Sage Therapeutics Announces First Quarter 2023 Financial Results and Highlights Pipeline and Business Progress

May 2, 2023

New Drug Application (NDA) for zuranolone in the treatment of Major Depressive Disorder (MDD) and Postpartum Depression (PPD) under priority review by U.S. Food and Drug Administration (FDA) with a PDUFA date of August 5, 2023

Sage and Biogen progressing key commercial preparations to support a potential launch of zuranolone in late 2023, following DEA scheduling period, if approved and expected timelines are met

Continued progress across pipeline with nine studies advancing across neuropsychiatry and neurology

Data demonstrating severe economic burden associated with depression presented at the Academy of Managed Care Pharmacy and The Professional Society for Health Economics and Outcomes Research

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 2, 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 first quarter ended March 31, 2023.

"The first quarter was marked by important advancements across our brain health pipeline and product engine, which lay the groundwork for continued execution and the potential for long-term value creation, particularly as we approach the PDUFA target action date for zuranolone in MDD and PPD," said Barry Greene, Chief Executive Officer at Sage Therapeutics. "We are laser focused on progressing launch readiness activities in collaboration with Biogen and we believe that our planned strategic approach to the commercialization of zuranolone, if approved, will help us to achieve our vision of transforming the way depression is treated."

First Quarter 2023 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 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 14-day 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 February 2023, Sage and Biogen announced the FDA accepted the filing of an NDA for zuranolone for the treatment of MDD and PPD. The application was granted priority review and assigned a Prescription Drug User Fee Act (PDUFA) action date of August 5, 2023.

In March, Sage and Biogen presented important health economics and outcomes research at the Academy of Managed Care Pharmacy Annual Meeting that reinforced the significant negative impacts MDD can have on patients, their families and society. These presentations highlighted the associations between MDD symptoms and reduced health-related quality of life scores, and the burden that extends to other adults living in a home with someone with MDD. They also showed the increase in all-health related and MDD-related costs during the 90-day period following treatment with a current antidepressant.

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, and following DEA scheduling period
  - 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 has received Fast Track Designation from the FDA and Orphan Drug Designation from the European Medicines Agency (EMA) for the potential treatment of HD.

Sage is advancing a robust clinical program for SAGE-718 with ongoing studies across multiple disease areas, including cognitive impairment associated with HD as well as cognitive impairment due to AD and PD.

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 mild cognitive impairment 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, 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 on 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 movement disorders, such as essential tremor (ET), epilepsy and PD. SAGE-689, a Sage wholly-owned program, is an intramuscular balanced GABA$_A$ receptor PAM in development as a potential therapy for disorders associated with GABA hypofunction.

Sage and its collaborator, Biogen, are actively 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 targeted for completion in late 2023.

Sage is also currently enrolling 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:

- Targeted 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 continues to progress its early development programs, SAGE-319 and SAGE-421. SAGE-319 is currently in Phase 1 studies and IND-enabling work is underway for SAGE-421.

- **SAGE-319:** an oral, extra-synaptic preferring $GABA_A$ receptor 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 FIRST QUARTER 2023

- **Cash Position:** Cash, cash equivalents and marketable securities as of March 31, 2023 were $1.1 billion compared to $1.3 billion at December 31, 2022.

- **Revenue:** Net revenue from sales of ZULRESSO was $3.3 million in the first quarter of 2023 compared to $1.6 million in the same period of 2022.

- **R&D Expenses:** Research and development expenses were $92.8 million, including $8.8 million of non-cash stock-based compensation expense, in the first quarter of 2023 compared to $78.0 million, including $8.6 million of non-cash stock-based compensation expense, in the same period of 2022. The increase in spending was 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 research and development operations. The reimbursement from Biogen to us for R&D expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $17.3 million in the first quarter of 2023 compared to $18.5 million in the same period of 2022.

- **SG&A Expenses:** Selling, general and administrative expenses were $65.7 million, including $11.3 million of non-cash stock-based compensation expense, in the first quarter of 2023 compared to $46.5 million, including $9.9 million of non-cash stock-based compensation expense, in the same period of 2022. The increase in SG&A expenses was primarily due to hiring employees to support ongoing activities in anticipation of potential launch of zuranolone. The reimbursement from us to Biogen for SG&A expenses pursuant to the Sage/Biogen Collaboration and License Agreement was $3.0 million in the first quarter of 2023 compared to $1.5 million of reimbursement from Biogen to us in the same period of 2022.

- **Net Loss:** Net loss was $146.8 million in the first quarter of 2023 compared to $122.1 million in the same period of 2022.

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 for the treatment of 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, Tuesday, May 2, at 8:00 a.m. ET to review its first quarter 2023 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 potential for value creation opportunities; the mission and goals for our business; and our expectations with respect to potential receipt of milestones from collaborations, potential future revenue, cash runway; 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 or with limitations or restrictions; 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 or may find other deficiencies in our development program, data, processes, or manufacturing sites that causes the FDA not to approve our NDA; the FDA 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 or may impose review extensions; 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 for any of our products or product candidates at any stage that negatively impact further development, the

potential for approval or the potential for successful commercialization 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 to 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 cash run-way, the 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 for 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 March 31,	
	2023	**2022**
Product revenue, net	$ 3,294	$ 1,582
Operating costs and expenses:		
Cost of goods sold	230	286
Research and development	92,826	78,018
Selling, general and administrative	65,708	46,477
Total operating costs and expenses	158,764	124,781
Loss from operations	(155,470)	(123,199)
Interest income, net	8,830	1,168
Other expense, net	(188)	(24)
Net loss	$ (146,828)	$ (122,055)
Net loss per share - basic and diluted	$ (2.46)	$ (2.07)
Weighted average shares outstanding - basic and diluted	59,674,127	59,028,858

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

	March 31, 2023	**December 31, 2022**
Cash, cash equivalents and marketable securities	$ 1,129,585	$ 1,272,494
Total assets	1,220,686	1,356,449
Total liabilities	87,557	103,850
Total stockholders' equity	1,133,129	1,252,599

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/20230501005482/en/

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