Sage Therapeutics Announces Third Quarter 2020 Financial Results and Highlights Pipeline and Business Progress

November 5, 2020

Ongoing zuranolone Phase 3 pivotal trials in major depression and postpartum depression progressing well; expect to initiate dosing in CORAL Study in 4Q 2020

Continued execution across brain health franchises highlighted during 2nd annual FutureCast event

First patient dosed in PARADIGM Study investigating SAGE-718 in patients with Parkinson's disease cognitive dysfunction

Conference call today at 8:30 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 5, 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 third quarter ended September 30, 2020.

"Today I'm pleased to report that our clinical programs across three franchises remain on track, with a series of key milestones anticipated over the next 12 to 18 months," said Mike Cloonan, chief operating officer at Sage Therapeutics. "During the third quarter, we continued progress across our deep and robust clinical pipeline, a pipeline that spans multiple disease states with programs in early, mid and late stage development. The Sage team continues to execute well during the COVID-19 pandemic and remains determined to provide much needed options to patients suffering with debilitating brain health disorders."

Recent updates

Sage recently reported positive, interim topline results from a July data cut of the ongoing Phase 3 open-label SHORELINE Study of zuranolone in major depressive disorder (MDD). The data analyzed to date show that zuranolone was generally well-tolerated in the 30 mg dose and among the initial patients treated with the 50 mg dose. Adverse events reported in the trial during the period analyzed were generally consistent with results seen in previous zuranolone clinical trials.

As the first naturalistic, longitudinal, clinical development trial conducted in MDD, the SHORELINE Study provides real world insight into the potential use of zuranolone, if successfully developed and approved as an as-needed treatment for MDD, and builds on the data assembled in the LANDSCAPE clinical program. The Company plans to report comprehensive data from the 30 mg dose of the SHORELINE Study in the first half of 2021 and will include additional analyses of the data set.

Portfolio Updates

Sage is advancing a portfolio of novel, new 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 Franchise

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 U.S. Food and Drug Administration (FDA) as the first treatment specifically indicated for postpartum depression (PPD). Zuranolone has received breakthrough therapy designation from the FDA for the treatment of MDD.

- **Zuranolone ongoing studies:** Sage is evaluating the potential of zuranolone as a rapid-acting, short-course treatment for PPD and MDD. Sage recently initiated three new short-term clinical studies in 2020, with the potential along with the rest of the program, if successful, to support three distinct indications: PPD, acute rapid response therapy (RRT) in MDD when co-initiated with a new standard antidepressant, and as-needed, or episodic, treatment of MDD. Enrollment and dosing are now ongoing in two of these trials:
    - SKYLARK (PPD-301) Study investigating zuranolone as an oral therapy in women with PPD:
        - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in women with PPD, with additional short-term follow-up.
        - *Topline data from this study are anticipated in 2021.*
    - WATERFALL (MDD-301B) Study investigating zuranolone for the as-needed, or episodic, treatment of MDD:
        - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg in patients with MDD, with

additional short-term follow-up.
- *Topline data from this study are anticipated in the first half of 2021.*

Sage expects to initiate dosing of the third new zuranolone Phase 3 trial in 2020:

- CORAL (MDD-305) Study investigating zuranolone for acute RRT in patients with MDD when co-initiated with a newly administered standard antidepressant therapy:
  - Placebo-controlled trial evaluating a two-week course of zuranolone 50 mg, when co-initiated with a new open-label antidepressant, in patients with MDD, with additional short-term follow-up.
  - *Topline data from this study are anticipated in 2021.*

- Sage is also currently evaluating the ongoing zuranolone clinical pharmacology and safety program and plans to finalize requirements to support a potential future new drug application (NDA) with the FDA.
- **ZULRESSO® (brexanolone) CIV injection:**
  - Revenue in the third quarter of 2020 from sales of ZULRESSO was $1.6 million, compared to $1.5 million in the third quarter of 2019. As previously announced, due to the ongoing impact of the COVID-19 pandemic, the Company expects de minimis revenue for the balance of 2020, and expects future revenue growth to be limited even after the pandemic as a result of the significant barriers to treatment and the refocus of Sage's commercialization efforts after the April 2020 restructuring.
  - The Company has received clearance from the FDA, under the Coronavirus Treatment Acceleration Program (CTAP), to initiate a Phase 3 study with brexanolone in patients with advanced COVID-19 related acute respiratory distress syndrome (ARDS). The Company expects to initiate patient dosing in this study in the fourth quarter of 2020.
    - *Topline data from this study are anticipated in 2021.*

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 (PD).

- **KINETIC Study:** The KINETIC Study (324-ETD-201), a placebo-controlled Phase 2 study evaluating the safety and efficacy of SAGE-324 in patients with ET is ongoing. Patients in the study receive a once-daily, four-week course of SAGE-324 60 mg or placebo.
  - *Topline data from this study are now anticipated in 1Q 2021.*

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, potentially including Huntington's disease (HD), PD and Alzheimer's disease (AD).

