposes of this Agreement, "Good Reason" shall mean that the Executive has complied with the "Good Reason Process" (hereinafter defined) following, the occurrence of any of the following events:

(i) a material diminution in the Executive's responsibilities, authority or duties;

(ii) a material diminution in the Executive's base salary except for across-the-board salary reductions based on the Company's financial performance similarly affecting all or substantially all senior management employees of the Company;

(iii) a material change, defined as miles or more, in the geographic location at which the Executive is required to provide services to the Company, not including business travel and short-term assignments; or

(iv) a material breach of this Agreement by the Company.

"Good Reason Process" shall mean that (i) the Executive reasonably determines in good faith that a "Good Reason" condition has occurred; (ii) the Executive notifies the Company in writing of the first occurrence of the Good Reason condition within 60 days of the first occurrence of such condition; (iii) the Executive cooperates in good faith with the Company's efforts, for a period not less than 30 days following such notice (the "Cure Period"), to remedy the condition; (iv) notwithstanding such efforts, the Good Reason condition continues to exist; and (v) the Executive provides a Notice of Termination to the Company within 60 days after the end of the Cure Period. If the Company cures the Good Reason condition during the Cure Period, Good Reason shall be deemed not to have occurred.

4. **Change in Control Payment.** In the event a Terminating Event occurs on or within the 12 months immediately after a Change in Control (such 12-month period, the "Change in Control Period"), subject to the Executive signing a separation agreement containing, among other provisions, a general release of claims in favor of the Company and related persons and entities,

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confidentiality, return of property and non-disparagement, in the form attached hereto as Attachment A (the “Separation Agreement and Release”) and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination or end of the Cure Period , the following shall occur

(a) the Company shall pay to the Executive an amount equal to the sum of (i) 9 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event (or the Executive’s annual base salary in effect immediately prior to the Change in Control, if higher), and (ii) a pro rata portion of the Executive’s target bonus for the fiscal year in which the termination of employment occurs, determined by multiplying the target bonus by a fraction, the numerator of which shall be the number of days during the fiscal year in which the Executive was employed by the Company and the denominator of which shall be 365;

(b) if the Executive was participating in the Company’s group health plan immediately prior to the Date of Termination and elects COBRA health continuation , then the Company shall pay to the Executive a lump sum payment, in an amount equal to 12 times the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company;

(c) notwithstanding anything to the contrary in any applicable option agreement or stock-based award agreement, all stock options and other stock-based awards with time-based vesting held by the Executive shall immediately accelerate and become fully exercisable and nonforfeitable as of the Executive’s Date of Termination conditioned upon the Separation Agreement and Release becoming irrevocable; and

(d) the amounts payable under this Section 4 shall be paid out in a lump sum commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year and ends in a second calendar year, the amounts shall be paid in the second calendar year by the last day of such 60-day period. All other wages earned, including, but not limited to, accrued vacation, to the Date of Termination shall be paid on the Date of Termination.

5. **Severance Outside the Change in Control Period**. In the event a Terminating Event occurs at any time other than during the Change in Control Period, subject to the Executive signing the Separation Agreement and Release and the Separation Agreement and Release becoming irrevocable, all within 60 days after the Date of Termination, the following shall occur:

(a) the Company shall pay to the Executive an amount equal to 12 months times the Executive’s annual base salary in effect immediately prior to the Terminating Event;

(b) if the Executive was participating in the Company’s group health plan immediately prior to the Date of Termination and elects COBRA health continuation, then the Company shall pay to the Executive a monthly cash payment for 12 months in an amount equal to the monthly employer contribution that the Company would have made to provide health insurance to the Executive if the Executive had remained employed by the Company; and

(c) the amounts payable under this Section 5 shall be paid out in substantially equal installments in accordance with the Company’s payroll practice over 12 months commencing within 60 days after the Date of Termination; provided, however, that if the 60-day period begins in one calendar year

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and ends in a second calendar year, the Severance Amount shall begin to be paid in the second calendar year by the last day of such 60-day period; provided, further, that the initial payment shall include a catch-up payment to cover amounts retroactive to the day immediately following the Date of Termination. Each payment pursuant to this Agreement is intended to constitute a separate payment for purposes of Treasury Regulation Section 1.409A-2(b)(2).

#### **6. Additional Limitation.**

(a) Anything in this Agreement to the contrary notwithstanding, in the event that the amount of any compensation, payment or distribution by the Company to or for the benefit of the Executive, whether paid or payable or distributed or distributable pursuant to the terms of this Agreement or otherwise, calculated in a manner consistent with Section 280G of the Code and the applicable regulations thereunder (the “Compensatory Payments”), would be subject to the excise tax imposed by Section 4999 of the Internal Revenue Code of 1986, as amended (the “Code”), (or any successor provision), then the Compensatory Payments shall be reduced so that the sum of all of the Compensatory Payments shall be \$1.00 less than the amount at which the Executive becomes subject to the excise tax imposed by Section 4999 of the Code (or any successor provision); provided that such reduction shall only occur if it would result in the Executive receiving a higher After Tax Amount (as defined below) than the Executive would receive if the Compensatory Payments were not subject to such reduction. In such event, the Compensatory Payments shall be reduced in the following order, in each case, in reverse chronological order beginning with the Compensatory Payments that are to be paid the furthest in time from consummation of the transaction that is subject to Section 280G of the Code: (i) cash payments not subject to Section 409A of the Code; (ii) cash payments subject to Section 409A of the Code; (iii) equity-based payments and acceleration; and (iv) non-cash forms of benefits; provided that in the case of all the foregoing Compensatory Payments all amounts or payments that are not subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c) shall be reduced before any amounts that are subject to calculation under Treas. Reg. §1.280G-1, Q&A-24(b) or (c).

