Sage Therapeutics Announces Fourth Quarter and Full Year 2018 Financial Results and Highlights Pipeline and Business Progress

February 19, 2019

Planned U.S. commercial launch of ZULRESSO™ (brexanolone) injection, if approved, on track for June 2019, based on PDUFA target date of March 19, 2019 and anticipated DEA scheduling

Topline data from Phase 3 trial of SAGE-217 in MDD expected in Q4 2019 or 1Q 2020

Neurology and neuropsychiatry franchises continue to progress with positive Phase 1 data

Conference call today at 8:00 AM ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 19, 2019-- Sage Therapeutics, Inc. (NASDAQ: SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-altering central nervous system (CNS) disorders, today reported business highlights and financial results for the fourth quarter and full year ended December 31, 2018.

“Eight years ago, Sage was founded to address the innovation void in CNS drug development. Today we are establishing Sage as a CNS leader by building multiple franchise opportunities - in depression, neurology and neuropsychiatry, with the potential to treat millions of patients. Our focused execution across these three franchises has led to a pipeline of four clinical candidates across several indications, all using novel mechanisms and approaches,” said Jeff Jonas, M.D., chief executive officer at Sage. “The expected near-term approval of our lead product candidate, ZULRESSOin the treatment of postpartum depression, will mark a major milestone in our company’s journey and, along with our broader portfolio, may help support a paradigm-shifting approach to mental health. We want people to be treated as people with depression, not depressed people, and we believe our development programs, if successful, can help define this new normal.”

Depression Franchise:

Led by ZULRESSO™ (brexanolone) injection, which has been designated as a breakthrough therapy by the U.S. Food and Drug Administration (FDA) for the treatment of postpartum depression (PPD), and SAGE-217, which has been designated as a breakthrough therapy for the treatment of major depressive disorder (MDD).

- ZULRESSO: Prescription Drug User Fee Act (PDUFA) goal date is March 19, 2019.
  - If approved, Sage plans to launch ZULRESSO in the U.S. in June 2019, following expected scheduling by the Drug Enforcement Administration (DEA), which is to occur within 90 days of approval. The Company’s commercial infrastructure build is complete and the sales organization is launch ready, pending approval and scheduling.
- SAGE-217: Multiple studies are underway across the pivotal program studying SAGE-217 as a short-course oral treatment for depression, which includes two completed positive pivotal trials in MDD and PPD.
  - Based on enrollment progress in the ongoing Phase 3 placebo-controlled MOUNTAIN Study in patients with MDD, topline results are now expected in Q4 2019 or Q1 2020.

        - The MOUNTAIN Study is evaluating two weeks of 20mg or 30mg SAGE-217 treatment compared to placebo and four weeks of follow-up in approximately 450 patients with MDD.
        - As a separate observational protocol, the Company will continue to follow patients from the MOUNTAIN Study after completion for up to 6 months.
    - Topline readouts from Phase 3 RAINFOREST and SHORELINE studies anticipated in 2020. Additional MDD-302 Study planned.
        - The RAINFOREST Study is evaluating two weeks of 30mg SAGE-217 treatment compared to placebo in patients with MDD and co-morbid insomnia.
        - The SHORELINE Study will evaluate 30mg SAGE-217 open-label treatment, treatment-free intervals and as-needed retreatment for return of major depressive episodes over the course of up to a year.
        - Based on the positive results of the ROBIN Study in PPD and the ongoing Breakthrough dialog with the FDA, the SAGE-217 depression program will be expanded to generate monotherapy maintenance data through an additional study, MDD-302. This placebo-controlled trial will evaluate fixed interval SAGE-217 monotherapy (treatment without traditional antidepressants) for up to a year, and, if positive, would generate data that the Company believes will maximize value, help fulfill FDA registration requirements, and offer more treatment options to clinicians, if SAGE-217 is successfully developed and approved.
        - Sage believes that these studies will provide support for Sage's vision to transform the treatment paradigm for MDD.
    - The open-label Phase 2 ARCHWAY Study is evaluating SAGE-217 as a treatment for bipolar depression, with topline results expected in the first half of 2019.
        - The ARCHWAY Study is evaluating open-label SAGE-217 treatment in up to 30 patients with bipolar I/II disorder with a current major depressive episode. Primary endpoints are safety and tolerability; secondary endpoints will measure improvements in depressive symptoms and sleep.

Neurology Franchise:

Led by SAGE-324, a next-generation positive allosteric modulator (PAM) of $GABA_A$ receptors in development as a potential therapy for neurological conditions, such as essential tremor and epileptiform disorders.

