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## **Sage Therapeutics Announces The Lancet Publishes Positive Phase 2 Brexanolone (SAGE-547) Clinical Data in Severe Postpartum Depression**

- Study showed significant mean reduction in the 17-item Hamilton Rating Scale for Depression (HAM-D) total score compared to placebo -

- Seventy percent of subjects in the study experienced remission of symptoms within 60 hours of treatment with brexanolone and maintained effect until 30-day follow-up -

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 that *The Lancet* has published (online) results from a Phase 2, double-blind, randomized and placebo-controlled study of brexanolone (SAGE-547) in women with severe postpartum depression (PPD). The study found that treatment with brexanolone resulted in a clinically meaningful and statistically significant mean reduction in the 17-item Hamilton Rating Scale for Depression (HAM-D) total score, a common measure of depression severity, that began at 24 hours and was maintained at similar magnitude until the 30-day follow-up. Brexanolone was well-tolerated in this study with no observations of deaths, serious adverse events or discontinuations.

"There is a significant unmet need for new treatment options in PPD, for mothers suffering from the disorder, as well as their children and families. Currently available pharmacologic treatment options for PPD do not target the underlying mechanism or biology," said Samantha Meltzer-Brody, M.D., M.P.H., Associate Professor and Director of the UNC Perinatal Psychiatry Program of the UNC Center for Women's Mood Disorders and primary investigator of the study. "The rapid onset of action and duration of effect observed in this study compared to placebo suggest that brexanolone has the potential to address unmet needs in the treatment of patients suffering from PPD. If successfully developed and approved, this would be an enormous step forward for the field."

"Postpartum depression is a common, biological complication of childbirth. It is a serious mood disorder associated with a range of debilitating symptoms that impact a women's ability to function, and is a leading cause of maternal suicide," said Steve Kaner, M.D., Ph.D., Chief Medical Officer of Sage and lead author of the paper. "The publication of these data in *The Lancet* highlights the potential for brexanolone to be a treatment option for PPD. We are hopeful these findings will aid in the understanding of this disorder and the development of effective therapies."

The study's primary efficacy endpoint was the mean change from baseline in the 17-item HAM-D total score in subjects who received brexanolone compared with subjects who received placebo at the 60-hour time point. As previously reported, at the end of the 60-hour infusion, brexanolone-treated subjects demonstrated a mean reduction in HAM-D total score of 20.97 points, a 12.2-point difference [95 %CI, -3.67 to -20.77] from placebo ( $p=0.008$ ). The effect was statistically significant from 24 hours after initiation of treatment (-19.37 vs -8.12,  $p=0.006$ ) until the 30-day follow-up (-20.77 vs -8.84,  $p=0.010$ ). No deaths, serious adverse events or discontinuations were observed. Overall, fewer patients who received brexanolone experienced adverse events compared with placebo (4 of 10 on brexanolone and 8 of 11 on placebo). The most commonly reported adverse events in the trial were dizziness (2 brexanolone-treated subjects; 3 placebo-treated subjects) and somnolence (2 brexanolone-treated subjects; 0 placebo-treated subjects) and an equal number of patients reported the cluster of dizziness, sedation or somnolence (3 in brexanolone group and 3 in the placebo group).

### **PPD-202A Study Design and Additional Highlights**

The paper, titled "[Brexanolone \(SAGE-547 injection\) in post-partum depression: a randomized controlled trial.](#)" reports findings from a double-blind, randomized, placebo-controlled, Phase 2 registration study of brexanolone in 21 women with severe PPD (10 in the brexanolone group and 11 in the placebo group). At baseline, the mean HAM-D scores for both groups was greater than 28. Subjects were randomized 1:1 to receive either a single, continuous intravenous (IV) infusion of brexanolone or placebo for 60 hours.

Prespecified secondary endpoints of the study were assessed using validated and clinically relevant rating and diagnostic scales to evaluate severity of depression and to serve as a guide to evaluate recovery from baseline at 2 hours through 30 days. The outcomes were consistent with the primary endpoint results and included significant findings in measures assessed with the HAM-D, CGI (Clinical Global Impression Scale), and MADRS (Montgomery-Åsberg Depression Rating Scale) scales.

## **About Postpartum Depression**

Postpartum depression (PPD) is a distinct and readily identified major depressive disorder that is a biological complication of childbirth, affecting a subset of women typically commencing in the third trimester of pregnancy or within four weeks after giving birth. 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.<sup>1,2</sup> There are no approved therapies for PPD and there is a high unmet medical need for improved pharmacological therapy in PPD.

## **About the Hamilton Rating Scale for Depression (HAM-D)**

HAM-D is a validated rating scale used to provide an assessment of depression, and as a guide to evaluate recovery. This scale is an accepted regulatory endpoint for depression. The scale is used to rate the severity of a patient's depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation, anxiety, weight loss, and somatic symptoms.

## **About Brexanolone (SAGE-547)**

Brexanolone is an allosteric modulator of both synaptic and extrasynaptic GABA<sub>A</sub> receptors. Brexanolone has been granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) and Priority Medicines (PRIME) designation from the European Medicines Agency (EMA) for the treatment of postpartum depression (PPD). Brexanolone 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 brexanolone 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 brexanolone in PPD with two randomized, placebo-controlled Phase 3 clinical trials to explore dose-ranging of brexanolone in severe PPD patients (202B) and to evaluate brexanolone efficacy in moderate PPD patients (202C). For more information about these trials, please visit <https://thehummingbirdstudy.com/>.

Brexanolone 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](http://www.statustrial.com). Brexanolone 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, 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](http://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 the potential for brexanolone in the treatment of PPD; our view as to the unmet need for additional treatment options in PPD and how brexanolone might address the needs of PPD patients and families, if successfully developed and approved; our estimate as to the number of patients with PPD; and our plans and expectations with respect to development of brexanolone and our other 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 be able to successfully demonstrate the efficacy and safety of brexanolone or any of our other product candidates at each stage of development; success in early stage clinical trials may not be repeated or observed in ongoing or future studies of brexanolone; the efficacy data generated in ongoing or future clinical trials may be less robust or we may encounter unexpected safety or tolerability issues; ongoing or future clinical trials may not support further development of brexanolone or our other product candidates or be sufficient to gain regulatory approval to market any product; decisions or actions of regulatory agencies may affect the initiation, timing, progress, number, size and cost of clinical trials, and our ability to proceed with further clinical trials of a product candidate in a particular indication, or at all, or our ability to obtain marketing approval; we may decide that a development pathway for a product candidate in one or more indications is no longer feasible or advisable or that the unmet need no longer exists; the number of patients with PPD or the unmet need for additional treatment options 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.*

<sup>1</sup> 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](http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_12.pdf).

<sup>2</sup> 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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