(b) For purposes of this Section 6, the “After Tax Amount” means the amount of the Compensatory Payments less all federal, state, and local income, excise and employment taxes imposed on the Executive as a result of the Executive’s receipt of the Compensatory Payments. For purposes of determining the After Tax Amount, the Executive shall be deemed to pay federal income taxes at the highest marginal rate of federal income taxation applicable to individuals for the calendar year in which the determination is to be made, and state and local income taxes at the highest marginal rates of individual taxation in each applicable state and locality, net of the maximum reduction in federal income taxes which could be obtained from deduction of such state and local taxes.

(c) The determination as to whether a reduction in the Compensatory Payments shall be made pursuant to Section 6(a) shall be made by an accounting firm selected by the Company (the “Accounting Firm”), which shall provide detailed supporting calculations both to the Company and the Executive within 15 business days of the Date of Termination, if applicable, or at such earlier time as is reasonably requested by the Company or the Executive. Any determination by the Accounting Firm shall be binding upon the Company and the Executive.

#### **7. Section 409A.**

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(a) Anything in this Agreement to the contrary notwithstanding, if at the time of the Executive's "separation from service" within the meaning of Section 409A of the Code, the Company determines that the Executive is a "specified employee" within the meaning of Section 409A(a)(2)(B)(i) of the Code, then to the extent any payment or benefit that the Executive becomes entitled to under this Agreement on account of the Executive's separation from service would be considered deferred compensation subject to the 20 percent additional tax imposed pursuant to Section 409A(a) of the Code as a result of the application of Section 409A(a)(2)(B)(i) of the Code, such payment shall not be payable and such benefit shall not be provided until the date that is the earlier of (A) six months and one day after the Executive's separation from service, or (B) the Executive's death.

(b) The parties intend that this Agreement will be administered in accordance with Section 409A of the Code. To the extent that any provision of this Agreement is ambiguous as to its compliance with Section 409A of the Code, the provision shall be read in such a manner so that all payments hereunder comply with Section 409A of the Code. The parties agree that this Agreement may be amended, as reasonably requested by either party, and as may be necessary to fully comply with Section 409A of the Code and all related rules and regulations in order to preserve the payments and benefits provided hereunder without additional cost to either party.

(c) All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by the Executive during the time periods set forth in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit.

(d) To the extent that any payment or benefit described in this Agreement constitutes "non-qualified deferred compensation" under Section 409A of the Code, and to the extent that such payment or benefit is payable upon the Executive's termination of employment, then such payments or benefits shall be payable only upon the Executive's "separation from service." The determination of whether and when a separation from service has occurred shall be made in accordance with the presumptions set forth in Treasury Regulation Section 1.409A-1(h).

(e) The Company makes no representation or warranty and shall have no liability to the Executive or any other person if any provisions of this Agreement are determined to constitute deferred compensation subject to Section 409A of the Code but do not satisfy an exemption from, or the conditions of, such Section.

8. **Term.** This Agreement shall take effect on the date first set forth above and shall terminate upon the earlier of (a) the termination of the Executive's employment with the Company for any reason other than the occurrence of a Terminating Event, or (b) the date all amounts have been paid to the Executive upon a Terminating Event pursuant to Section 4 or Section 5 hereof.

9. **Withholding.** All payments made by the Company to the Executive under this Agreement shall be net of any tax or other amounts required to be withheld by the Company under applicable law.

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#### 10. **Notice and Date of Termination.**

(a) **Notice of Termination.** After a Change in Control and during the term of this Agreement, any purported termination of the Executive's employment (other than by reason of death) shall be communicated by written Notice of Termination from one party hereto to the other party hereto in accordance with this Section 10. For purposes of this Agreement, a "Notice of Termination" shall mean a notice which shall indicate the specific termination provision in this Agreement relied upon.

(b) **Date of Termination.** "Date of Termination" shall mean: (i) if the Executive's employment is terminated by his death, the date of his death; (ii) if the Executive's employment is terminated on account of Executive's Disability or by the Company for Cause, the date on which Notice of Termination is given; (iii) if the Executive's employment is terminated by the Company without Cause the date on which a Notice of Termination is given; (iv) if the Executive's employment is terminated by the Executive without Good Reason, 30 days after the date on which a Notice of Termination is given, and (v) if the Executive's employment is terminated by the Executive with Good Reason, the date on which a Notice of Termination is given after the end of the Cure Period. Notwithstanding the foregoing, in the event that the Executive gives a Notice of Termination to the Company, the Company may unilaterally accelerate the Date of Termination and such acceleration shall not result in a termination by the Company for purposes of this Agreement.

