Sage Therapeutics Inc Logo

Sage Therapeutics Announces Fourth Quarter and Full Year 2019 Financial Results and Highlights Pipeline and Business Progress

February 27, 2020

ZULRESSO™ (brexanolone) CIV injection net revenues of $2M and $4M for fourth quarter and full year 2019, respectively

Evaluating path forward for the zuranolone (SAGE-217) Landscape Program

Continued expansion of Neurology and Neuropsychiatry franchises with planned initiation of additional SAGE-324 and SAGE-718 studies in 2020

Conference call today at 8:00 a.m. EST

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 27, 2020-- Today, Sage Therapeutics, Inc. (NASDAQ: SAGE), a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain, reported business highlights and financial results for the fourth quarter and full year ended December 31, 2019.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20200227005220/en/

“The progress we made in 2019 across our depression, neuropsych and neurology franchises supports our vision to make medicines that matter,” said Jeff Jonas, chief executive officer of Sage Therapeutics. “Our focus in 2020 will be guided by perseverance, disciplined execution and rigorous prioritization designed to achieve an optimal pace of innovation for what we believe is a leading, novel portfolio of NCEs dedicated to treating brain health disorders. Our most immediate goal is to find the most efficient pathway to bring new treatments to patients as quickly as possible.”

Portfolio Updates
Sage is advancing a portfolio of novel and differentiated product candidates designed to improve brain health by targeting the GABA and NMDA receptor systems. Dysfunction in these systems is thought to be at the core of numerous neurological and neuropsychiatric disorders.

Depression Franchise
The Depression Franchise is led by ZULRESSO™ (brexanolone) CIV injection, approved by the U.S. Food and Drug Administration (FDA) as the first treatment specifically indicated for postpartum depression (PPD), and zuranolone (SAGE-217), Sage’s next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors, being evaluated in clinical development as a treatment for various affective disorders. Zuranolone has received breakthrough therapy designation from the FDA for the treatment of major depressive disorder (MDD).

- **ZULRESSO™ (brexanolone) CIV injection:** Enabling broad access to ZULRESSO for women with PPD and helping to activate treatment-ready sites of care remain the key focus in the launch of ZULRESSO. The Company continues to see positive indicators suggesting the long-term potential of ZULRESSO, including strong patient and health care provider (HCP) demand, as well as broad and favorable payor coverage.
    - Sites of care
        - Sage continues to help sites of care advance through the actions required to be treatment-ready to ensure women with PPD have access to a healthcare setting capable of administering ZULRESSO.

        - Based on experience during the initial six months of the ZULRESSO launch, Sage now anticipates the majority of interested sites will take nine months or longer to complete the actions required to be treatment ready. Many large hospital and healthcare systems are estimated to take 12 months or longer.
        - As of December 31, 2019, more than 175 healthcare facilities were ZULRESSO REMS certified across 75 of the top 140 Metropolitan Statistical Areas in the U.S., compared to 140 healthcare facilities as of the end of the third quarter of 2019. Of these healthcare facilities, 29 have completed all of the steps required to be treatment-ready and infused patients with ZULRESSO by the end of the year 2019, compared to 11 sites as of the end of the third quarter of 2019.
    - Payor coverage & reimbursement
        - As of December 31, 2019, plans representing in aggregate 80 percent of all covered lives have committed to favorable coverage with either light or no restrictions.
        - Sites must often negotiate the reimbursement amount for each payor under commercial coverage. Availability and sufficiency of Medicaid reimbursement varies by state and often depends on whether the state treats the ZULRESSO infusion as an outpatient or inpatient administration.
        - The Centers for Medicare & Medicaid Services assigned ZULRESSO an HCPCS C-code in January 2020. The C-code is being adopted by commercial and state Medicaid plans and is available for use on qualifying claims reflecting ZULRESSO utilization to treat women with PPD through the hospital out-patient department. Sage anticipates activation by the end of the first quarter of 2020, which could improve reimbursement transparency.
    - Patient demand & support
        - Sage continues to see strong patient demand with more than 300 start forms in the fourth quarter of 2019 compared to more than 200 in the third quarter of 2019, bringing the total to more than 500 start forms by end of year 2019. Additionally, the number of referring HCPs more than doubled in the fourth quarter of 2019 compared to the third quarter of 2019, bringing the total to more than 300 referring HCPs by the end of year 2019.
        - Sage Central, Sage's patient support center, continues to provide a range of patient resources to assist women with PPD and their families in the treatment journey. As of December 31, 2019, more than 95% of referred patients used Sage Central's resources.
    - Revenue
        - Sage expects ZULRESSO revenue growth will be modest over the next couple of quarters with an increase in the rate of growth of ZULRESSO revenue anticipated in the second half of 2020, assuming an increase in the number of treatment-ready sites, including larger hospitals administering ZULRESSO to treat women with PPD, and an increase in the volume of patients treated at existing sites. To accomplish this objective, Sage is guiding large sites through the steps necessary to become treatment-ready and supporting hospital administrations' efforts to reduce the complexity of those steps.

