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SAGE Therapeutics Announces Positive Top-Line Data in Exploratory Trial of SAGE-547 in Postpartum Depression

Marked Improvement Demonstrated in HAM-D Scores in Patients with PPD Enrolled in Open-Label Trial

Plan to Initiate Placebo-Controlled Trial of SAGE-547 by Year End and Advance Novel Product Candidates for Potential Development

CAMBRIDGE, Mass., June 9, 2015 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE) today announced top-line data from an exploratory clinical trial that indicate a statistically significant improvement from baseline in depression in four women with postpartum depression (PPD) within 24 hours after administration of intravenous SAGE-547 (paired t-test p=0.001). During the SAGE-547 treatment period, all four patients rapidly achieved remission, as measured by the Hamilton Rating Scale for Depression (HAM-D). The patients had a mean HAM-D score of 26.5 at baseline and improved to a mean HAM-D score of 1.8 at the end of the 60-hour treatment period. All four patients also demonstrated consistent improvement as measured by the Clinical Global Impression-Improvement (CGI-I) scale. SAGE-547 was well-tolerated in all patients treated with no serious adverse events observed on therapy or during the 30-day follow-up period.

"Severe postpartum depression is a serious and debilitating form of major depressive disorder," said Samantha Meltzer-Brody, M.D., Director of the Perinatal Psychiatry Program, University of North Carolina Center for Women's Mood Disorders and Principal Investigator of the trial. "The signal of SAGE-547's activity is highly encouraging for women and their families facing the devastating consequences of this condition. I look forward to continuing to study this treatment approach in the placebo-controlled trial."

PPD is estimated to affect up to 20% of women following childbirth. The HAM-D scale is used by clinicians to rate the severity of 17 symptoms observed in depression, such as low mood, insomnia, agitation, anxiety and weight loss. A HAM-D rating of greater than 24.0 is considered severe and a score below 7.0 is considered symptom-free.

"These top-line results demonstrate an early but encouraging signal of activity in women with severe PPD and we believe further validate that the SAGE-547 mechanism of action has the potential to impact a broad range of disorders beyond epilepsy," said Jeff Jonas, M.D., chief executive officer of SAGE. "Given the severity of this disorder and the strength of the initial signal, we plan to move from the initial open-label exploratory trial into a placebo-controlled trial to validate the activity signal as rapidly as possible. In parallel, we plan to advance several novel product candidates from our extensive compound library into development that we believe may be uniquely suited for the treatment of this devastating disorder."

The exploratory open-label trial recruited women with PPD for treatment with a proprietary dosing schedule of SAGE-547 as an adjunctive therapy, a therapy combined with current therapeutic approaches. The trial was designed to provide data regarding safety, tolerability, pharmacokinetics and the acute effect of SAGE-547 on depressive symptoms as measured by the HAM-D and CGI-I. All of the patients enrolled had a Major Depressive Episode, as diagnosed by Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and were treated as inpatients. All four patients had an inadequate response to prior antidepressant therapy. The initial trial planned to enroll up to 15 patients or until 10 patients were deemed to be evaluable, whichever occurred first, aged 18 to 45 years, but after the consistent responses observed, the initial findings justified accelerating the program into a placebo-controlled trial.

SAGE-547 was well-tolerated with no serious adverse events reported during the treatment and follow-up periods and no discontinuations due to adverse events. A total of 14 adverse events were reported in four patients. The only adverse event reported in more than one patient was sedation, observed in two patients.

"I would like to thank these patients for participating in the trial and the nurses, physicians and staff at the Perinatal Psychiatry Inpatient Unit at UNC Neurosciences Hospital, along with our clinical team for the rapid completion of this first phase of clinical testing," added Stephen Kanes, M.D., Ph.D., chief medical officer of SAGE. "Given that PPD has been associated with abnormalities of allopregnanolone levels, we believe this disorder represents an opportunity to evaluate SAGE-547's mechanism of action in this patient population where there is a significant need for new treatment options."