11. **No Mitigation.** The Company agrees that, if the Executive's employment by the Company is terminated during the term of this Agreement, the Executive is not required to seek other employment or to attempt in any way to reduce any amounts payable to the Executive by the Company pursuant to Section 4 or Section 5 hereof. Further, the amount of any payment provided for in this Agreement shall not be reduced by any compensation earned by the Executive as the result of employment by another employer.

12. **Consent to Jurisdiction.** The parties hereby consent to the jurisdiction of the Superior Court or the Commonwealth of Massachusetts and the United States District Court for the District of Massachusetts. Accordingly, with respect to any such court action, the Executive (a) submits to the personal jurisdiction of such courts; (b) consents to service of process; and (c) waives any other requirement (whether imposed by statute, rule of court, or otherwise) with respect to personal jurisdiction or service of process.

13. **Integration.** This Agreement constitutes the entire agreement between the parties with respect to severance pay, benefits and accelerated vesting in connection with any termination of employment, to the extent inconsistent with any prior agreements supersedes the inconsistent provisions of such prior agreements between the parties concerning such subject matter, including without limitation any provisions of any offer letter or employment agreement relating to severance pay or benefits in connection with the ending of Executive's employment relationship with the Company. In the interest of clarity, any agreement relating to confidentiality, noncompetition, nonsolicitation or assignment of inventions shall not be affected by the Agreement.

14. **Successor to the Executive.** This Agreement shall inure to the benefit of and be enforceable by the Executive's personal representatives, executors, administrators, heirs, distributees, devisees and legatees. In the event of the Executive's death after a Terminating Event but prior to the completion by the Company of all payments due him under this Agreement, the Company shall

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continue such payments to the Executive's beneficiary designated in writing to the Company prior to his death (or to his estate, if the Executive fails to make such designation).

15. **Enforceability.** If any portion or provision of this Agreement (including, without limitation, any portion or provision of any Section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

16. **Waiver.** No waiver of any provision hereof shall be effective unless made in writing and signed by the waiving party. The failure of any party to require the performance of any term or obligation of this Agreement, or the waiver by any party of any breach of this Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

17. **Notices.** Any notices, requests, demands and other communications provided for by this Agreement shall be sufficient if in writing and delivered in person or sent by a nationally recognized overnight courier service or by registered or certified mail, postage prepaid, return receipt requested, to the Executive at the last address the Executive has filed in writing with the Company, or to the Company at its main office, attention of the Board of Directors.

18. **Amendment.** This Agreement may be amended or modified only by a written instrument signed by the Executive and by a duly authorized representative of the Company.

19. **Effect on Other Plans and Agreements.** An election by the Executive to resign for Good Reason under the provisions of this Agreement shall not be deemed a voluntary termination of employment by the Executive for the purpose of interpreting the provisions of any of the Company's benefit plans, programs or policies. Nothing in this Agreement shall be construed to limit the rights of the Executive under the Company's benefit plans, programs or policies except as otherwise provided in Section 6 hereof, and except that the Executive shall have no rights to any severance benefits under any Company severance pay plan, offer letter or otherwise. In the event that the Executive is party to an agreement with the Company providing for payments or benefits under such agreement and this Agreement, the terms of this Agreement shall govern and Executive may receive payment under this Agreement only and not both. Further, Section 4 and Section 5 of this Agreement are mutually exclusive and in no event shall Executive be entitled to payments or benefits pursuant to Section 4 and Section 5 of this Agreement.

20. **Governing Law.** This is a Massachusetts contract and shall be construed under and be governed in all respects by the laws of the Commonwealth of Massachusetts, without giving effect to the conflict of laws principles of such Commonwealth. With respect to any disputes concerning federal law, such disputes shall be determined in accordance with the law as it would be interpreted and applied by the United States Court of Appeals for the First Circuit.

21. **Successor to Company.** The Company shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company expressly to assume and agree to perform this Agreement to the same extent that the Company would be required to perform it if no succession had taken place. Failure of the

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Company to obtain an assumption of this Agreement at or prior to the effectiveness of any succession shall be a material breach of this Agreement.

22. **Gender Neutral**. Wherever used herein, a pronoun in the masculine gender shall be considered as including the feminine gender unless the context clearly indicates otherwise.

23. **Counterparts**. This Agreement may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original; but such counterparts shall together constitute one and the same document.

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**IN WITNESS WHEREOF**, the parties have executed this Agreement effective on the date and year first above written.

**SAGE THERAPEUTICS, INC.**

By: /s/ Barry Greene

Name: Barry Greene

Title: Chief Executive Officer

/s/ Laura Gault

Employee Name: Laura Gault

[Signature Page to Severance and Change in Control Agreement]

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## AMENDMENT TO SEVERANCE AND CHANGE IN CONTROL AGREEMENT

This Amendment to Severance and Change in Control Agreement (this “Amendment”) is made as of February 15, 2023 (the “Amendment Effective Date”) by and between Sage Therapeutics, Inc., a Delaware corporation (the “Company”), and Laura Gault (the “Executive”).