- **Zuranolone:** The Landscape Program, the clinical program evaluating the potential of zuranolone as a rapid-acting, durable, short-course treatment for MDD and PPD, currently includes three completed pivotal efficacy studies, one in PPD (ROBIN Study) and two in MDD (MDD-201, MOUNTAIN Study), and three other initiated Phase 3 pivotal studies (REDWOOD, SHORELINE, RAINFOREST).
    - Study updates
        - MOUNTAIN Study (MDD-301): The Company announced topline data from the pivotal Phase 3 study in December 2019.
            - The MOUNTAIN study did not meet its primary endpoint of a statistically significant reduction from baseline compared to placebo in the 17-item Hamilton Rating Scale for Depression (HAM-D) total score at Day 15. Patients in the zuranolone 30 mg group achieved statistically significant reductions in the HAM-D total score at Days

3, 8 and 12.
        - Zuranolone was generally well-tolerated and showed a similar safety profile as seen in earlier studies.
    - REDWOOD Study (MDD-302): The study is a placebo-controlled pivotal trial evaluating the efficacy – time to first relapse – and long-term safety of fixed interval zuranolone 30 mg monotherapy maintenance treatment. Randomized patients receive a two-week course of zuranolone 30 mg or placebo every two months until the first relapse for up to one year.
        - The Company paused enrollment in the study in the fourth quarter of 2019 and is evaluating potential study amendments as the Company determines next steps in the Landscape Program.
    - SHORELINE Study (MDD-303): The study is an open-label, long-term pivotal trial evaluating the safety of as-needed repeat treatment with zuranolone. Patients receive an initial two-week course of zuranolone 30 mg and as needed retreatment. Patients are assessed for potential relapse of depressive symptoms for up to one year.
        - The Company anticipates reporting topline data from the SHORELINE Study in 2020.
        - The Company is also assessing the potential of adding an additional cohort to the study evaluating a higher dose of zuranolone in patients with MDD.
    - RAINFOREST Study (MDD-304): The study is a placebo-controlled pivotal trial evaluating zuranolone 30 mg in patients with comorbid MDD and insomnia. The primary endpoint of the study is change from baseline in sleep efficiency as assessed by polysomnography.
        - The Company paused enrollment in the study in the fourth quarter of 2019 and is evaluating potential study amendments as the Company determines next steps in the Landscape Program.
  - Program next steps
    - Sage previously announced that a meeting with the FDA to discuss zuranolone would occur in the first quarter of 2020. The Company continues to evaluate data from the MOUNTAIN Study and will announce next steps in the Landscape Program upon completion of relevant correspondence with the FDA, including receipt of meeting minutes, and the determination of the development and regulatory path forward.

Neurology Franchise
SAGE-324, a next-generation PAM of $GABA_A$ receptors and Sage's lead neurology asset, is in development as a potential oral therapy for neurological conditions, such as essential tremor (ET), epilepsy and Parkinson's disease.

- **SAGE-324:** The Company plans to initiate a placebo-controlled Phase 2 study evaluating the safety and efficacy of SAGE-324 in patients with ET in the first half of 2020. Patients will receive a once-daily, four-week course of SAGE-324 60 mg or placebo.
  - The planned progression of SAGE-324 in ET is based on results from a Phase 1 open-label study evaluating the safety and pharmacokinetics of SAGE-324 in patients with ET. Data from the study will be presented in 2020.

