Sage Therapeutics Announces Fourth Quarter and Full Year 2022 Financial Results and Highlights Pipeline and Business Progress

February 16, 2023

U.S. Food and Drug Administration (FDA) accepts filing of New Drug Application (NDA) for zuranolone and grants Priority Review in the treatment of Major Depressive Disorder (MDD) and Postpartum Depression (PPD) following submission of rolling NDA in December 2022

Robust pipeline advancing nine studies across neuropsychiatry and neurology in 2023

Year-end 2022 cash, cash equivalents and marketable securities of $1.3 billion along with ongoing collaboration funding, and potential revenue, expected to support operations into 2025

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 16, 2023-- Sage Therapeutics, Inc. (Nasdaq: SAGE), a biopharmaceutical company leading the way to create a world with better brain health, today reported business highlights and financial results for the fourth quarter and full year ended December 31, 2022.

“We set out in 2022 to deliver on a bold agenda; starting with the goal of transforming the treatment of depression. We have been laser focused on the opportunity to help millions of people who are desperate for new treatment options and the recent acceptance of the NDA filing for zuranolone in MDD and PPD puts us one step closer to that goal,” said Barry Greene, Chief Executive Officer at Sage Therapeutics. “We are also progressing a promising and targeted pipeline with the goal of being able to launch new drugs or indications for years to come. This momentum puts us in a position of strength as we kick off 2023 and progress in our plan to become the leader in brain health and a top tier biopharmaceutical company.”

Key 2022 Highlights

Advanced Regulatory Path and Commercialization Plans for Zuranolone: In December 2022, Sage and its collaborator Biogen announced the completion of the rolling NDA submission for zuranolone in MDD and PPD. Sage and Biogen recently announced that the FDA accepted the filing of the NDA for zuranolone and that the application was granted Priority Review, with a Prescription Drug User Fee Act (PDUFA) action date of August 5, 2023.

- The NDA submission includes data from the LANDSCAPE and NEST clinical development programs as well as a Phase 2 study of zuranolone completed by Shionogi in Japan in adults with MDD for zuranolone. The LANDSCAPE program includes five studies of zuranolone in adults with MDD (MDD-201B, MOUNTAIN, SHORELINE, WATERFALL, and CORAL Studies). The NEST program includes two studies of zuranolone in adult women with PPD (ROBIN and SKYLARK Studies). Zuranolone, if approved, could represent the first oral, short course (14-day) medication with rapid onset for MDD and PPD.
- In 2022, Sage and Biogen advanced commercialization plans for zuranolone through scientific exchange, permitted interactions with payers and disease state education in MDD and PPD. Sage expects these efforts and other permitted pre-launch activities to advance in 2023.

Reported Positive Topline Data from Phase 3 SKYLARK Study in 2022 and Multiple Data Presentations Supporting Zuranolone Potential: Sage and its collaborator Biogen announced positive topline data from the SKYLARK Study in 2022. The companies also presented multiple datasets from the LANDSCAPE and NEST clinical development programs that support the potential efficacy and safety of zuranolone for the treatment of MDD and PPD, respectively.

- The Phase 3 SKYLARK Study of zuranolone in PPD met its primary endpoint and all key secondary endpoints, demonstrating significant and clinically meaningful improvement in depressive symptoms as early as day 3 for participants treated with zuranolone 50mg, which was sustained at all measured timepoints through day 45.
- Multiple new analyses across the zuranolone development program were presented at key congresses throughout the year, including new analyses from the SHORELINE Study and Health Economics and Outcomes Research.
- Across the clinical program in MDD and PPD, zuranolone showed consistent rapid and sustained improvement of depressive symptoms with a generally well-tolerated and consistent safety profile.

Presented Encouraging Data from Phase 2 Open Label LUMINARY and Open Label PARADIGM Studies of SAGE-718: SAGE-718 demonstrated improvements across multiple domains of cognition, including executive performance and learning and memory, in patients with mild cognitive impairment (MCI) and mild dementia due to Alzheimer’s disease (AD) in the Phase 2 open-label LUMINARY Study and in patients with mild cognitive impairment (MCI) due to Parkinson’s disease (PD) in the Phase 2 open-label PARADIGM Study.