**WHEREAS**, the Company and the Executive previously entered into a certain Severance and Change in Control Agreement dated as of October 18, 2022 (the “Agreement”); and

**WHEREAS**, the Agreement contains a scrivener’s error and the parties desire to amend the terms of the Agreement to clarify the intent of the parties.

**NOW THEREFORE**, for good and valuable mutual consideration, including, but not limited to, your continued employment and access to Company confidential information, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree to amend the Agreement as follows:

1. Section 5(a) of the Agreement is hereby deleted in its entirety and replaced with the following:

“(a) the Company shall pay to the Executive an amount equal to 12 months of the Executive’s annual base salary in effect immediately prior to the Terminating Event;”

2. All other terms and conditions of the Agreement, as amended and modified, are hereby ratified, confirmed and approved. Except as set forth in this Amendment the Agreement is unaffected and shall continue in full force and effect in accordance with its terms. If there is a conflict between the Agreement and this Amendment, the terms of this Amendment will prevail.
3. This Amendment may be executed in any number of counterparts, each of which when so executed and delivered shall be taken to be an original, but such counterparts shall together constitute one and the same document.

**IN WITNESS WHEREOF**, the parties have executed this Amendment as of the Amendment Effective Date.

**LAURA GAULT**

**By:** /s/ Laura Gault  
duly authorized

**Print Name:** Laura Gault

**Title:** Chief Medical Officer

**SAGE THERAPEUTICS, INC.**

**By:** /s/ Barry Greene  
duly authorized

**Print Name:** Barry Greene

**Title:** Chief Executive Officer

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**CNS INNOVATION ADVISORY BOARD  
CONSULTING AGREEMENT**

Jeffrey M. Jonas, M.D.

Dear Dr. Jonas:

Sage Therapeutics, Inc. (“Sage”) would like to engage you to provide services as a member of Sage’s CNS Innovation Advisory Board commencing on November 8, 2022 (the “Effective Date”), under the following terms and conditions (the “Agreement”):

1. *Description of Services.* You will serve as member of Sage’s CNS Innovation Scientific Advisory Board (the “Scientific Advisory Board”). The Scientific Advisory Board is comprised of a small group of physicians and researchers with expertise in the area of brain and other central nervous system diseases and disorders, including the diagnosis and treatment of such disorders, clinical research in the area, and areas of unmet need (collectively, the “Focus Area”). The primary Sage participants in meetings of the Scientific Advisory Board will be Sage’s Chief Executive Officer, Chief Development Officer, Chief Medical Officer, Senior Vice President, R&D Strategy and Business Management, and Senior Vice President, Medical Affairs. The purpose of the Scientific Advisory Board is to allow Sage’s leadership team to gain insights in the Focus Area that will inform Sage’s development of ongoing and future programs, clinical research activities, life-cycle innovation, efforts to address areas of unmet need, efforts to improve treatment paradigms and access for patients, and potential new areas of interest. As a member of the Scientific Advisory Board, you will use your best efforts to participate in meetings of the Scientific Advisory Board, expected to be held 4 to 5 times per year, and, in between meetings, to be available, on a regular ad hoc reasonable basis for discussions and consulting with the Chief Executive Officer, Chief Innovation Officer and/or Chief Medical Officer of Sage (collectively, the “Services”). During the Term, this Agreement shall be the sole agreement and relationship between the parties with respect to consulting and advisory services provided by you to Sage.

2. *Contract Term and Termination.* This initial term of this Agreement will commence on the Effective Date and will end on November 8, 2023, and shall thereafter be automatically renewed for successive renewal terms of one calendar year each (the initial term and each applicable renewal term collectively, the “Term”), unless the Term is earlier terminated. The Agreement may be terminated at any time for any reason by either party upon ten (10) days’ prior written notice or upon breach by the other party that is not cured within thirty (30) days of prior written notice from the other party. Upon termination, you shall (i) immediately stop performing the Services, (ii) deliver all Work Product (as defined below) to Sage, and (iii) promptly return all Confidential Information (as defined below) to Sage.

3. *Payment of Fees and Expenses.* Sage will pay you a retainer in the amount of \$10,000 per quarter during the Term for the Services to be provided by you under this Agreement, including your participation in meetings of the Scientific Advisory Board, regular ad hoc discussions and/or consulting with Sage’s Chief Executive Officer, Chief Development Officer, Chief Medical Officer, Senior Vice President, R&D Strategy and Business Management, and Senior Vice President, Medical Affairs, and preparation for such activities. You acknowledge and agree that the retainer to be paid to you represents fair market value for your participation as a member of the Scientific Advisory Board and the other Services to be provided under this Agreement. This Agreement shall not be construed under any circumstances as an inducement or reward for you to promote, recommend, or use any products manufactured or distributed by Sage. Sage will reimburse you for any pre-approved actual expenses reasonably incurred by you in connection with the provision of Services hereunder. In the event you are unable to attend a scheduled meeting or event

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necessary to the Services, including if cancelled by Sage, for which Sage has provided you with airline tickets, you must promptly return the airline tickets to Sage. In the case of returned airline tickets, you agree to assist Sage in any efforts to obtain any refund available for such tickets.