- SAGE-324: Results from a Phase 1 single ascending dose study demonstrated that the profile of SAGE-324 includes good oral bioavailability and a pharmacokinetic profile consistent with once-daily dosing. SAGE-324 demonstrated clear target engagement in the brain using pharmaco-EEG (β-band power) as a functional biomarker.
- SAGE-324 was generally well-tolerated with no serious adverse events and with a safety profile consistent with $GABA_A$ positive allosteric modulation.
- The Phase 1 multiple ascending dose study is ongoing and a Phase 1 study to determine the safety, tolerability and pharmacokinetics of SAGE-324 in patients with essential tremor has been initiated.

Neuropsychiatry Franchise:

Led by first-in-class NMDA receptor PAM, SAGE-718, which is in development as a potential therapy for certain cognition-related disorders impacted by NMDA receptor dysfunction.

- SAGE-718: Results from Phase 1 studies demonstrated that the profile of SAGE-718 includes good oral bioavailability and a pharmacokinetic profile consistent with once-daily dosing.
- SAGE-718 was generally well-tolerated with no serious adverse events reported.

- Results from target engagement biomarker studies in healthy volunteers, focusing on electrophysiology and imaging, are ongoing with results expected later in 1H 2019.
- Initiated a Phase 1 study to determine the safety, tolerability and pharmacokinetics of SAGE-718 in patients with early manifest Huntington’s disease.

Expected Milestones

- **Data readouts:**
  - SAGE-217 Phase 2 ARCHWAY Study in bipolar depression (1H 2019)
  - SAGE-718 Phase 1 biomarker data (1H 2019)
  - SAGE-324 Phase 1 MAD study (2H 2019)
  - SAGE-324 essential tremor Phase 1 cohort data (2H 2019)
  - SAGE-718 Huntington’s Disease Phase 1 cohort data (2H 2019)
  - SAGE-217 MDD Phase 3 MOUNTAIN Study (Q4 2019/Q1 2020)
  - SAGE-217 MDD Phase 3 RAINFOREST and SHORELINE studies (2020)
- **Regulatory and commercial:**
  - ZULRESSO in PPD PDUFA target date (March 19, 2019)
  - ZULRESSO in PPD commercial launch, if approved (June 2019)

Financial Results for the Fourth Quarter and Full Year 2018

- **Cash Position:** Cash, cash equivalents, and marketable securities as of December 31, 2018 were $922.8 million, compared with $518.8 million at December 31, 2017. The increase was primarily due to net proceeds of $631.2 million from Sage's follow-on public offering completed in February 2018, and an upfront milestone payment from Shionogi & Co., Ltd. related to the strategic collaboration on SAGE-217 in Japan, Taiwan and South Korea that we entered into in June 2018.
- **R&D Expenses:** Research and development expenses were $88.8 million, including $15.9 million of non-cash stock-based compensation expense, in the fourth quarter of 2018, compared to $50.9 million, including $5.7 million of non-cash stock-based compensation expense, for the same period of 2017. For the year ended December 31, 2018, research and development expenses were $282.1 million, including $50.9 million of non-cash stock-based compensation expense, compared to $210.3 million, including $19.9 million of non-cash stock-based compensation expense, for the same period of 2017. The increase in R&D expenses year-over-year was primarily due to Phase 3 clinical development of SAGE-217 in PPD and MDD; the continuation of Phase 1 studies of SAGE-324 and SAGE-718 and supporting clinical activities; ongoing early-stage R&D programs and discovery efforts focused on identifying new development candidates and additional indications of interest; and investments in R&D headcount to support the growth in Sage's pipeline and operations. These expenses were offset by a decrease in expense related to the ZULRESSO clinical development program.
- **G&A Expenses:** General and administrative expenses were $75.7 million, including $15.8 million of non-cash stock-based compensation expense, in the fourth quarter of 2018, compared to $19.6 million, including $4.6 million of non-cash stock-based compensation expense, for the same period of 2017. For the year ended December 31, 2018, G&A expenses were $201.4 million, including $51.1 million of non-cash stock-based compensation expense, compared to $62.9 million, including $15.6 million of non-cash stock-based compensation expense, for the same period of 2017. The increase in G&A expenses was primarily due to the increase in personnel-related expenses, professional fees to support expanding operations, costs related to continued preparations for a potential commercial launch, and facilities-related costs to support expanding operations.
- **Net Loss:** Net loss was $158.4 million for the fourth quarter of 2018 and $372.9 million for the year ended December 31, 2018, compared to a net loss of $69.4 million and $270.1 million, respectively, for the comparable periods of 2017.

Financial Guidance

- Based upon its current operating plan, Sage now anticipates that its existing cash, cash equivalents and marketable securities, and estimated product sales of ZULRESSO, if the product is approved, will enable Sage to fund its operating expenses and capital expenditure requirements into 2H 2020.
- Sage expects that its operating expenses will increase year over year in 2019 to support continued pipeline advancement and anticipated commercialization of ZULRESSO in PPD.