- Data from the Phase 2 open-label PARADIGM Study (Part A, 14 days of dosing) presented at the AD/PD 2022 Advances in Science & Therapy International Conference on Alzheimer’s and Parkinson’s Diseases and Related Neurological

Disorders, showed that SAGE-718 was associated with improvements in executive function and learning and memory at Day 14 in patients with MCI due to PD. Additionally, sustained effects and improving trends were observed at 14 days post-treatment.
- Additional results from the Phase 2 open-label PARADIGM Study (Part B, 28 days of dosing) were presented at ECNP and showed that improvements in executive function could be sustained through 28 days of dosing.
- Data from the Phase 2 open-label LUMINARY Study in individuals with MCI and mild dementia due to AD presented at the American Academy of Neurology showed that SAGE-718 given once daily for 14 days was generally well-tolerated and associated with improved executive performance and learning and memory.
- SAGE-718 has been well-tolerated in studies to date.

Strengthened Executive Leadership Team: In 2022, the Company strengthened its leadership team with several key appointments including Laura M. Gault, M.D., Ph.D. as Chief Medical Officer and Mark Pollack, M.D. as Senior Vice President, Medical Affairs. Sage also made key leadership hires, further building out the commercial team.

Fourth Quarter 2022 Portfolio Updates

Sage is advancing a portfolio of clinical-stage programs featuring internally discovered novel chemical entities with the potential to become differentiated products designed to improve brain health by targeting the $GABA_A$ and NMDA receptor systems. Dysfunction in these systems is thought to be at the core of numerous neurological and neuropsychiatric disorders.

Depression

Sage's depression franchise features zuranolone, Sage's next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors being evaluated in clinical development as a treatment for various affective disorders, and ZULRESSO® (brexanolone) CIV injection, approved by the FDA as the first treatment specifically indicated for PPD. Zuranolone has received Breakthrough Therapy and Fast Track Designation for the treatment of MDD and Fast Track Designation for the treatment of PPD from the FDA.

Zuranolone is being evaluated as a potential rapid-acting, once-daily, oral two-week treatment for MDD and PPD. Across the LANDSCAPE and NEST clinical development programs to date, zuranolone has demonstrated rapid and sustained relief of depressive symptoms in people with MDD and PPD. In December 2022, Sage and its collaborator Biogen completed the rolling NDA submission for zuranolone in MDD and PPD. The companies recently announced the NDA for zuranolone was accepted for filing by the FDA and granted priority review with a PDUFA action date of August 5th.

The Company expects the following milestones across the depression franchise in 2023:

- Mid 2023:
  - Present additional data from the SHORELINE Study
- Late 2023:
  - PDUFA date for zuranolone in MDD and PPD (August 5th)
  - Commercial availability of zuranolone in MDD and PPD, if zuranolone is approved with no review extensions
  - Initiate a lifecycle innovation study with zuranolone
- Present additional analyses of data from LANDSCAPE and NEST clinical programs, including health economics and patient reported outcomes

Neuropsychiatry

Sage's neuropsychiatry franchise features SAGE-718, the Company's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). SAGE-718 received Fast Track Designation from the FDA for the potential treatment of HD.

Sage is advancing a robust clinical program for SAGE-718 with multiple ongoing or planned Phase 2 studies across multiple disease areas, including its potential lead indication, cognitive impairment associated with HD, as well as cognitive impairment due to AD and PD. The Company recently initiated LIGHTWAVE (CNA-202), a Phase 2 study of SAGE-718 in people with mild cognitive impairment and mild dementia due to AD and PURVIEW (CIH-301), a Phase 3 extension study in people with cognitive impairment due to HD.

Sage is currently enrolling in the following studies:

- DIMENSION (CIH-201) Study: The DIMENSION Study is a double-blind, placebo-controlled Phase 2 study in people with HD cognitive impairment. The study is designed to evaluate the efficacy of once-daily SAGE-718 dosed over three months, with a target enrollment of approximately 178 people. Sage expects the DIMENSION Study to include more than 40 clinical sites.
- SURVEYOR (CIH-202) Study: The SURVEYOR Study is a double-blind, placebo-controlled Phase 2 study in people with HD cognitive impairment and healthy volunteers, with the goal of generating evidence linking efficacy signals on cognitive performance to domains of real-world functioning.
- PURVIEW (CIH-301) Study: The PURVIEW Study is an open-label Phase 3 safety study of SAGE-718 in people with HD cognitive impairment. The study is designed to evaluate the long-term safety profile and benchmark performance against HD natural history studies.
- PRECEDENT (CNP-202) Study: The PRECEDENT Study is a double-blind, placebo-controlled Phase 2 study in people