As additional compensation for the Services, if in connection with your resignation as an employee of Sage (which the parties acknowledge was effective as of the Effective Date) you elect COBRA health continuation coverage (“COBRA”), then Sage will reimburse you for the payments you make for COBRA for a period of up to six (6) months, provided you timely elect and pay for COBRA. COBRA reimbursements shall be made by Sage to you consistent with Sage’s normal expense reimbursement policy, provided that you submit reasonable documentation to Sage substantiating your payments for COBRA.

4. *Safety Information Reporting.* If, during the performance of the Services you receive notice or become aware of any Safety Information (as defined in **Exhibit A**) about a Sage product, you must comply with the safety reporting requirements set forth in **Exhibit A**.

5. *Product Complaints.* If, during the performance of the Services under this Agreement, you become aware of any Product Complaint (as defined below) of a Sage Product, you shall report such to Sage as soon as reasonably possible but in no event later than one (1) business day to [ProductComplaints@sagerx.com](mailto:ProductComplaints@sagerx.com). For purposes of this Agreement, “**Product Complaint**” is defined as any written, electronic, or verbal expression of dissatisfaction regarding the identity, quality, reliability, safety, purity, potency, effectiveness or performance (as applicable for marketed products) of a Sage product after it is released for distribution.

6. *Performance of Services; Compliance with Laws.* You represent and warrant that you will render Services in a professional manner and in compliance with all applicable laws, rules and regulations, as amended from time to time, and all professional standards applicable to the Services, including but not limited to the Anti-Kickback Statute, the Food, Drug and Cosmetic Act, and relevant regulations, including U.S. Food and Drug Administration (“**FDA**”) promotional guidelines, the provisions of applicable federal and state transparency and disclosure laws, all national and trans-national anti-bribery and anti-corruptions laws, applicable privacy laws, and the PhRMA Code on Interactions with Healthcare Professionals. Sage will report to relevant government entities information about compensation, expenses, and other payments or transfers of value (including in-kind payments and expense reimbursements) that Sage provides to you as required by law or regulation, and such government entities may make the information public. You agree to provide Sage with any information requested to allow for timely, accurate, and complete reporting.

You represent and warrant that you (i) are not currently under consideration to be, and will notify Sage immediately if you become, excluded or debarred by the FDA in any capacity; (ii) are not suspended or otherwise ineligible to participate in federal healthcare programs or in federal procurement or non-procurement programs by the Office of Inspector General (“**OIG**”) or the General Services Administration (“**GSA**”); (iii) if applicable, have a valid state medical license; and (iv) have not been subject to disciplinary action by any healthcare licensing authority. In the event that Sage becomes aware that exclusion, debarment, suspension, or other declaration of ineligibility has been brought or threatened against you, Sage shall have the right to terminate this Agreement immediately.

You acknowledge that Sage may be required to publicly disclose, either directly or through an applicable government agency, information relating to the Services hereunder including, without limitation, the existence and nature of your relationship with Sage, your name, address, contact details, professional identification number and any fees, expenses and other transfers of value provided to you.

7. *Compliance with Obligations to Third Parties.* You represent and warrant to Sage that the terms of this Agreement and your performance of Services do not and will not conflict with any of your

obligations to any third parties, and that, if required, you have disclosed, or will disclose, this Agreement, and have obtained, or will obtain, approval, prior to beginning the Services.

You represent that you have not brought and will not bring with you to Sage or use in the performance of Services any equipment, confidential information or trade secrets of any third party which are not generally available to the public, unless you have obtained written authorization for their possession and use in the performance of Services.

8. *Work Product.* You hereby transfer and assign, and to the extent cannot presently assign, shall assign, to Sage and/or its designee all ownership and right, title and interest in Work Product. "Work Product" means work product, results, reports, original works of authorship, developments, improvements, ideas, know-how, techniques, methods, processes, research, or documents, whether or not having patent, copyright, trade secret, mask work or any other statutory right associated therewith, that is created or generated in connection with the performance of the Services, and which you may solely or jointly with others conceive or develop or reduce to practice, or cause to be conceived or developed or reduced to practice, in the course of the performance of Services. You agree not to make any substantial use of any space, facilities, materials or other resources of any Institution or any other entity of which you are an employee or consultant in the performance of your Services under this Agreement. For sake of clarity, the use of office space and word processors of Institution alone shall not be considered a "substantial use" for the purposes of this paragraph. You shall promptly make full written disclosure of Work Product to Sage and will hold Work Product in trust for the sole right and benefit of Sage. You shall keep and maintain adequate and current written records of all Work Product, and such records will be available to and remain the sole property of Sage at all times. Without limiting the foregoing, all original works of authorship which are made by you (solely or jointly with others) within the scope of this Agreement and which are protectable by copyright are "works made for hire", as that term is defined in the United States Copyright Act. You warrant that you have and will have the right to transfer and assign to Sage ownership of all works of authorship as a result of their status as "works made for hire" by those individuals engaged by you to render Services for the purposes of the U.S. Copyright Act. You shall execute all documents, and take any and all actions needed, all without further consideration, in order to confirm Sage's rights as outlined above. In the event that you should fail or refuse to execute such documents within a reasonable time, you appoint Sage as attorney to execute and deliver any such documents on your behalf.

