Sage Therapeutics Announces Third Quarter 2018 Financial Results and Highlights Pipeline and Business Progress

November 6, 2018

FDA Advisory Committee Meeting outcome supports approval of ZULRESSO™ (brexanolone) injection asthe first medicine specifically indicated for the treatment of postpartum depression (PPD)

Continuing to execute commercial strategy for ZULRESSO in PPD ahead of PDUFA target date of December 19, 2018 and readiness for planned U.S. launch in late March

Completion of enrollment in Phase 3 clinical trial of SAGE-217 in PPD – top-line results expected in January 2019

Expansion of depression franchise with initiation of Phase 2 clinical trial of SAGE-217 in bipolar depression and multiple near-term trial initiations expected in major depressive disorder

Continued progress for SAGE-324 and SAGE-718 in early clinical pipeline

Conference call today at 8:00 AM ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 6, 2018-- 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 third quarter ended September 30, 2018.

“At Sage, our approach to scientific discovery and development is focused on transforming the lives of people with life-altering CNS disorders. Our first program, in PPD, exemplifies this philosophy. Members of the PPD patient advocacy community and healthcare providers across the country have shared their sense of urgency with us – they are seeking a new way of thinking about PPD and an opportunity to rapidly alleviate suffering from this condition. If approved, ZULRESSO has the potential to meet these needs and to be an important new tool that healthcare providers can use to ease the burden of PPD for patients and their families,” said Jeff Jonas, M.D., chief executive officer of Sage. “Sage is committed to helping women diagnosed with PPD access ZULRESSO, if it is approved. We are currently assessing potential patient support options to help lessen financial barriers to access for women with PPD in need of treatment, where appropriate and permitted. We aspire to define a new normal for brain health and we’re just getting started.”

ZULRESSO™ (brexanolone) Injection Regulatory and Pre-Launch Activities Updates:

- On November 2nd, the U.S. Food and Drug Administration (FDA) Psychopharmacologic Drugs Advisory Committee (PDAC) and Drug Safety and Risk Management Advisory Committee (DSaRM) jointly voted (17 yes, 1 no) that data support the favorable benefit-risk profile of ZULRESSO™ (brexanolone) injection for the treatment of postpartum depression (PPD) when administered by qualified staff in a facility that has been certified under a Risk Evaluation and Mitigation Strategies (REMS) program. The joint committee based their joint recommendation on the safety and efficacy data from three placebo-controlled clinical studies.
- The New Drug Application (NDA) for ZULRESSO for the treatment of PPD has been accepted for

Priority Review by the FDA. The FDA has assigned a Prescription Drug User Fee Act (PDUFA) target date of December 19, 2018.
- If approved, ZULRESSO is expected to be scheduled by the U.S. Drug Enforcement Administration (DEA), consistent with other approved GABAergic therapies. The DEA is required to issue an interim final rule controlling the drug within 90 days of approval.
- Preparations continue for a potential U.S. commercial launch of ZULRESSO for the treatment of PPD in late March 2019, if the NDA is approved and post-DEA scheduling.
- Sage is continuing discussions with the European Medicines Agency (EMA) to determine the European regulatory pathway for a marketing authorization application (MAA) filing for brexanolone injection for PPD. Sage plans to seek additional Scientific Advice to help determine what additional data or information will be needed prior to filing, as is permissible under the PRIority MEdicines (PRIME) designation program.

Pipeline Updates:
Beyond ZULRESSO, Sage is advancing a portfolio of novel CNS product candidates targeting the GABA and NMDA receptor systems. Dysfunction in these systems is known to be at the core of numerous psychiatric and neurological disorders.