with MCI due to PD. The study is designed to evaluate the safety and efficacy of SAGE-718 in people with MCI due to PD over 42 days, followed by a controlled follow-up period.
- LIGHTWAVE (CNA-202) Study: The LIGHTWAVE Study is a double-blind, placebo-controlled Phase 2 study of SAGE-718 in people with MCI and mild dementia due to AD. The study is designed to evaluate the safety and efficacy of SAGE-718 dosed over an 84-day period (across an initial dose and a lower dose), followed by a controlled follow-up period.

The Company expects the following milestones across the neuropsychiatry franchise in 2023:

- Progress recruitment in the ongoing DIMENSION, SURVEYOR, PURVIEW, PRECEDENT, and LIGHTWAVE Studies
- Present additional analyses of data from clinical development program as well as disease state and burden of disease research in Huntington's, Parkinson's and Alzheimer's diseases

Neurology

Sage's neurology franchise features SAGE-324 and SAGE-689. SAGE-324, a next-generation PAM of GABA $_A$ receptors and Sage's lead neurology program, is in development as a potential oral therapy for neurological conditions, such as essential tremor (ET), epilepsy and PD. SAGE-689 is an intramuscular GABA$_A$ receptor PAM in development as a potential therapy for disorders associated with acute GABA hypofunction.

Sage and its collaborator, Biogen, are currently enrolling participants in the Phase 2b KINETIC 2 placebo-controlled study of SAGE-324 in ET following positive results from the KINETIC Study. The KINETIC 2 Study is a Phase 2b dose-ranging study with the primary goal of defining the dose for SAGE-324 in ET with a good tolerability profile and a dosing schedule to maintain plasma concentrations needed for sustained tremor symptom control in treating ET. Enrollment in the KINETIC 2 Study is expected to be completed in late 2023.

Sage is also currently dosing patients in a Phase 2 long-term open label safety study, to evaluate the long-term safety and tolerability of SAGE-324 in ET. The primary endpoint is incidence of treatment-emergent adverse events.

SAGE-689 continues in Phase 1 development.

The Company expects the following milestones across the neurology franchise in 2023:

Late 2023:

- Anticipate completion of enrollment in the Phase 2b KINETIC 2 Study
- Present additional analyses of data from clinical development program as well as disease state and burden of disease research in ET

Early Development

Sage is progressing its early development programs, SAGE-319 and SAGE-421. IND-enabling work is underway for SAGE-421 and the Company plans to move SAGE-319 to Phase 1 studies.

- **SAGE-319:** an oral, extra-synaptic GABA$_A$ receptor preferring PAM that Sage plans to study for potential use in disorders of social interaction.
- **SAGE-421:** an oral, NMDA receptor PAM that Sage plans to study for potential use in neurodevelopmental disorders and cognitive recovery and rehabilitation.

FINANCIAL RESULTS FOR THE FOURTH QUARTER AND FULL YEAR 2022

- **Cash Position:** Cash, cash equivalents and marketable securities as of December 31, 2022 were $1.3 billion compared to $1.4 billion at September 30, 2022.

- **Revenue:** Net revenue from sales of ZULRESSO was $2.9 million in the fourth quarter of 2022, compared to $1.6 million in the same period of 2021. For the year ended December 31, 2022, net revenue from sales of ZULRESSO was $7.7 million compared to $6.3 million in the same period of 2021.

- **R&D Expenses:** Research and development expenses were $89.3 million, including $4.9 million of non-cash stock-based compensation expense, in the fourth quarter of 2022 compared to $75.4 million, including $9.1 million of non-cash stock-based compensation expense, for the same period in 2021. For the year ended December 31, 2022, R&D expenses were $326.2 million, including $25.9 million of non-cash stock-based compensation expense, compared to $283.2 million, including $49.7 million of non-cash stock-based compensation expense, for the same period in 2021. For the year, the increase in R&D expenses was primarily due to increased spending on SAGE-324 and Sage's wholly owned pipeline, including SAGE-718 and other programs. Increases were partially offset by the completion of the WATERFALL Study and the CORAL Study for zuranolone and decreases in non-cash stock-based compensation expense. The reimbursement from Biogen for R&D expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $73.2 million in 2022 compared to $79.8 million in the same period of 2021.