9. *Confidentiality & Non-Use.* You shall hold all Confidential Information (as defined below) in confidence, shall exercise reasonable precautions to physically protect all Confidential Information, and shall not disclose any Confidential Information to any third party. You shall not use Confidential Information for any purpose except as may be necessary in the ordinary course of performing Services or in connection with your service on the Sage board of directors without the prior written consent of Sage. "Confidential Information" means (a) all Work Product, and (b) all confidential and proprietary data, trade secrets, business plans, and other information of a confidential or proprietary nature, belonging to Sage or its subsidiaries or third parties with whom Sage may have business dealings, disclosed or otherwise made available to you by Sage or on behalf of Sage. You may disclose Confidential Information to a governmental authority or by order of a court of competent jurisdiction only if required and provided that the disclosure is subject to all applicable governmental or judicial protection available for like material, reasonable advance notice is given to Sage, and you reasonably cooperate with Sage in obtaining such order.

You hereby acknowledge that Confidential Information may contain material, non-public information about Sage and hereby agrees that you may not purchase or sell any securities of Sage while in possession of such information.

Upon the termination of this Agreement, or upon the written request by Sage, you shall promptly deliver to Sage all Confidential Information and all copies and embodiments thereof (including notes and abstracts) then in your custody, control or possession, except for those portions of the Confidential

Information that constitutes analyses, compilations, studies or similar documents prepared by or on behalf of you not specifically as part of Services, which shall be destroyed by you. You shall, at the written request of Sage, deliver within five (5) days after the termination of this Agreement or request by Sage, a written statement to Sage certifying to such actions.

10. *Sage Property.* All documents, data, records, apparatus, equipment and other physical property furnished or made available to you in connection with this Agreement shall be and remain the sole property of Sage and shall be returned promptly to Sage when requested. In any event, you shall return and deliver all such property, including any copies thereof, upon termination or expiration of this Agreement, irrespective of the reason for such termination.

You agree that Sage, and anyone acting on behalf of Sage, may interview, photograph and record you and use, copy, publish, and/or distribute your name, likeness, voice, biographical data and statements in connection with the Services in any media now known or hereafter to become known for the purpose stated in this Agreement, including without limitation for use on its website, in press releases, brochures, offering documents, presentations, reports or other documents in printed or electronic form. Sage may modify and edit such information and may also use the information as often and for as long as necessary without payment of any consideration to you. Sage is not required to provide you the opportunity to review or approve such information or material prior to such use.

11. *Publication; Publicity.* Work Product may not be published or referred to, in whole or in part, by you without the prior express written consent of Sage. You shall not use the name, logo, trade name, service mark, or trademark, or any simulation, abbreviation, or adaptation of same, or the name of Sage or its subsidiaries for publicity, promotion, or similar uses without Sage's prior written consent.

12. *Independent Contractor Relationship.* Nothing contained in this Agreement shall be deemed to constitute you an employee of Sage, it being the intent of the parties to establish an independent contractor relationship, nor shall you have authority to bind Sage in any manner whatsoever by reason of this Agreement. You shall at all times while on Sage premises observe all security and safety policies of Sage. You shall bear sole responsibility for paying and reporting your own applicable federal and state income taxes, social security taxes, unemployment insurance, workers' compensation, and health or disability insurance, retirement benefits, and other welfare or pension benefits, if any, and you shall indemnify and hold Sage harmless from and against any liability with respect thereto.

13. *Conflict of Interest.* You represent and warrant that you have no outstanding agreement or obligation (regardless of whether in written form) that is in conflict with any of the provisions of this Agreement, or that would preclude you from fully complying with the provisions hereof, and further certify that you will not enter into such conflicting agreement during the term of this Agreement. You will advise Sage at such time as any activity of either Sage or another business presents you with a conflict of interest or the appearance of a conflict of interest. You will take whatever action is requested by Sage to resolve any conflict or appearance of conflict which Sage finds to exist. You further represent and warrant that you have full power and authority to enter into this Agreement and perform the obligations hereunder.

14. *Notices.* Any notice given under this Agreement shall be deemed delivered when delivered by hand, by certified mail, or by air courier to the parties at their respective addresses set forth above or at such other address as either party may provide to the other in writing from time to time.

15. *Assignment.* The rights and obligations of the parties hereunder shall inure to the benefit of and be binding upon their respective successors and assigns. This Agreement may not be assigned by you, and your obligations under this Agreement may not be subcontracted or delegated by you, without the prior written consent of Sage. For clarity, this Agreement may be assigned by Sage with prompt notice of such assignment to you.

You acknowledge that Sage may not have adequate remedy at law in the event you breach the terms of this Agreement. In addition to any other rights it may have, Sage shall have the right to seek in any court of competent jurisdiction injunctive or other relief to restrain any breach or threatened breach of this Agreement.

16. *Survival.* Any termination of this Agreement shall be without prejudice to any obligation of either party that shall have accrued and then be owing prior to termination. Sections 6 through 17 of this Agreement shall survive any termination of this Agreement.