About SAGE-547

SAGE-547 is an allosteric modulator of both synaptic and extra-synaptic $GABA_A$ receptors. $GABA_A$ receptors are widely regarded as validated drug targets for a variety of disorders, with decades of research and multiple approved drugs targeting these receptor systems. SAGE-547 is an intravenous agent entering Phase 3 clinical development as an adjunctive therapy, a therapy combined with current therapeutic approaches, for the treatment of super-refractory status epilepticus (SRSE), as well as in exploratory development for the treatment of essential tremor and postpartum depression. SAGE plans to begin enrollment of its planned Phase 3 clinical trial, called the STATUS Trial, in mid-2015. SAGE-547 has been granted both Fast Track and orphan drug designations by the U.S. Food and Drug Administration (FDA) for the treatment of SRSE. The active pharmaceutical ingredient for SAGE-547 has been contributed under agreement by the Regents of the University of California and the University of California, Davis.

About Postpartum Depression

Postpartum Depression (PPD) is distinct and readily identified form of depressive disorder estimated to affect up to 20% of women following childbirth[1,2]. PPD may have devastating consequences for a woman and for her family, which may include 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, poor self-esteem and suicidality. PPD is reported to be the most under-diagnosed obstetric complication in the U.S.[3] and there is a continued need for improved pharmacological therapy for PPD.

About SAGE Therapeutics

SAGE Therapeutics is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system, or CNS, disorders. SAGE's lead program, SAGE-547, is entering Phase 3 clinical development for super-refractory status epilepticus, or SRSE, and is the first of several compounds the Company is developing in its portfolio of potential anti-seizure medicines. SAGE's proprietary chemistry platform has generated multiple new compounds that target $GABA_A$ and NMDA receptors, which are broadly accepted as impacting many psychiatric and neurological disorders. For more information, please visit www.sagerx.com.

Forward-Looking Statements

Various statements in this release concerning SAGE's future expectations, plans and prospects, including without limitation, SAGE's expectations regarding SAGE-547 as a treatment for SRSE, essential tremor and severe postpartum depression, statements concerning the potential safety and efficacy of SAGE-547 and durability of response, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. In addition, it should be noted that there is limited data concerning the safety and efficacy of SAGE-547. These data may not be repeated or observed in ongoing or future studies involving SAGE-547 or SAGE's other product candidates. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, SAGE's ability to successfully demonstrate the efficacy and safety of its drug candidates, the pre-clinical and clinical results for its product candidates, which may not support further development of product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting intellectual property, SAGE's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, competition from others developing products for similar uses, SAGE's ability to manage operating expenses, SAGE's ability to obtain additional funding to support its business activities and establish and maintain strategic business alliances and new business initiatives, SAGE's dependence on third parties for development, manufacture, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in SAGE's annual report on Form 10-K for the fiscal year ended December 31, 2014 and quarterly report on Form 10-Q for the quarter ended March 31, 2015, as well as discussions of potential risks, uncertainties, and other important factors in SAGE's subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent SAGE's views only as of today and should not be relied upon as representing its views as of any subsequent date. SAGE explicitly disclaims any obligation to update any forward-looking statements.

[1] O'Hara MW, Wisner KL. Perinatal mental illness: definition, description and aetiology. *Best Pract Res Clin Obstet Gynaecol* 2014;28(1):3-12. doi: 10.1016/j.bpobgyn.2013.09.002

[2] Gavin NI, Gaynes BN. Perinatal Depression A Systematic Review of Prevalence and Incidence. *Obstetrics & Gynecology* 12/2005; 106(5 Pt 1):1071-83. doi: 10.1097/01.AOG.0000183597.31630.db

[3] Earls MF; Committee on Psychosocial Aspects of Child and Family Health American Academy of Pediatrics. Incorporating recognition and management of perinatal and postpartum depression into pediatric practice. *Pediatrics* 2010;126(5):1032-9. doi: 10.1542/peds.2010-2348

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