- **SG&A Expenses:** Selling, general and administrative expenses were $67.3 million, including $10.4 million of non-cash

stock-based compensation expense, in the fourth quarter of 2022, compared to $51.6 million, including $11.5 million of non-cash stock-based compensation expense, for the same period in 2021. For the year ended December 31, 2022, SG&A expenses were $227.7 million, including $35.7 million of non-cash stock-based compensation expense, compared to $183.5 million, including $54.9 million of non-cash stock-based compensation expense, for the same period in 2021. The increase in SG&A expenses was primarily due to hiring employees to support ongoing activities in anticipation of the potential launch of zuranolone. The reimbursement from Biogen for SG&A expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $2.2 million in 2022 compared to $11.3 million in the same period of 2021.

- **Net Loss:** Net loss was $147.1 million for the fourth quarter of 2022 compared to $124.7 million for the same period in 2021. For the year ended December 31, 2022, net loss was $532.8 million compared to $457.9 million for the same period in 2021.

FINANCIAL GUIDANCE

- Based upon the Company's current operating plan, Sage anticipates that its existing cash, cash equivalents and marketable securities, anticipated funding from ongoing collaborations, and potential revenue, will support its operations into 2025.
    - This includes the potential to achieve milestones totaling $225.0 million from Biogen related to first commercial sales of zuranolone in MDD and PPD in the U.S., if approved.
- The Company anticipates R&D and SG&A spending to increase as it prepares for the potential launch of zuranolone and advances planned and ongoing studies for SAGE-718 and SAGE-324.

Conference Call Information

Sage will host a conference call and webcast today, Thursday, February 16, at 8:00 a.m. ET to review its fourth quarter and full year 2022 financial results and discuss recent corporate updates. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. A replay of the webcast will be available on Sage's website following the completion of the event and will be archived for up to 30 days.

About Sage Therapeutics

Sage Therapeutics is a biopharmaceutical company fearlessly leading the way to create a world with better brain health. Our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. For more information, please visit http://www.sagerx.com.

Forward-Looking Statements

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: the potential profile and benefit of zuranolone in MDD and PPD; the potential for regulatory approval and commencement of launch and commercialization of zuranolone and potential timing of such activities; our belief in our readiness for commercial launch of zuranolone, if approved; other planned next steps for the zuranolone program and planned commercialization activities; anticipated timelines for commencement of trials, completion of dosing, initiation of new activities and other plans for our other programs and early stage pipeline; our belief in the potential profile and benefit of our product candidates; potential indications for our product candidates; the potential for success of our programs, and the opportunity to help patients in various indications; the mission and goals for our business; and our expectations with respect to potential receipt of milestones from collaborations, funding of future operations and increases in expenses. These statements constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: the FDA may find that the data included in our NDA for zuranolone are not sufficient for approval and may not approve the NDA in MDD or PPD, or both, or may approve zuranolone for only a subset of such patients; the FDA may decide that the design, conduct or results of our completed and ongoing clinical trials for zuranolone, even if positive, are not sufficient for approval in MDD or PPD and may require additional trials or data which may significantly delay and put at risk our efforts to obtain approval and may not be successful; the FDA may not meet expected review timelines for our NDA; other decisions or actions of the FDA or other regulatory agencies may affect our efforts with respect to zuranolone and our plans, progress, results and expected timelines; results of ongoing or future studies may impact our ability to obtain approval of zuranolone or impair the potential profile of zuranolone; success in earlier clinical trials of any of our other product candidates may not be repeated or observed in ongoing or future studies, and ongoing and future clinical trials may not meet their primary or key secondary endpoints which may substantially impair development; unexpected concerns may arise from additional data, analysis or results from any of our completed studies; we may encounter adverse events at any stage that negatively impact further development, the potential for approval or the potential for successful commercialization of any our product candidates or that require additional nonclinical and clinical work which may not yield positive results; we may encounter delays in initiation, conduct, completion of enrollment or completion of our ongoing and planned clinical trials, including as a result of slower than expected site initiation, slower than expected enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines and increase our costs; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development or may impair the potential for successful development; the anticipated benefits of our ongoing collaborations, including the achievement of events tied to milestone payments or the successful development or commercialization of products and generation of revenue, may never be achieved; the need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; our business may be adversely affected and our costs may increase if any of our key collaborators fails to perform its obligations or terminates our collaboration; the internal and external costs required for our ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected which may cause us to use cash more quickly than we expect or change or curtail some of our plans or both; we may never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels we expect or at levels necessary to justify our investment; we may not be successful in our efforts to gain regulatory approval of products beyond ZULRESSO; we may not achieve revenues from zuranolone, if approved, or any other of our products that may be successfully developed, at the levels we expect; our expectations as to sufficiency of cash to fund future operations and expense levels may prove not to be correct for these and other reasons such as changes in plans or actual events being different than our assumptions; we may be

