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SAGE Therapeutics Initiates Phase 2a Trial of SAGE-547 in Postpartum Depression

CAMBRIDGE, Mass., Jan. 12, 2015 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-threatening, rare central nervous system (CNS) disorders, today announced dose administration of the first patient in a Phase 2a clinical trial of SAGE-547, an allosteric modulator of $GABA_A$ receptors, in women with severe postpartum depression (PPD), a distinct and readily identified form of major depressive disorder estimated to affect 15 to 20 percent of women following childbirth. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and efficacy of SAGE-547 for the treatment of severe PPD.

"Postpartum depression is a serious medical condition that can have a devastating effect on the patient and her family. Therapeutic options for PPD are extremely limited, and there is a great need for new medicines to aid patients suffering with this disorder," said Steve Kanes, M.D., Ph.D., chief medical officer of SAGE Therapeutics. "This form of depression has been characterized by demonstrated abnormalities of allopregnanolone levels and has a stereotypical time of onset, allowing for the identification of a homogeneous patient population. Given preclinical data demonstrating that SAGE-547 impacts biological processes that are dysregulated in reproductive hormone-related mood disorders like PPD, we believe this represents an important opportunity to evaluate SAGE-547's mechanism of action in this indication."

This Phase 2a trial is an open-label study of SAGE-547 as an adjunctive therapy, or treatment given with current therapeutic approaches, in patients with severe PPD. This trial is expected to enroll at least 10 women with severe PPD who have experienced a major depressive episode within four weeks following delivery. This trial is designed to provide data regarding safety, tolerability and the acute effect of SAGE-547 on depressive symptoms as measured by the Hamilton Rating Scale for Depression (HAM-D) and Clinical Global Impression-Improvement Scale (CGI-I), respectively. Patients will be administered SAGE-547 intravenously for 48 hours and will be monitored for up to 30 days following treatment. The study is being conducted by 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 study.

"SAGE-547 is a potent and selective modulator of $GABA_A$, a receptor that plays a role in many CNS disorders but has been difficult to target effectively without considerable accompanying side effects," said Jeff Jonas, M.D., chief executive officer of SAGE Therapeutics. "Given the clinical data already available regarding the activity of SAGE-547, we believe this study will provide important insights into the potential for SAGE-547 and related compounds to impact the treatment of this disorder."

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 in Phase 1/2 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 Phase 2 clinical trials for the treatment of essential tremor and as an adjunctive therapy for the treatment of severe postpartum depression (PPD). In 2014, the U.S. Food and Drug Administration (FDA) granted both Fast Track and orphan drug designation to SAGE-547 for the treatment of SRSE.

About Postpartum Depression

Postpartum Depression (PPD) is a major depressive disorder that occurs in approximately 15 to 20 percent of women who have recently given birth, with up to 10 percent classified as suffering from severe PPD[1,2]. PPD may have devastating consequences for a woman and for her family, including 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 current therapeutic options for severe PPD are limited.

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 in 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 seizure medicines. The active pharmaceutical ingredient has been contributed under agreement by the Regents of the University of California and the University of California, Davis. 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 the potential safety, pharmacological effect and efficacy of SAGE-547 as a treatment for SRSE and PPD, the expected development pathway for SAGE-547 and its other product candidates and its expectations with respect to the timing and success of its clinical trials, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. 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 product 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 most recent quarterly report on Form 10-Q, 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] Edge D. Ethnicity, psychosocial risk, and perinatal depression - a comparative study among inner-city women in the United Kingdom. *J Psychosom Res* 2007;63(3):291-5. Epub 2007 Aug 1.

[2] 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

[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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