- SAGE-217 in Major Depressive Disorder (MDD) and PPD:
    - PPD Phase 3 trial enrollment completed: Enrollment was recently completed for the Phase 3 placebo-controlled trial evaluating SAGE-217 in patients with PPD, and Sage plans to announce top-line results in January 2019.
    - MDD Phase 3 trial initiated: Plans are on-track for enrollment to begin in a Phase 3 placebo-controlled trial of SAGE-217 in MDD in 4Q 2018. The trial will evaluate the potential of episodic treatment through a protocol including two weeks of 20mg or 30mg SAGE-217 treatment compared to placebo in approximately 450 patients with MDD, with four weeks of additional follow-up.
    - Long-term retreatment study: Additional data regarding patient safety and potential treatment of recurrent or new major depressive episodes will be acquired through a long-term retreatment study evaluating SAGE-217 treatment and episodic retreatment as needed.

- SAGE-217 in Other Psychiatric Indications:
    - Bipolar depression: Dosing of patients is underway in Part A of a two-part Phase 2 clinical trial evaluating open-label SAGE-217 treatment in up to 30 patients with bipolar I/II disorder with a current major depressive episode. If Part A is successful, the Company plans to progress to a randomized, placebo-controlled Part B study. The Part A trial is intended to evaluate the safety and tolerability of SAGE-217 and secondary endpoints, including efficacy in improving depressive symptoms and sleep. The top-line results from Part A are planned to be announced in 1H 2019.
    - Sleep disorders: Additional data from a placebo-controlled trial in a model of insomnia demonstrating an encouraging impact of SAGE-217 on sleep architecture was recently presented at the 31stEuropean College of Neuropsychopharmacology Congress. Sage plans to initiate a Phase 3 placebo-controlled polysomnography trial of SAGE-217 in MDD patients with co-morbid insomnia in 4Q 2018, and also plans to seek feedback in 2019 from the FDA on potential development plans for SAGE-217 for the treatment of sleep disorders and other indications.

- SAGE-324 in Neurological Indications:
    - Phase 1 program: A Phase 1 single-ascending dose trial of SAGE-324 in healthy volunteers, which is intended to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamic profile of SAGE-324, is ongoing, and Sage plans to complete this trial in 4Q 2018. Based on initial findings from this trial, Sage plans to initiate a Phase 1 multiple-ascending dose trial of

SAGE-324 in healthy volunteers in 4Q 2018. SAGE-324 is being developed as a potential treatment for patients impacted by neurological conditions such as epileptiform disorders, essential tremor, and Parkinson’s disease.

- NMDA Programs:
  - SAGE-718: The healthy volunteer portion of the Phase 1 multiple ascending dose trial of SAGE-718 has been completed. As part of the Phase 1 program, Sage has initiated target engagement biomarker studies, focusing on electrophysiology and imaging, to evaluate SAGE-718 in healthy volunteers, and is considering plans to evaluate the safety, tolerability, pharmacokinetic and pharmacodynamic profile of SAGE-718 in a patient cohort.
  - SAGE-904 is currently in IND-enabling studies.

Expected Milestones

- **Trial Enrollment Initiations:**
  - SAGE-217 Phase 3 placebo-controlled trial in MDD (4Q 2018)
  - SAGE-217 Phase 3 placebo-controlled polysomnography trial in MDD patients with co-morbid insomnia (4Q 2018)
  - SAGE-324 Phase 1 multiple ascending dose trial (4Q 2018)
- **Data Readouts:**
  - SAGE-217 Phase 3 placebo-controlled trial in PPD (January 2019)
  - SAGE-217 Phase 2 trial in bipolar depression (1H 2019)
  - SAGE-718 Phase 1 target engagement studies (1H 2019)
  - SAGE-324 Phase 1 multiple ascending dose trial (1H 2019)
- **Regulatory and Commercial:**
  - ZULRESSO in PPD PDUFA target date (December 19, 2018)
  - ZULRESSO in PPD commercial launch, if approved (late March 2019)