- **PARADIGM Study:** The Company initiated enrollment and dosing in the PARADIGM Study (718-CNP-201), a Phase 2a open-label study evaluating SAGE-718 in patients with PD cognitive dysfunction.
  - *Topline data from this study are now anticipated in the first quarter of 2021.*

- **LUMINARY Study:** The Company expects to initiate dosing in the LUMINARY Study (718-CNP-201), a Phase 2a open-label study evaluating SAGE-718 in patients with AD cognitive dysfunction and mild dementia in the fourth quarter of 2020.

Results from these studies will inform potential advancement of SAGE-718 into further development.

Corporate Updates

During the third quarter, the Company strengthened its leadership with two key additions:

- **Barry Greene** was appointed to Sage's Board of Directors. He was most recently President of Alnylam Pharmaceuticals, Inc.

- **Tammy Phinney** joined the Company's management team as senior vice president, regulatory affairs. Her extensive experience leading regulatory functions in the neurology therapeutic area over the last 15 years is well-aligned with Sage's significant regulatory needs as the Company is anticipating several potential FDA engagements as its pipeline advances. Most recently, she served as Vice President, Head of US, Regulatory Affairs at EMD Serono.

The Company also hosted the 2nd annual "FutureCast: An R&D Portfolio Review" in the third quarter to review the Company's research and development strategy, and clinical progress in its key depression, neurology, and neuropsychiatry franchise programs.

Anticipated Upcoming Milestones

Q4 2020

- Zuranolone:
  - Initiate dosing in Phase 3 CORAL Study (MDD-305) evaluating zuranolone 50 mg, when co-initiated with a new open-label antidepressant, as an acute rapid response therapy in patients with MDD.
- Brexanolone:
  - Initiate dosing in Phase 3 study in patients with advanced COVID-19 related acute respiratory distress syndrome (ARDS).
- SAGE-718
  - Initiate dosing in Phase 2a LUMINARY open-label, signal finding study in patients with Alzheimer's disease cognitive dysfunction and mild dementia.

2021

- Zuranolone:
  - Report topline data from Phase 3 WATERFALL Study (1H 2021).
  - Report topline data from Phase 3 SKYLARK Study.
  - Report topline data from Phase 3 CORAL Study.
  - Report topline data from Phase 3 SHORELINE Study (30 mg full data set – 1H 2021; 50 mg topline data – 2H 2021).
- SAGE-324:
  - Report topline data from Phase 2 placebo-controlled KINETIC Study in essential tremor (1Q 2021).
- SAGE-718:
  - Report topline data from Phase 2a PARADIGM open-label, signal finding study in patients with Parkinson's disease cognitive dysfunction (1Q 2021).
- Brexanolone:
  - Report topline data from Phase 3 study in patients with advanced COVID-19 related ARDS.

Financial Results for the Third Quarter 2020

- **Revenue**: Sage recorded $1.6 million in net revenue in the third quarter of 2020 from sales of ZULRESSO, compared to $1.5 million for the same period in 2019. Sage recorded no collaboration revenue in the third quarter of 2020 compared to $2.1 million in collaboration revenue from Shionogi & Co., Ltd. related to reimbursement of product expense for the same period in 2019.

- **Cash Position**: Cash, cash equivalents, restricted cash, and marketable securities as of September 30, 2020 were $671 million compared to $759 million at June 30, 2020.

- **R&D Expenses**: Research and development expenses were $74.1 million, including $9.9 million of non-cash stock-based compensation expense, in the third quarter of 2020 compared to $102.1 million, including $17.1 million of non-cash stock-based compensation expense, for the same period in 2019. The decrease in R&D expenses was primarily related to the completion of the MOUNTAIN Study, a Phase 3 clinical trial of zuranolone in MDD; the decrease in non-cash stock-based compensation expense and decreased spending for clinical pharmacology studies, partially offset by an increase in spending for the WATERFALL Study, a Phase 3 clinical trial of zuranolone in MDD.

- **SG&A Expenses**: Selling, general and administrative expenses were $35.1 million, including $10.2 million of non-cash stock-based compensation expense, in the third quarter of 2020 compared to $88.5 million, including $26.6 million of non-cash stock-based compensation expense, for the same period in 2019. The decrease in SG&A expenses was primarily due to the restructuring that the Company announced during the second quarter of 2020.

- **Net Loss**: Net loss was $105.7 million for the third quarter of 2020, compared to $180.0 million for the same period in 2019.

Financial Guidance

- Sage anticipates a cash balance of at least $550 million at end of 2020, which the Company anticipates will support operations into 2022 based on current operating plans.