Neuropsychiatry Franchise
SAGE-718, Sage's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, including Huntington's disease (HD).

- **SAGE-718:** The Company reported data from a Phase 1 open-label study evaluating the safety and pharmacokinetics of SAGE-718 in a cohort of patients with early HD in December 2019.
  - Study results

        - SAGE-718 was well tolerated, with no serious adverse events or adverse events leading to treatment discontinuation.
        - Patients demonstrated improved performance, compared to baseline, on assessments of executive functioning; executive dysfunction is a core feature of early HD. Additional data will be presented at an upcoming medical meeting.
    - Next steps
        - SAGE-718 is being developed as a potential treatment for disorders where cognitive function is impaired. In 2020, the Company plans to initiate one or more Phase 2a open-label studies evaluating SAGE-718 in patients with impaired cognitive function, which may include Parkinson's disease, Alzheimer's disease, and other neuropsychiatric disorders. Results from these studies will inform advancement of SAGE-718 into further Phase 2 development.

Anticipated Upcoming Milestones

- **Regulatory Updates**
    - The Company previously announced that a meeting with the FDA to discuss zuranolone would occur in the first quarter of 2020. The Company continues to evaluate data from the MOUNTAIN Study and will announce next steps in the Landscape Program upon completion of relevant correspondence with the FDA, including receipt of meeting minutes, and determination of the development and regulatory path forward (2020)
- **Topline Data**
    - Zuranolone Phase 3 MDD SHORELINE Study (2020)
- **Planned Clinical Trial Initiations**
    - SAGE-324 Phase 2 placebo-controlled study in ET (1H 2020)
    - SAGE-718 Phase 2a open-label study or studies in various disorders associated with cognitive dysfunction (2020)

Financial Results for the Fourth Quarter and Full Year 2019

- **Revenues**: Sage recorded $2.0 million in revenues in the fourth quarter of 2019 from sales of ZULRESSO. Sage recorded $0.3 million in collaboration revenues from Shionogi & Co., Ltd. related to reimbursement of product expense for the same period of 2018. For the year ended December 31, 2019, revenues were $6.9 million, including $4.0 million of net product revenues related to sales of ZULRESSO and $2.9 million in collaboration revenues from Shionogi & Co., Ltd. related to reimbursement of product expense, compared to $90.3 million in collaboration revenues from Shionogi & Co., Ltd., for the year ended December 31, 2018.
- **Cash Position**: Cash, cash equivalents, restricted cash, and marketable securities as of December 31, 2019 were approximately $1.0 billion compared to $925.1 million at December 31, 2018.
- **R&D Expenses**: Research and development expenses were $91.3 million, including $11.4 million of non-cash stock-based compensation expense, in the fourth quarter of 2019, compared to $88.8 million, including $15.9 million of non-cash stock-based compensation expense, for the same period of 2018. For the year ended December 31, 2019, research and development expenses were $368.8 million, including $62.9 million of non-cash stock-based compensation expense, compared to $282.1 million, including $50.9 million of non-cash stock-based compensation expense, for the year ended December 31, 2018. The increase in R&D expenses was primarily due to the advancement of the pivotal program for zuranolone in MDD and continued research and development efforts across the Company's early-stage clinical and discovery pipeline.
- **SG&A Expenses**: Selling, general and administrative expenses were $85.1 million, including $19.3 million of non-cash stock-based compensation expense, in the fourth quarter of 2019, compared to $75.7 million, including $15.8 million of non-cash stock-based compensation expense, for the same period in 2018. For the year ended December 31, 2019, SG&A expenses were $345.8 million,

including $90.3 million of non-cash stock-based compensation expense, compared to $201.4 million, including $51.1 million of non-cash stock-based compensation expense, for the year ended December 31, 2018. The increase in SG&A expenses was primarily due to an increase in personnel-related expenses, along with facilities and corporate infrastructure costs to support expanding operations and the ZULRESSO commercial launch.
- **Net Loss:** Net loss was $168.7 million for the fourth quarter of 2019 and $680.2 million for the year ended December 31, 2019, compared to a net loss of $158.4 million and $372.9 million, respectively, for the comparable periods of 2018.