17. *Prior Agreements; Governing Law; Severability; Amendment.* This Agreement, including all Exhibits and Schedules hereto, embodies the entire understanding between the parties with respect to the subject matter of this Agreement and supersedes any prior or contemporaneous agreements with respect to the subject matter of this Agreement. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts, without regard to any choice of law principle that would dictate the application of the law of another jurisdiction, and you submit to the jurisdiction and agree to the proper venue of all state and federal courts located within the Commonwealth of Massachusetts. In the event that any provision of this Agreement shall, for any reason, be held to be invalid or unenforceable in any respect, such invalidity or unenforceability shall not affect any other provision of this Agreement, and this Agreement shall be construed as if such invalid or unenforceable provision had not been included in this Agreement. This Agreement may not be amended, and its terms may not be waived, except pursuant to a written amendment or waiver signed by both parties.

*IN WITNESS WHEREOF*, the parties enter into this Agreement as of the Effective Date.

**Jeffrey M. Jonas, M.D.**

**SAGE THERAPEUTICS, INC.**

/s/ Jeffrey M. Jonas, M.D.

/s/ Erin Lanciani

Name: Jeffrey M. Jonas, M.D.

Name: Erin Lanciani

Address: 215 First Street

Cambridge, MA 02142

**EXHIBIT A**

**SAFETY INFORMATION REPORTING**

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**Sage Therapeutics, Inc.**

**Amended and Restated Non-Employee Director Compensation Policy**

The purpose of this Amended and Restated Non-Employee Director Compensation Policy (this “Policy”) of Sage Therapeutics, Inc., a Delaware corporation (the “Company”), is to provide a total compensation package that enables the Company to attract and retain, on a long-term basis, high-caliber directors who are not employees or officers of the Company. In furtherance of this purpose, all non-employee directors shall be paid compensation for services provided to the Company as set forth below:

**Cash Retainers**

The cash retainers to be paid to non-employee directors for their participation on the Company’s Board of Directors (the “Board”) and committees of the Board are as follows:

Annual Retainer for Board Membership: \$50,000 for general availability and participation in meetings and conference calls of our Board. No additional compensation for attending individual Board meetings.

Additional Annual Retainer for Non-Executive Chairman of the Board: \$40,000

Additional Annual Retainers for Committee Membership:

Audit Committee Chairperson:	\$20,000
Audit Committee member:	\$10,000
Compensation Committee Chairperson:	\$15,000
Compensation Committee member:	\$7,500
Nominating and Corporate Governance Committee Chairperson:	\$10,000
Nominating and Corporate Governance Committee member:	\$5,000
Science and Technology Committee Chairperson:	\$15,000
Science and Technology Committee member:	\$7,500

No additional compensation for attending individual committee meetings.

All cash retainers will be paid quarterly, in arrears, or upon the earlier resignation or removal of the non-employee director. Cash retainers shall be annualized, meaning that, with respect to non-employee directors who join the Board during the calendar year, such amounts shall be pro-rated based on the number of calendar days served by such director. Notwithstanding anything to the

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contrary in this Policy, the cash retainers paid to non-employee directors will not exceed the 75th percentile paid by the Company's peer group, as then-approved by the Compensation Committee of the Board (the "Peer Group"), to non-employee directors in the prior calendar year.

### **Election to Receive Options In Lieu of Cash Retainers.**

Each non-employee director may elect to receive a stock option to purchase the Company's common stock, par value \$0.0001 per share ("Common Stock") in lieu of payment of all (but not a portion) of the cash retainers specified above that would have otherwise been paid for service on the Board and committees of the Board in a given calendar year.

Election. To elect to receive an option to purchase shares of Common Stock in lieu of cash retainers for any calendar year, the non-employee director must notify the Company's Corporate Secretary in writing of such election prior to the commencement of the calendar year for which the cash retainers would otherwise have been paid (the "Payment Year"). A newly elected or appointed non-employee director may not make an election for the year in which he or she first becomes a non-employee director. All elections shall remain in effect for future calendar years unless revoked by written notice to the Corporate Secretary. A revocation of an election received after the start of a calendar year will not be effective until the next calendar year.

Number of Option Shares and Terms of Grant. The number of shares underlying each stock option to be granted to a non-employee director who has made an election to receive an option in lieu of cash retainers for any year shall be determined on the first business day of the Payment Year, and shall equal the total amount of the cash retainers the non-employee director would have received in the Payment Year under this Policy divided by the product of (x) the closing trading price of the Common Stock on such first business day of the Payment Year and (y) 70%. Each stock option granted pursuant to such election shall be granted on the second business day of the Payment Year and shall fully vest on the last business day of such year, subject to the non-employee director's continued service through such date. If a non-employee director who has elected to receive a stock option in lieu of cash retainers is appointed to one or more additional committees of the Board after the start of the relevant Payment Year (but not where the individual is departing the same number of Board committees), such director may receive a cash retainer for such additional services.

See also *General Terms Applicable to Option Grants* for additional terms.

