May 9, 2017

Sage Therapeutics Announces First Quarter 2017 Financial Results and Provides Pipeline Update

Phase 3 STATUS Trial of brexanolone in SRSE nearing completion of enrollment - expects top-line results in Q3 2017

Advancing SAGE-217 into Part B open-label Phase 2 trial in Parkinson's disease based on initial activity signal

First patient dosed in placebo-controlled Phase 2 clinical trial of SAGE-217 in major depressive disorder

Conference call today at 4:30 PM ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- 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 first quarter ended March 31, 2017.

"We continue to make good progress in building Sage into a leading CNS company with the potential to deliver differentiated medicines for a variety of central nervous system disorders. We are focused on closing the innovation gap in areas of brain disorders where more breakthroughs for patients are needed," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "We are now nearing completion of enrollment in our lead Phase 3 program in super-refractory status epilepticus (SRSE), and remain focused on completing Phase 3 clinical development of brexanolone in both SRSE and postpartum depression (PPD) in 2017. Further, we continue to advance our growing pipeline of novel product candidates, including our lead oral compound, SAGE-217, in four clinical programs in both mood and movement disorders."

Brexanolone in SRSE - Phase 3 STATUS Trial Update

Sage is nearing completion of enrollment in the Phase 3 STATUS Trial, the first ever global, randomized, double-blind, placebo-controlled trial in SRSE. The Company expects to report top-line results from the STATUS Trial in the third quarter of 2017 after enrollment of an anticipated 126 evaluable patients and completion of all study follow-up periods and data analysis. Sage expects top-line results to include the primary endpoint, safety and tolerability, and select secondary endpoints, including open-label retreatment arm response and the Clinical Global Impression scale.

Top-Line Results from Part A of SAGE-217 Phase 2 in Parkinson's Disease

Sage today announced top-line results from the Part A open-label portion of a Phase 2 clinical trial of SAGE-217 in Parkinson's disease:

- SAGE-217 was studied in an exploratory open-label trial designed to understand the safety, tolerability, pharmacokinetics and activity of SAGE-217 in a cohort of 12 Parkinson's disease patients in order to determine whether there is a suitable activity signal to justify further development, and if so, to help develop the methodology needed to expedite progress into further Phase 2 testing.
- Twelve Parkinson's disease patients with moderate disease severity (Hoehn and Yahr stage 2 or 3) who were on stable doses of the anti-Parkinsonian agent levodopa/carbidopa prior to the study were evaluated. As an exploratory study, the Part A phase enrolled an all-comer population that was not enriched based on tremor severity or for any other particular Parkinson's disease symptom complex. Patients were withdrawn from maintenance therapy and administered their baseline medicine (levodopa/carbidopa morning dose only) for three days, followed by a single morning dose of SAGE-217 administered as a monotherapy for the subsequent four days.
- For the overall population in the trial, levodopa/carbidopa activity was primarily focused on the motor symptoms of bradykinesia and rigidity, while SAGE-217 activity as a monotherapy was primarily focused on tremor symptoms.
- In the five subjects with overt tremor (tremor score over five at baseline), an approximate 20-30% improvement in tremor symptoms was observed on the four days of SAGE-217 open-label treatment, as assessed by change in the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part III tremor score. This improvement in tremor score during the SAGE-217 dosing phase was longer-lasting than the effect on tremor observed in these subjects during the levodopa/carbidopa-only phase.

- Administration of SAGE-217 during the day was found to be generally well-tolerated with no serious adverse events or discontinuations reported. Similar to findings in the Phase 1 clinical program, the most common adverse events were sedation and somnolence (occurring 2 to 4 hours post dose). While dosing was initiated at the 30 mg per day maximum tolerated dose established in the Phase 1 program, the majority of patients were down-titrated to 10 to 20 mg of SAGE-217 per day.
- Based on the signal of activity in reducing Parkinsonian tremor in these patients, Sage plans to proceed to an open-label Part B study evaluating SAGE-217 as an adjunctive treatment to anti-Parkinsonian agents in tremor-predominant patients, and intends to further evaluate non-motor symptoms of Parkinson's disease, including depression, anxiety, cognition and sleep.