Financial Guidance

- Sage expects ZULRESSO revenue growth will be modest over the next couple of quarters with an increase in the rate of growth of ZULRESSO revenue anticipated in the second half of 2020.

Conference Call Information
Sage will host a conference call and webcast today, Thursday, February 27, 2020, at 8:00 a.m. EST to discuss its fourth quarter and full year 2019 financial results and 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 approximately two hours after the completion of the event and will be archived for up to 30 days.

About Sage Therapeutics
Sage Therapeutics is a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain. We are pursuing new pathways with the goal of improving brain health, and our depression, neurology and neuropsychiatry franchise programs aim to change how brain disorders are thought about and treated. Our mission is to make medicines that matter so people can get better, sooner. For more information, please visit www.sagerx.com.

Forward-Looking Statements
Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation: our views and expectations regarding our commercial launch of ZULRESSO and its long-term potential, including the potential timing for sites to become ready to administer ZULRESSO and expectations regarding an increase in the number of activated sites, the potential timing of revenue growth, an increase in the volume of treated patients at existing sites, and the potential for favorable reimbursement of ZULRESSO; our development plans, goals and strategy and the potential timing and results of our development efforts; our plans to determine next steps with respect to the development and regulatory path forward for zuranolone and the Landscape Program, including any potential amendments to our clinical trials of zuranolone; our belief in the potential of our product candidates in various indications; the potential profile and benefit of our product candidates; and the goals, opportunity and potential for our business. 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: we may encounter issues or other challenges in commercializing ZULRESSO, including issues related to market acceptance by healthcare providers, healthcare settings and women with PPD, issues related to the willingness of sites to administer ZULRESSO, issues related to reimbursement, issues related to the requirements of the REMS, and challenges associated with execution of our sales and patient support activities, which in each case could limit the potential of ZULRESSO and the timing and amount of future revenues; results achieved with use of ZULRESSO in the treatment of PPD in commercial use may be different than observed in clinical trials, and may vary among patients; the number of women with PPD or the unmet need for additional treatment options may be significantly smaller than we

expect; we may encounter unexpected safety or tolerability issues with ZULRESSO or any of our product candidates, including, for zuranolone or other product candidates, as a result of any increase in dosing in our clinical trials; we may not be successful in our development of any of our current or future product candidates in any indication we are currently pursuing or may in the future pursue; success in prior clinical trials or nonclinical studies may not be repeated or observed in ongoing or future studies of any of our product candidates; ongoing and future clinical or nonclinical results for our product candidates may generate results that are different than we expect or may not support further development of the product candidate or be sufficient to gain regulatory approval of our product candidates on the timelines we expect or at all, or may require additional clinical trials or nonclinical studies; we may decide that a development pathway for one of our product candidates in one or more indications is no longer feasible or advisable or that the unmet need no longer exists; the FDA may decide that the development program for any of our product candidates, even if positive, is not sufficient for a new drug application filing or approval; 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; we may experience slower than expected initiation or enrollment in ongoing or future clinical trials; the internal and external costs required for our ongoing and planned research and development efforts, and to manage our organization in connection with such activities, and the resulting expense increases and use of cash, may be higher than expected which may cause us to change or curtail some of our plans; we may change our plans for other business reasons; and we may encounter technical and other unexpected hurdles in the development of our product candidates; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent annual report filed with the Securities and Exchange Commission (SEC), and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. 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.

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,	
	2019	**2018**	**2019**	**2018**
Product revenue, net	$ 1,960	$ -	$ 3,957	$ -
Collaboration revenue	-	273	2,911	90,273
Total revenue	1,960	273	6,868	90,273
Operating costs and expenses:				
Cost of goods sold	219	-	400	-

Research and development	91,250	88,805	368,815	282,107
Selling, general and administrative	85,129	75,695	345,777	201,404
Total operating costs and expenses	176,598	164,500	714,992	483,511
Loss from operations	(174,638)	(164,227)	(708,124)	(393,238)
Interest income, net	5,915	5,851	27,804	20,334
Other income (expense), net	70	(12)	82	22
Net loss	$ (168,653)	$ (158,388)	$ (680,238)	$ (372,882)
Net loss per share - basic and diluted	$ (3.25)	$ (3.38)	$ (13.38)	$ (8.08)
Weighted average shares outstanding - basic and diluted	51,834,880	46,876,452	50,833,837	46,121,194