Conference Call Information

Sage will host a conference call and webcast today at 8:00 AM ET to discuss its fourth quarter and full year 2018 financial results and recent corporate updates. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. The conference call can be accessed by dialing 1-866-450-8683 (toll-free domestic) or 1-281-542-4847 (international) and using the conference ID 6968949. 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 clinical-stage biopharmaceutical company committed to developing novel medicines to transform the lives of patients with life-altering CNS disorders. Sage's lead product candidate, ZULRESSO™ (brexanolone) injection, has completed Phase 3 clinical development for postpartum depression and a New Drug Application is currently under review with the U.S. Food and Drug Administration. Sage is developing a portfolio of novel product candidates targeting critical CNS receptor systems, including SAGE-217, which is in Phase 3 development in major depressive disorder and postpartum depression. 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 expectations regarding approval of our new drug application (NDA) for ZULRESSO in the treatment of PPD, including the target timing of a decision by the FDA; our plans regarding the timing of launch of ZULRESSO in PPD, future commercial activities, and the potential for future revenues, if the NDA for ZULRESSO is approved; our statements regarding plans and timelines for development of SAGE-217 and our other product candidates, including planned clinical and regulatory activities; our view of the potential for the data from our development program with SAGE-217 in MDD, if positive, to create value and be supportive of a regulatory submission and approval; our views as to the opportunity represented by Sage's portfolio and business in CNS, including the potential, if we are successful, to treat millions of patients and to change treatment paradigms; and our expectations regarding increases in operating expense, use of cash and future cash needs. 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 decide not to approve our NDA for ZULRESSO in PPD; the clinical and non-clinical data we have generated with ZULRESSO to date may be determined by the FDA to be insufficient to gain regulatory approval to launch and commercialize our product in PPD and FDA may determine that additional trials or data are necessary in order to file for or obtain approval; the FDA may not complete its review of our filing within the target timelines; even if ZULRESSO is successfully approved for PPD in the U.S., we may encounter issues, delays or other challenges in launching or commercializing the product, including issues related to market acceptance and reimbursement, challenges associated with restrictions or conditions that may be imposed by regulatory authorities, including challenges related to limiting the site of administration to a certified healthcare facility monitored by a qualified healthcare provider, and the necessity for a REMS; and challenges associated with execution of our sales and patient support activities, which in each case could limit the potential of our

product; we may encounter unexpected safety or tolerability issues with ZULRESSO, SAGE-217 or any of our other product candidates in ongoing or future development; we may not be successful in our development of SAGE-217 or any of our other product candidates in any indication we are currently pursuing or may in the future pursue; success in early stage clinical trials may not be repeated or observed in ongoing or future studies of SAGE-217 or any of our other product candidates; ongoing and future clinical results may not support further development or be sufficient to gain regulatory approval of our product candidates; 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 our development program for SAGE-217, even if positive, is not sufficient for an NDA 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 or may impact the regulatory pathway; we may experience slower than expected enrollment in ongoing clinical trials; the internal and external costs required for our activities, and to build our organization in connection with such activities, and the resulting use of cash, may be higher than expected, or we may conduct additional clinical trials or pre-clinical studies, or engage in new activities, requiring additional expenditures and using cash more quickly than anticipated; and we may encounter technical and other unexpected hurdles in the development, manufacture and potential future commercialization of our product candidates; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent 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,	
	2018	**2017**	**2018**	**2017**
Collaboration revenue	$ 273	$ -	$ 90,273	$ -
Operating expenses:				
Research and development	88,805	50,890	282,107	210,277
General and administrative	75,695	19,558	201,404	62,878
Total operating expenses	164,500	70,448	483,511	273,155
Loss from operations	(164,227)	(70,448)	(393,238)	(273,155)
Interest income, net	5,851	1,042	20,334	3,099
Other income (expense), net	(12)	(15)	22	(64)
Net loss	$ (158,388)	$ (69,421)	$ (372,882)	$ (270,120)
Net loss per share - basic and diluted	$ (3.38)	$ (1.75)	$ (8.08)	$ (7.09)
Weighted average shares outstanding - basic and diluted	46,876,452	39,583,004	46,121,194	38,113,678

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

(Unaudited)

	December 31, 2018	December 31, 2017
Assets		
Current Assets:		
Cash and cash equivalents	$ 190,943	$ 306,235
Marketable securities	731,833	212,613
Prepaid expenses and other current assets	21,919	6,227
Total current assets	944,695	525,075
Property and equipment and other long-term assets	8,010	4,862
Total assets	$ 952,705	$ 529,937
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 34,036	$ 9,350
Accrued expenses	51,994	42,601
Total current liabilities	86,030	51,951
Other liabilities	3,704	2,511
Total liabilities	89,734	54,462
Total stockholders' equity	862,971	475,475
Total liabilities and stockholders' equity	$ 952,705	$ 529,937

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