### **Equity Retainers**

Initial Equity Grant: Each new non-employee director will, on the business day after his/her election to the Board is first effective, be granted a one-time option to purchase shares of Common Stock in such amount and on such terms as authorized by the Board, or by a committee appointed by the Board (the "Initial Equity Grant"). Such Initial Equity Grant shall vest in equal monthly installments during the 36 months following the grant date, subject to the director's continued service on the Board. Notwithstanding anything to the contrary in this Policy, an Initial Equity Grant will not exceed two times the Annual Equity Grant (as defined below) most recently awarded to the Company's incumbent non-employee directors.

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**Annual Equity Grant**: Each non-employee director serving on the Board immediately following the Company's annual meeting of stockholders for a given year will, on the date of the meeting, be granted an option to purchase shares of Common Stock in such amount and on such terms as authorized by the Board, or by a committee appointed by the Board (the "**Annual Equity Grant**"). Such Annual Equity Grant shall vest on the earlier of the one-year anniversary of the grant date or the day prior to the Company's next annual meeting of stockholders, subject to the director's continued service on the Board. Notwithstanding anything to the contrary in this Policy, the Annual Equity Grant in any year will not exceed the lesser of (i) a percent of the Company equal to the 65th percentile of the annual equity compensation awarded to non-employee directors by the Company's Peer Group, calculated as a percent of the company, as reported by the Peer Group in the prior year and (ii) a Black-Scholes value (calculated in accordance with FASB Topic 718) equal to the highest reported value of the annual equity compensation awarded to non-employee directors by any member of the Peer Group in the prior year. See also *General Terms Applicable to Option Grants* for additional terms.

### **General Terms Applicable to Option Grants.**

Options granted to non-employee directors under this Policy, whether in lieu of cash retainers or as initial or annual equity retainers, will have the following additional terms:

- (i) the exercise price will be the closing price of the Common Stock on the Nasdaq Global Market on the date of grant;
- (ii) each option will become fully vested and immediately exercisable upon the death or disability of such director or upon a change in control of the Company;
- (iii) each option will be exercisable as to vested shares during the term of the non-employee director's service on the Board and for a period of six months following cessation of service as a director, provided that the director has not been removed for cause;
- (iv) each option will be granted under the Company's 2014 Stock Option and Incentive Plan (the "**Plan**") and subject to the terms of the Plan;
- (v) each option will be documented on the Company's standard form of non-qualified stock option agreement as modified to reflect the specific terms of this Policy; and
- (vi) each option will expire on the tenth anniversary of the date of grant if not earlier terminated or forfeited under the terms of the Plan or the applicable stock option agreement.

For avoidance of doubt, all equity grants described in this Policy shall be effective by their terms, without additional action or approval from the Board or any committee thereof.

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## **Expenses**

The Company shall reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending Board and committee meetings.

ADOPTED: April 30, 2014

EFFECTIVE: July 17, 2014

AMENDED: March 5, 2015

AMENDED: December 15, 2016

AMENDED: September 19, 2017

AMENDED: March 30, 2018

AMENDED: September 20, 2018

AMENDED: April 8, 2022

AMENDED: December 16, 2022

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## SUBSIDIARIES

	<u>Subsidiary</u>	<u>Jurisdiction of Incorporation</u>
1	Sage Securities Corporation	Massachusetts
2	Sage (Bermuda) Ltd.	Bermuda
3	Sage Therapeutics Limited	England and Wales
4	Sage Therapeutics GmbH	Switzerland
5	Sage Therapeutics GmbH	Germany
6	Sage Therapeutics, Inc.	Canada

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CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (File No. 333-261708) and on Forms S-8 (File Nos. 333-197498, 333-204549, 333-209831, 333-216202, 333-223146, 333-228246, 333-229732, 333-236680, 333-253431, 333-262948 and 333-266455) of Sage Therapeutics, Inc. of our report dated February 16, 2023 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP  
Boston, Massachusetts  
February 16, 2023

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## CERTIFICATIONS UNDER SECTION 302

I, Barry E. Greene, certify that:

1. I have reviewed this Annual Report on Form 10-K of Sage Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 16, 2023

/s/ Barry E. Greene

Name: Barry E. Greene  
Title: Chief Executive Officer, President and Director  
(Principal Executive Officer)

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## CERTIFICATIONS UNDER SECTION 302

I, Kimi Iguchi, certify that:

1. I have reviewed this Annual Report on Form 10-K of Sage Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal controls over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
  - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
  - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
  - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
  - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
  - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 16, 2023

/s/ Kimi Iguchi

Name: Kimi Iguchi  
Title: Chief Financial Officer (Principal Financial and Accounting Officer)

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CERTIFICATIONS PURSUANT TO  
18 U.S.C. SECTION 1350,  
AS ADOPTED PURSUANT TO  
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with this Annual Report on Form 10-K of Sage Therapeutics, Inc. (the “Company”) for the fiscal year ended December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the “Report”), each of the undersigned officers hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his or her knowledge:

- (1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Barry E. Greene

Name: Barry E. Greene

Title: Chief Executive Officer, President and Director (Principal Executive Officer)

Date: February 16, 2023

/s/ Kimi Iguchi

Name: Kimi Iguchi

Title: Chief Financial Officer (Principal Financial and Accounting Officer)

Date: February 16, 2023

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