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

	December 31, 2019	December 31, 2018
Cash, cash equivalents, restricted cash and investments	$ 1,010,760	$ 925,143
Total assets	$ 1,084,150	$ 952,705
Total liabilities	$ 139,495	$ 89,734
Total stockholders' equity	$ 944,655	$ 862,971

About ZULRESSO™ (brexanolone) CIV injection
ZULRESSO, the first medicine specifically approved by the U.S. Food and Drug Administration (FDA) for the treatment of postpartum depression (PPD) in adults, is a positive allosteric modulator of both synaptic and extrasynaptic GABAA receptors. Allosteric modulation of neurotransmitter receptor activity results in varying degrees of desired activity rather than complete activation or inhibition of the receptor.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ZULRESSO?

ZULRESSO can cause serious side effects, including:

- **Excessive sedation and sudden loss of consciousness.** ZULRESSO may cause you to feel very sleepy (excessive sedation) or pass out (loss of consciousness). Your healthcare provider should check you for symptoms of excessive sleepiness every 2 hours while you are awake.
    - During your ZULRESSO infusion, tell your healthcare provider right away if you feel like you cannot stay awake during the time you are normally awake or if you feel like you are going to pass out. Your healthcare provider may lower your dose or stop the infusion until symptoms go away.
    - You must have a caregiver or family member with you to help care for your child(ren) during your ZULRESSO infusion.
- Because of the risk of serious harm resulting from excessive sedation or sudden loss of consciousness, ZULRESSO is only available through a restricted program called the ZULRESSO REMS.

Before receiving ZULRESSO, tell your healthcare provider about all your medical conditions, including if you:

- drink alcohol
- have kidney problems
- are pregnant or think you may be pregnant. It is not known if ZULRESSO will harm your unborn baby.
    - There is a pregnancy registry for females who are exposed to ZULRESSO during pregnancy. The purpose of the registry is to collect information about the health of females exposed to ZULRESSO and their baby. If you become pregnant during treatment with ZULRESSO, talk to your healthcare provider about registering with the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visit https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/
- are breastfeeding or plan to breastfeed. ZULRESSO passes into breast milk. Talk to your healthcare provider about the risks and benefits of breastfeeding and about the best way to feed your baby while receiving ZULRESSO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

ZULRESSO and some medicines may interact with each other and cause serious side effects.

Especially tell your healthcare provider if you take other antidepressants, opioids, or Central Nervous System (CNS) depressants (such as benzodiazepines).

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine. Your healthcare provider will decide if other medicines can be taken with ZULRESSO.

How will I receive ZULRESSO?
ZULRESSO is given to you by continuous intravenous (IV) infusion into your vein. The infusion will last for a total of 60 hours (2.5 days).

What should I avoid while receiving ZULRESSO?

- ZULRESSO may make you feel dizzy and sleepy. Do not drive a car or do other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away. See "**What is the most important information I should know about ZULRESSO?**"

- Do not drink alcohol while receiving ZULRESSO.

What are the possible side effects of ZULRESSO?

ZULRESSO can cause serious side effects, including:

- See "**What is the most important information I should know about ZULRESSO?**"
- **Increased risk of suicidal thoughts or actions.** ZULRESSO and other antidepressant medicines may increase suicidal thoughts and actions in some people 24 years of age and younger. Depression or other serious mental illnesses are the most important causes of suicidal thoughts or actions.

How can I watch for and try to prevent suicidal thoughts and actions?

- Pay close attention to any changes, especially sudden changes in mood, behavior, thoughts, or feelings, or if you develop suicidal thoughts or actions.
- Tell your healthcare provider right away if you have any new or sudden changes in mood, behavior, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

Tell your healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

- Attempts to commit suicide, thoughts about suicide or dying, new or worse depression, other unusual changes in behavior or mood

The most common side effects of ZULRESSO include:

- Sleepiness, dry mouth, passing out, flushing of the skin or face.

These are not all the side effects of ZULRESSO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see **Full Prescribing Information including Boxed Warning** and **Medication Guide** for ZULRESSO and discuss any questions you may have with your healthcare provider.

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