opportunistic in our future financing plans even if available cash is sufficient; additional funding may not be available on acceptable terms when we need it; the number of patients with the diseases or disorders for which zuranolone or any of our other products are developed, the unmet need for additional treatment options, and the potential market for zuranolone, if approved, or any other future products, if successfully developed, may be significantly smaller than we expect; zuranolone, if approved or any of our other products that may be successfully developed in the future may not achieve the clinical benefit, clinical use or market acceptance we expect or we may encounter reimbursement-related or other market-related issues that impact the success of our commercialization efforts; and we may encounter technical and other unexpected hurdles in the development and manufacture of our product candidates or the commercialization of any current or future marketed product which may delay our timing or change our plans, increase our costs or otherwise negatively impact our business; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent quarterly report, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

Financial Tables

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Product revenue, net	$ 2,865	$ 1,642	$ 7,686	$ 6,308
Operating costs and expenses:				
Cost of goods sold	143	87	813	553
Research and development	89,295	75,443	326,163	283,166
Selling, general and administrative	67,329	51,599	227,699	183,498
Total operating costs and expenses	156,767	127,129	554,675	467,217
Loss from operations	(153,902)	(125,487)	(546,989)	(460,909)
Interest income, net	6,793	751	14,190	2,883
Other income (expense), net	(37)	24	15	134
Net loss	$ (147,146)	$ (124,712)	$ (532,784)	$ (457,892)
Net loss per share - basic and diluted	$ (2.47)	$ (2.12)	$ (8.98)	$ (7.80)
Weighted average shares outstanding - basic and diluted	59,494,613	58,897,195	59,306,094	58,670,230

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets
(in thousands)
(unaudited)

	December 31, 2022	December 31, 2021
Cash, cash equivalents and marketable securities	$ 1,272,494	$ 1,742,296
Total assets	$ 1,356,449	$ 1,825,288
Total liabilities	$ 103,850	$ 96,257
Total stockholders' equity	$ 1,252,599	$ 1,729,031

ZULRESSO (brexanolone) SELECT IMPORTANT SAFETY INFORMATION

This does not include all the information needed to use ZULRESSO safely and effectively. See full prescribing information for ZULRESSO.

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

See full prescribing information for complete boxed warning

Patients are at risk of excessive sedation or sudden loss of consciousness during administration of ZULRESSO.

Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren).

ZULRESSO is available only through a restricted program called the ZULRESSO REMS.

WARNINGS AND PRECAUTIONS

Suicidal Thoughts and Behaviors: Consider changing the therapeutic regimen, including discontinuing ZULRESSO, in patients whose PPD becomes worse or who experience emergent suicidal thoughts and behavior.

ADVERSE REACTIONS: Most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) were sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** ZULRESSO may cause fetal harm. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/clinical-and-researchprograms/pregnancyregistry/antidepressants/

- **Renal Impairment:** Avoid use of ZULRESSO in patients with end stage renal disease (ESRD)

Controlled Substance: ZULRESSO contains brexanolone, a Schedule IV controlled substance under the Controlled Substances Act.

To report SUSPECTED ADVERSE REACTIONS, contact Sage Therapeutics, Inc. at 1-844-4-SAGERX (1-844-472-4379) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information including Boxed Warning.

View source version on businesswire.com: https://www.businesswire.com/news/home/20230215005948/en/

Investor Contact
Helen Rubinstein
315-382-3979
helen.rubinstein@sagerx.com

Media Contact
Matthew Henson
917-930-7147
matthew.henson@sagerx.com

Source: Sage Therapeutics, Inc.