Pipeline Update

Sage is advancing a portfolio of novel central nervous system (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 is pursuing a data-driven approach to CNS drug development by employing efficient human proof-of-concept studies both to uncover activity signals and to help understand future trial methodology, before investing in larger clinical programs.

- **Brexanolone (SAGE-547):** Sage is currently developing brexanolone in separate Phase 3 clinical programs as an acute interventional treatment for super-refractory status epilepticus (SRSE) and postpartum depression (PPD). Brexanolone is Sage's proprietary intravenous (IV) formulation of allopregnanolone, a naturally occurring neuroactive steroid that acts as a synaptic and extrasynaptic modulator of the $GABA_A$ receptor.
  - **SRSE:** Sage is evaluating brexanolone in the Phase 3 STATUS Trial, a global, randomized, double-blind, placebo-controlled trial, designed to evaluate brexanolone as a potential adjunctive therapy for SRSE, a life-altering and persistent seizure condition with no treatments currently approved by the U.S. Food and Drug Administration (FDA). The Phase 3 clinical program is being conducted in agreement with the FDA under a Special Protocol Assessment (SPA). Sage has also received positive scientific advice from the European Medicines Agency (EMA) with respect to development of brexanolone for SRSE. Based on this advice, the Company believes the Phase 3 clinical program, if successful, will be sufficient to support submission of a marketing authorization application (MAA) to the EMA seeking approval of brexanolone for SRSE in the EU.

- **PPD:** Sage is currently enrolling its Phase 3 clinical program evaluating brexanolone as a potential treatment for PPD, consisting of separate placebo-controlled trials in severe PPD patients (202B) and in moderate PPD patients (202C), collectively known as the Hummingbird Study. In 2016, the FDA granted Breakthrough Therapy Designation and the EMA granted PRIority MEdicines (PRIME) designation to brexanolone for the treatment of PPD. Sage recently conducted its PRIME meeting with EMA authorities, and is now in process of seeking formal scientific advice. Sage expects to report top-line results from the Phase 3 clinical trials of brexanolone in PPD in the second half of 2017.

- **SAGE-217:** Sage's most advanced, next-generation product candidate is SAGE-217, a novel, orally-active neuroactive steroid that, like brexanolone, is a positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors. SAGE-217 is currently in Phase 2 development in both mood and movement disorders, with four Phase 2 clinical programs now underway.
  - **Mood Disorders:**
    - **Major Depressive Disorder (MDD):** Sage recently initiated dosing of patients in the Part B randomized, double-blind, placebo-controlled Phase 2 clinical trial of SAGE-217 in MDD. Earlier this year, Sage reported positive clinical results from the open-label Part A portion of the Phase 2 clinical program evaluating SAGE-217 in patients with moderate to severe MDD. The Part B study is expected to evaluate up to 66 patients with moderate to severe MDD for two weeks of treatment with SAGE-217 compared to placebo. Top-line results from the Part B study are expected in the first half of 2018.
    - **PPD:** Sage is currently enrolling a Phase 2 clinical trial of SAGE-217 in PPD. The Phase 2 multi-center, double-blind, placebo-controlled, randomized trial will evaluate the efficacy, safety, tolerability, and pharmacokinetics of SAGE-217 in the treatment of patients with severe PPD. Top-line results from the SAGE-217 PPD study are expected in the second half of 2017.
  - **Movement Disorders:**
    - **Essential tremor:** Sage is currently enrolling its Phase 2 clinical trial of SAGE-217 in essential tremor. The efficacy, safety, tolerability, and pharmacokinetics of SAGE-217 are being evaluated in a Phase 2 multi-center, double-blind, placebo-controlled, randomized withdrawal trial in the treatment of patients with essential tremor. Top-line results from the SAGE-217 essential tremor study are expected in the second half of 2017.
    - **Parkinson's disease:** Based on a positive activity signal observed in the Part A open-label portion of the Phase 2 program of SAGE-217 in Parkinson's disease, Sage is planning to initiate an open-label Part

B study to evaluate SAGE-217 as an adjunctive treatment in tremor-predominant Parkinson's disease patients. The Part B study is expected to be initiated in the first half of 2017 with top-line results anticipated in the second half of 2017.