Conference Call Information

Sage will host a conference call and webcast today, Thursday, November 5, at 8:30 a.m. ET to discuss its third quarter 2020 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 revenues from sales of ZULRESSO; our clinical development plans and expected timelines; our expectations with respect to 2020 operating expenses and year-end cash; our belief that existing cash will support operations into 2022; 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 never be able to generate meaningful revenues from sales of ZULRESSO or to generate revenues at levels necessary to justify our investment; the impact of the COVID-19 pandemic on sales of ZULRESSO may last longer than we expect or may reoccur in waves; our post-restructuring focus on geographies where there are existing, active ZULRESSO treating sites may not be sufficient for us to achieve success from the sale of ZULRESSO or to generate revenues at meaningful levels or at levels necessary to justify our investment even after the impact of the COVID-19 pandemic lessens; we may not be able to overcome the barriers to treatment with ZULRESSO or we may continue to encounter other issues or challenges in commercializing ZULRESSO which could further 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 patients with the diseases or disorders for which our products are developed or the unmet need for additional treatment options may be significantly smaller than we expect; we may encounter delays in initiation, conduct or completion of our ongoing and planned clinical trials, including as a result of slower than expected site initiation or enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected time-lines and increase our costs; we may not be able to mitigate the impact of COVID-19 on our clinical development timelines and the impact may be more significant than we expect and may negatively impact expected site initiation, enrollment or conduct in our clinical trials, or cause us to pause trials or not be able to use data, in each case which may significantly impact our ability to meet our expected time-lines or may significantly impact the integrity or sufficiency of the data from our trials or increase our costs or cause us to have to change our plans; 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; our expectations as to expenses, year-end cash and cash needs may prove not to be correct for 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; we may not be successful in our development of any of our product candidates in any indication we are currently pursuing or may in the future pursue; success in our non-clinical studies or in earlier clinical trials may not be repeated or observed in ongoing or future studies, and ongoing and future non-clinical and clinical results or at interim time periods may not meet their primary or key secondary endpoints or be sufficient to file for or gain regulatory approval to market the product without further development work or may not support further development at all; we may encounter adverse events at any stage of development that negatively impact further development or that require additional nonclinical and clinical work which may not yield positive results; we may encounter different or more severe adverse events at the higher doses we are studying in new trials; we may encounter issues with the efficacy or durability of short-term treatment, or co-initiated treatment with zuranolone or safety and efficacy concerns with respect to retreatment that require additional studies be conducted; the FDA may ultimately decide that the design or results of our completed and planned clinical trials for any of our product candidates, even if positive, are not sufficient for regulatory approval in the indications that are the focus of our development plan; other 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 encounter technical and other unexpected hurdles in the development and manufacture of our product candidates which may delay our timing or change our plans or increase our costs; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Quarterly Report on Form 10-Q, 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.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2020	2019	2020	2019
Product revenue, net	$ 1,639	$ 1,478	$ 5,014	$ 1,997
Collaboration revenue	-	2,092	-	2,911
Total revenue	1,639	3,570	5,014	4,908
Operating costs and expenses:				
Cost of goods sold	149	137	429	181
Research and development	74,078	102,108	211,008	277,565
Selling, general and administrative	35,099	88,502	143,454	260,648
Restructuring	(529)	-	27,873	-
Total operating costs and expenses	108,797	190,747	382,764	538,394
Loss from operations	(107,158)	(187,177)	(377,750)	(533,486)
Interest income, net	1,347	7,227	8,763	21,889

Other income (expense), net	76	(8)	165	12
Net loss	$ (105,735)	$ (179,958)	$ (368,822)	$ (511,585)
Net loss per share - basic and diluted	$ (2.03)	$ (3.48)	$ (7.10)	$ (10.13)
Weighted average shares outstanding - basic and diluted	51,981,468	51,704,687	51,938,923	50,496,489

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

	September 30, 2020	December 31, 2019
Cash, cash equivalents, restricted cash and investments	$ 670,904	$ 1,010,760
Total assets	$ 738,628	$ 1,084,150
Total liabilities	$ 81,047	$ 139,495
Total stockholders' equity	$ 657,581	$ 944,655

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 $GABA_A$ receptors. Allosteric modulation of neurotransmitter receptor activity results in varying degrees of desired activity rather than complete activation or inhibition of the receptor.

SELECT IMPORTANT SAFETY INFORMATION

These are not all the side effects of 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 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 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.

ZULRESSO can cause other serious side effects, including:

- **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. **Pay close attention to and 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 or sudden changes in behavior or mood
  - Keep all follow-up visits and call your healthcare provider between visits as needed, especially if you have concerns about symptoms.

The most common side effects of ZULRESSO include:

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

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

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, or are breastfeeding or plan to breastfeed. It is not known if ZULRESSO will harm your unborn baby. If you become pregnant during treatment, talk with your healthcare provider about enrolling with the National Pregnancy Registry for Antidepressants at 1-844-405-6185.

While receiving ZULRESSO, avoid the following:

- Driving a car or doing other dangerous activities after your ZULRESSO infusion until your feeling of sleepiness has completely gone away
- Do not drink alcohol

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).

Please see the patient Medication Guide, including information about serious side effects, for Zulresso in the full Prescribing Information.

View source version on businesswire.com: https://www.businesswire.com/news/home/20201105005181/en/

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