September 27, 2016

Sage Reports Additional Positive Data on Secondary Endpoints from Phase 2 Clinical Trial of SAGE-547 in Severe Postpartum Depression at the Marcé Society for Perinatal Mental Health Biennial Scientific Meeting

Secondary endpoints showed significant difference in improvement from baseline for SAGE-547 compared to placebo over three weeks following end of treatment

Data are consistent with previously reported top-line results, including primary endpoint achieved with statistical significance at 60 hours and maintained through 30 days

Pursuing publication of comprehensive dataset in a peer-reviewed journal

Currently dosing patients with moderate or severe PPD in separate placebo-controlled trials; top-line data expected in 2017

Breakthrough Therapy Designation recently granted by FDA for treatment of postpartum depression; near-term meeting with FDA planned to discuss development pathway

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Sage Therapeutics (NASDAQ:SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-altering central nervous system disorders, today announced positive results on secondary endpoints from its Phase 2 clinical trial of SAGE-547 for the treatment of severe postpartum depression (PPD) at The Marcé Society for Perinatal Mental Health held September 26 - 28, 2016 in Melbourne, Australia. Secondary endpoints in the study, including the Edinburgh Perinatal Depression Scale (EPDS) and the Patient Health Questionnaire (PHQ-9) showed improvement through 30 days in the SAGE-547-treated group compared to the placebo group, demonstrating a strong durability of effect from SAGE-547 for over three weeks following the end of treatment. These data are consistent with previously reported top-line results showing SAGE-547 achieved the primary endpoint with a statistically significant reduction in the Hamilton Rating Scale for Depression (HAM-D) compared to placebo at 60 hours and maintained at similar magnitude through the 30-day follow-up. A similar statistically significant response was observed on other secondary endpoints including the Montgomery-Åsberg Depression Rating Scale (MADRS) and Remission from depression, as determined by a HAM-D of less than 7. The company is pursuing publication of a comprehensive dataset from the Phase 2 trial in severe PPD in a peer-reviewed journal. The U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy Designation to SAGE-547 for the treatment of postpartum depression (PPD). There are no approved therapies specifically for PPD.

Data from the EPDS showed a mean change from baseline at 30 days in the EPDS total score for the SAGE-547 group of -13.5 compared with a mean change from baseline of -5.3 in the placebo group, which was a statistically significant difference (p=0.024). The EPDS is a patient-rated depressive symptom severity scale specific to the perinatal period. Data from PHQ-9 showed that at day 30, six patients (60%) in the SAGE-547 group compared to one patient in the placebo group had a score of 0 to 4 indicating minimal or no depression (p=0.024). The PHQ-9 is a self-administered rating scale which is used to measure severity of symptoms and response to treatment. Items cover the core major depression symptoms.

The secondary endpoints were measured as part of a Phase 2, multi-center, placebo-controlled, double-blind, 1:1 randomization trial that was designed to enroll up to 32 women. The population studied were 21 women with severe PPD (HAM-D ≥26) who developed severe depression either in the third trimester or within four weeks of childbirth. At baseline, the mean HAM-D scores for both the SAGE-547-treated group and the placebo group were greater than 28. The primary objective of the trial was to evaluate the effect of SAGE-547 on depression as measured by the HAM-D score, compared to placebo, at 60 hours. In addition, patients were monitored during a 30-day follow-up period to assess both safety and efficacy. Top-line results from the trial were announced in July 2016. SAGE-547 was found to be generally well-tolerated with no serious adverse events reported during the treatment and follow-up periods. A greater number of adverse events were reported in the placebo arm than in the treatment arm of the trial (4 of 10 on SAGE-547 and 8 of 11 on placebo). Similar number of patients reported Nervous System Disorder Adverse Events: 3 of 10 on SAGE-547 and 4 of 11 on placebo. Equal number of patients reported the cluster of dizziness, sedation or somnolence: 3 in each group. Fewer SAGE-547 patients reported Psychiatric Disorder Adverse Events: 0 of 10 on SAGE-547 and 5 of 11 on placebo.

Based on the positive results from the Phase 2 clinical trial in severe PPD, Sage has expanded its development program evaluating SAGE-547 for PPD with the initiation of two additional multi-center, placebo-controlled trials, one of which is a

dose-ranging study of SAGE-547 in severe PPD patients and the other of which is studying the efficacy of SAGE-547 in moderate PPD patients. Top-line results from these two trials are expected in 2017.

"Postpartum depression represents a severely understudied and under-diagnosed class of patients. PPD is currently estimated to affect between 500,000 and 750,000 mothers in the U.S. each year. The unmet need for treatment in this vulnerable patient is significant. PPD carries an increased risk for suicide and it is one of the strongest predictors of suicidal ideation in new mothers," said Steve Kanes, M.D., Ph.D., Chief Medical Officer of Sage. "The results of the secondary endpoints in this Phase 2 study of SAGE-547, including the Edinburgh Perinatal Depression Scale and PHQ-9, support the primary endpoints achieved in the trial. Data from this clinical program show improvement in the SAGE-547 group compared with placebo and the secondary endpoints are suggestive of improvement through 30 days in the SAGE-547 treatment group. These collective findings have the potential to create a paradigm shift in how PPD is thought about and - if our program is successful - how PPD might be treated in the future."

The U.S. Food and Drug Administration (FDA) recently granted Breakthrough Therapy Designation to SAGE-547 for the treatment of PPD. Breakthrough Therapy Designation is intended to expedite the development and review of a drug candidate that is planned for use 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. In the near term, Sage plans to meet with the FDA to discuss the development pathway for SAGE-547 in PPD.

About the Marcé Society for Perinatal Mental Health

The principal aim of the Marcé Society is to promote, facilitate and communicate about research into all aspects of the mental health of women, their infants and partners around the time of childbirth. This involves a broad range of research activities ranging from basic science through to health services research.

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 GABAA 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 Phase 2 clinical program of SAGE-547 in PPD with two randomized, placebo-controlled Phase 2 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 program, SAGE-547, is in Phase 3 clinical development for super-refractory status epilepticus, a rare and severe seizure disorder, and is being developed for postpartum depression. Sage is developing its next generation modulators, including SAGE-217, SAGE-689 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 plans with respect to additional clinical trials of SAGE-547 in the treatment of PPD and the potential timing of data from these trials; our views as to the unmet need for additional treatment options in PPD and the estimated number of patients with PPD; our statements as to the potential for expedited development and review for SAGE-547 in PPD as a result of the breakthrough therapy designation; and our other 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; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, and progress of clinical trials, and our ability to proceed with further clinical studies of SAGE-547 in PPD or to obtain marketing approval; we may not be able to successfully demonstrate the efficacy and safety of our product candidates at each stage of development; success in early 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 clinical results may not support further development of a product candidate or be sufficient to gain regulatory approval to market any product; we may decide that a development pathway for one of our product candidates in one or more indications is no longer feasible or advisable; the number of patients with a particular disease or the unmet need for additional treatment options in a disease may be significantly smaller than we expect; and we may encounter technical and other unexpected hurdles in the development and manufacture 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, 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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