- **Other GABA Programs:** Sage is currently evaluating a series of novel $GABA_A$ receptor modulators in pre-clinical development, including SAGE-324, a novel, orally-active next-generation positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors. SAGE-324 is currently in IND-enabling studies, and is intended to be developed with a focus on orphan epilepsies and indications involving GABA hypofunction.
- **NMDA Programs:** Sage is also developing novel compounds that target the NMDA receptor. The first product candidate selected for development from this program is SAGE-718, a novel, oral, first-in-class oxysterol-based positive allosteric modulator of the NMDA receptor. Sage recently initiated Phase 1 clinical development of SAGE-718, and expects top-line results from a Phase 1 single ascending dose (SAD) trial of SAGE-718 in healthy volunteers in the second half of 2017. Positive modulation of NMDA receptors may have potential in the treatment of a range of neurological disorders associated with a variety of cognitive, neurological and behavioral symptoms.

Expected Near-Term Clinical Milestones

- **Trial Initiations:**
  - Part B of Phase 2 trial of SAGE-217 in Parkinson's disease (1H 2017)
- **Top-Line Data Readouts:**
  - Phase 3 STATUS Trial of brexanolone in SRSE (Q3 2017)
  - Phase 3 Hummingbird Study (202B) of brexanolone in PPD (2H 2017)
  - Phase 3 Hummingbird Study (202C) of brexanolone in PPD (2H 2017)
  - Phase 2 trial of SAGE-217 in essential tremor (2H 2017)
  - Phase 2 trial of SAGE-217 in PPD (2H 2017)
  - Part B of Phase 2 trial of SAGE-217 in Parkinson's disease (2H 2017)
  - Phase 1 single-ascending dose (SAD) trial of SAGE-718 (2H 2017)
  - Part B of Phase 2 trial of SAGE-217 in MDD (1H 2018)

Financial Results for the First Quarter of 2017

- **Cash Position:** Cash, cash equivalents and marketable securities as of March 31, 2017 were $342.6 million, compared with $397.5 million at December 31, 2016.
- **R&D Expenses:** Research and development expenses were $45.2 million, including $3.6 million of non-cash stock-based compensation expense, in the first quarter of 2017, compared to $23.6 million, including $1.6 million of non-cash stock-based compensation expense, for the same period of 2016. The increase in R&D expenses year-over-year was primarily due to the ongoing clinical development of brexanolone in SRSE and PPD; the ongoing Phase 2 development of SAGE-217; completion of IND-enabling studies and preparation for Phase 1 development for SAGE-718; continuing discovery efforts to identify new development candidates; and investments in R&D headcount to support the growth in Sage's pipeline and operations.
- **G&A Expenses:** General and administrative expenses were $12.3 million, including $2.6 million of non-cash stock-based compensation expense, in the first quarter of 2017, compared to $7.1 million, including $2.1 million of non-cash stock-based compensation expense, for the same period of 2016. The increase in G&A expenses year-over-year was primarily due to the increase in personnel-related expenses, professional fees, costs related to continued preparations for a potential commercial launch, and facilities-related costs to support expanding operations.
- **Net Loss:** Net loss was $56.8 million for the first quarter of 2017, compared to a net loss of $30.5 million for the comparable period of 2016.
- **Financial Guidance:** Sage expects that its existing cash, cash equivalents and marketable securities will fund its anticipated level of operations, based on its current operating plans, into the second quarter of 2018.