Financial Results for the Third Quarter of 2018

- **R&D Expenses:** Research and development expenses were $75.1 million, including $14.0 million of non-cash stock-based compensation expense, in the third quarter of 2018, compared to $58.3 million, including $5.4 million of non-cash stock-based compensation expense, for the same period of 2017. The increase in R&D expenses was primarily due to increases in expenses related to ongoing R&D programs and discovery efforts focused on identifying new clinical candidates and additional indications of interest and investments in R&D headcount to support the growth in Sage's pipeline and operations, offset by decreases in expenses due to the completion of Phase 3 clinical development of ZULRESSO.
- **G&A Expenses:** General and administrative expenses were $53.7 million, including $11.5 million of non-cash stock-based compensation expense, in the third quarter of 2018, compared to $16.1 million, including $4.3 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 $122.9 million for the third quarter of 2018 compared to a net loss of $73.7 million for the comparable period of 2017.
- **Cash Position:** Cash, cash equivalents, and marketable securities as of September 30, 2018 were $1.0 billion, 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 that was entered in June 2018.

Financial Guidance:

- Based on its current operating plan, Sage anticipates that its existing cash, cash equivalents and marketable securities as of September 30, 2018 will enable Sage to fund its operating expenses and capital expenditure requirements into 2020.
- Sage expects that its operating expenses will increase year-over-year in 2018 to support continued pipeline advancement, including ongoing Phase 3 development of SAGE-217, and potential commercialization of ZULRESSO in PPD, if approved.

Conference Call Information
Sage will host a conference call and webcast on Tuesday, November 6, 2018 at 8:00 AM ET to report its third quarter 2018 financial results and to discuss recent business 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 (866) 450-8683 (toll-free domestic) or (281) 542-4847 (international) and using the conference ID 1891169. 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 the potential for approval of our 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 and future commercial activities, if approved; our plans for determining the potential regulatory pathway for brexanolone injection in the EU; our statements regarding plans and timelines for development of SAGE-217 and our other product candidates, including planned clinical and regulatory activities;our views as to the opportunity represented by Sage's portfolio and business; 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 not agree with the recommendation of the Advisory Committees, and may decide not to approve our NDA for ZULRESSO in PPD; the clinical and non-clinical data we have generated with our proprietary formulation of brexanolone to date may be determined by the FDA, the EMA and other regulatory authorities to be insufficient to gain regulatory approval to launch and commercialize our product in PPD and regulatory authorities 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 issuccessfully 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 the build of our sales and patient support organizations and their 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; 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 Quarterly Report on Form 10-Q, and 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,	
	2018	**2017**	**2018**	**2017**
Collaboration revenue	$ -	$ -	$ 90,000	$ -
Operating expenses:				
Research and development	75,052	58,286	193,302	159,386
General and administrative	53,693	16,087	125,709	43,320
Total operating expenses	128,745	74,373	319,011	202,706
Loss from operations	(128,745)	(74,373)	(229,011)	(202,706)
Interest income, net	5,817	677	14,483	2,056
Other income (expense), net	10	(23)	34	(48)
Net loss	$ (122,918)	$ (73,719)	$ (214,494)	$ (200,698)
Net loss per share - basic and diluted	$ (2.63)	$ (1.97)	$ (4.68)	$ (5.37)
Weighted average shares outstanding - basic and diluted	46,706,770	37,470,912	45,866,676	37,367,802

Sage Therapeutics, Inc. and Subsidiaries
Condensed Consolidated Balance Sheets

(in thousands)
(unaudited)

	September 30, 2018	December 31, 2017
Assets		
Current Assets:		
Cash and cash equivalents	$ 253,123	$ 306,235
Marketable securities	768,278	212,613
Prepaid expenses and other current assets	18,511	6,227
Total current assets	1,039,912	525,075
Property and equipment and other long-term assets	7,087	4,862
Total assets	$ 1,046,999	$ 529,937
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 5,879	$ 9,350
Accrued expenses	48,647	42,601
Total current liabilities	54,526	51,951
Other liabilities	3,968	2,511
Total liabilities	58,494	54,462
Total stockholders' equity	988,505	475,475
Total liabilities and stockholders' equity	$ 1,046,999	$ 529,937

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