December 6, 2016

Sage Announces Expedited Development Plan for SAGE-547 in the Treatment of Postpartum Depression based on FDA Breakthrough Therapy Meeting

Current SAGE-547 clinical program is designed to support potential NDA submission; no additional controlled studies anticipated

The current trials will be expanded to Phase 3 trials to facilitate potential for global registration

If successfully developed, SAGE-547 has the potential to be the first FDA-approved treatment for postpartum depression

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Sage Therapeutics (NASDAQ:SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-altering central nervous system (CNS) disorders, today announced its expedited development plan for SAGE-547 following receipt of formal meeting minutes from a breakthrough therapy meeting with the U.S. Food and Drug Administration (FDA). This program is intended to support a potential filing for approval in the treatment of postpartum depression (PPD).

The current SAGE-547 program in PPD, along with prior Phase 2 data, were confirmed as supporting, if successful, a potential New Drug Application (NDA). Sage's PPD clinical program, now in Phase 3, will require only minor modifications, including an increase in sample size. Agreement with the FDA was achieved on the clinical endpoints for these pivotal trials. Sage anticipates announcing top-line data from the PPD registration trials in 2H 2017. In July 2016, Sage reported encouraging top-line results from the 202A placebo-controlled trial in women with severe PPD, in which SAGE-547 achieved a significant, rapid and durable reduction (at Day 30) in depression scores compared with placebo.

"We are encouraged by the FDA's feedback and appreciate their guidance regarding our SAGE-547 development program in postpartum depression," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "Based on our meeting, we have clear and efficient direction for the expedited development path forward for SAGE-547 to potentially support a New Drug Application (NDA) in 2018."

As confirmed by the FDA, the following are the elements of the expected clinical and regulatory path moving forward:

- Agreement and clarity was achieved with the FDA on an expedited path forward
- Current SAGE-547 clinical studies confirmed as appropriate to support registration, if successful
- No additional efficacy studies expected to be required beyond those currently underway
- Trial design of studies 202B and 202C are considered appropriate for registration, with increase in size and other minor modifications
- The primary clinical endpoint for these pivotal trials was unchanged and agreed upon with FDA
- Additional patient safety data may be acquired through an open-label program

Sage received Breakthrough Therapy Designation from the FDA for SAGE-547 in PPD in September, 2016. The Breakthrough Therapy Designation is intended to offer a potentially expedited development path and review for promising drug candidates, which includes increased interaction and guidance from the FDA. Sage achieved this regulatory designation based primarily on the positive results from the placebo-controlled 202A study of SAGE-547 in 21 patients with severe PPD. The trial met the primary endpoint of significant reduction in the Hamilton Rating Scale for Depression (HAM-D) score in the SAGE-547-treated group compared with placebo at 60 hours, with an effect that was maintained at similar magnitude through the 30-day follow-up period. SAGE-547 was generally well tolerated in the study. There were no deaths, serious adverse events or discontinuations due to adverse events.

About FDA Breakthrough Therapy Designation

The FDA's Breakthrough Therapy Designation is intended to expedite the development and review of a drug candidate that is planned for use, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing

therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy Designation include the same benefits as Fast Track Designation, plus an organizational commitment involving FDA's senior managers with more intensive guidance from the FDA. Breakthrough Therapy Designation does not change the standards for approval.

About Postpartum Depression

Postpartum depression (PPD) is an affective disorder impacting women after childbirth. PPD may have devastating consequences for a woman and for her family, which may include significant functional impairment, depressed mood and/or loss of interest in her newborn, and associated symptoms of depression such as loss of appetite, difficulty sleeping, motor challenges, lack of concentration, loss of energy and poor self-esteem. Suicide is the leading cause of maternal death following childbirth. It is estimated that PPD affects 500,000 to 750,000 mothers in the US each year[1,2]. A subset of these are severe enough to require hospitalization. There are no approved therapies for PPD and there is a high unmet medical need for improved pharmacological therapy in PPD.

About SAGE-547

SAGE-547 is an allosteric modulator of both synaptic and extra-synaptic $GABA_A$ receptors. SAGE-547 has been granted Breakthrough Therapy Designation by the FDA for the treatment of postpartum depression (PPD). SAGE-547 is an intravenous agent evaluated in the PPD-202A trial, a multi-center, randomized, double-blind, parallel-group, placebo-controlled study evaluating the efficacy, safety and pharmacokinetics of SAGE-547 in the treatment of adult female patients with severe PPD. Following top-line results in July 2016, Sage initiated an expansion of the clinical program of SAGE-547 in PPD with two randomized, placebo-controlled Phase 3 clinical trials to explore dose-ranging of SAGE-547 in severe PPD patients and to evaluate SAGE-547 efficacy in moderate PPD patients. For more information about participating in these trials, please contact clinicaltrials@sagerx.com.

SAGE-547 is also being developed as an adjunctive therapy for the treatment of super-refractory status epilepticus (SRSE) in the global Phase 3 STATUS Trial. For more information about the STATUS Trial, please visit www.statustrial.com. SAGE-547 has been granted both Fast Track and orphan drug designations by the FDA for the treatment of SRSE.

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 compound, 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, with a focus on acute and chronic 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 statements as to the potential for expedited development and review for SAGE-547 in PPD; our expectations as to the timing of results from our pivotal clinical trials in PPD; the potential for a future regulatory filing for approval of SAGE-547 in PPD, and our expectations for the potential timing of such a filing; the potential for approval of SAGE-547 in PPD; our estimates as to the number of patients with PPD; and our statements regarding the potential of Sage's product candidates. 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 not achieve expedited development or review of SAGE-547 as a result of the breakthrough therapy designation; despite the results of the breakthrough therapy meeting, the FDA may ultimately decide that the design or results of our clinical trials are not sufficient for regulatory approval; decisions or actions of the FDA or other regulatory agencies may affect the timing, design, size, progress and cost of our clinical trials, and our ability to proceed with further clinical studies of SAGE-547 in PPD or to obtain marketing approval; we may encounter delays in enrollment and site initiation that may impact our ability to meet our expected time-lines; we may not be successful in our development of SAGE-547 in PPD or 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 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 market any product; we may encounter adverse events at any stage of development that negatively impact further development; the actual size of the PPD patient population may be significantly lower than our estimates and, even if SAGE-547 is approved for PPD, only a subset of the PPD population will be considered for treatment with a drug delivered through IV administration; and we may encounter technical and other unexpected hurdles in the development and manufacture of our products which may delay our timing or change our plans, 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.

[1] Hamilton BE, Martin JA, Osterman MJK, et al. Births: Final data for 2014. *National Vital Statistics Reports*. National Center for Health Statistics, 2015, 64, 12. Available at http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_12.pdf.

[2] O'Hara MW, McCabe JE. Postpartum depression: Current status and future directions. *The Annual Review of Clinical Psychology,* 2013, 9, 379-407. doi: 10.1146/annurev-clinpsy-050212-185612.

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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

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