Conference Call Information

Sage will host a conference call and webcast today at 4:30 PM ET to discuss its first quarter 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 12287678. 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 central nervous system (CNS) disorders. Sage has a portfolio of novel product candidates targeting critical CNS receptor systems, GABA and NMDA. Sage's lead program, brexanolone (SAGE-547), is in Phase 3 clinical development for super-refractory status epilepticus, a rare and severe seizure disorder, and for postpartum depression. Sage is developing its next generation modulators, including SAGE-217 and SAGE-718, in various CNS disorders. 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 development of our product candidates and their potential in the treatment of various CNS disorders; the expected timing of initiation and completion of clinical trials; the anticipated availability and announcement of data and results from clinical trials of our product candidates; our plans for evaluation of new indications and new compounds; our expectations regarding the regulatory pathway for brexanolone (SAGE-547) in the treatment of SRSE in the EU, and our belief that the results of the current development program for brexanolone in SRSE, if successful, will be sufficient for an MAA filing in the EU; our expectations regarding a potential future new drug application and MAA filing and commercial launch of brexanolone, if successfully developed and approved; and our expectations with respect to future cash use and 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: we may continue to experience slower than expected enrollment and randomization of evaluable patients in the STATUS trial or slower than expected clinical site initiation and enrollment in our other clinical trials, or the potential need for additional analysis or data or the need to enroll additional patients, leading to possible delays in completion of trials or in the availability of data; we may not be able to generate supportive non-clinical data or to successfully demonstrate the efficacy and safety of our product candidates at each stage of clinical development; success in our non-clinical studies or in earlier stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and ongoing and future pre-clinical and clinical results may not support further development of product candidates or be sufficient to gain regulatory approval to launch and commercialize any product; decisions or actions of regulatory agencies may affect the initiation, timing, progress and cost of clinical trials, and our ability to proceed with further clinical studies of a product candidate or to obtain marketing approval or may result in restrictions in an approved indication or the need for additional clinical trials, including the risk that the EMA may, despite scientific advice, decide that the data from our Phase 3 trial in SRSE are not sufficient to support approval; 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 and manufacture of our products which may delay our timing or increase our expenses and use of cash, as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K, 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 Balance Sheets
(in thousands)
(Unaudited)

	March 31, 2017	December 31, 2016
Assets		
Current Assets:		
Cash and cash equivalents	$ 145,460	$ 168,517
Marketable securities	197,104	228,962
Prepaid expenses and other current assets	6,480	5,100
Total current assets	349,044	402,579
Property and equipment and other long-term assets	2,124	1,952
Total assets	$ 351,168	$ 404,531

Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 8,230	$ 12,817
Accrued expenses	23,652	22,352
Total current liabilities	31,882	35,169
Other liabilities	840	845
Total liabilities	32,722	36,014
Total stockholders' equity	318,446	368,517
Total liabilities and stockholders' equity	$ 351,168	$ 404,531

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

	Three Months Ended March 31,	
	2017	**2016**
Operating expenses:		
Research and development	$ 45,200	$ 23,581
General and administrative	12,280	7,133
Total operating expenses	57,480	30,714
Loss from operations	(57,480)	(30,714)
Interest income, net	707	175
Other expense, net	(5)	(4)
Net loss	$ (56,778)	$ (30,543)
Net loss per share - basic and diluted	$ (1.52)	$ (0.97)
Weighted average shares outstanding - basic and diluted	37,269,148	31,643,216

View source version on businesswire.com: http://www.businesswire.com/news/home/20170509006196/en/

Investors:
Sage Therapeutics
Paul Cox, 617-299-8377
paul.cox@sagerx.com
or
Media:
Suda Communications LLC
Maureen L. Suda, 585-387-9248
maureen.suda@sagerx.com

Source: Sage Therapeutics, Inc.