Sage Therapeutics Advances SAGE-217 into Placebo-Controlled Phase 2 Clinical Trial in Major Depressive Disorder

Open-label Pilot Study of Once Daily, Orally Administered Molecule Demonstrates Positive Signal of Activity and Tolerability

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 encouraging top-line results from its Phase 2 clinical trial of orally-administered SAGE-217 for the treatment of major depressive disorder (MDD). The primary endpoint of the 13 patient Part A open-label trial was to evaluate safety and tolerability. SAGE-217 was found to be generally well-tolerated with no serious adverse events or discontinuations reported. The trial also examined the effect of SAGE-217 on the Hamilton Rating Scale for Depression (HAM-D) total score, in addition to other secondary measures. Patients in the trial had a mean HAM-D total score of 27.2 at baseline. Data demonstrated a mean reduction from baseline in the HAM-D of 19.9 points at Day 15, with 85% (11 of 13) patients showing at least a 50% reduction of their HAM-D and 62% (8 of 13) of patients achieving remission, as determined by a HAM-D ≤7. Statistically significant mean change from baseline was observed by Day 2 of the study, following the first of once-daily, nighttime oral dosing of 30 mg of SAGE-217. A significant mean change from baseline was maintained throughout the treatment period (p < 0.0001 at Day 15). The reduction from baseline in depression ratings seen in Part A of the trial met the company's criteria for advancing SAGE-217 into a planned double-blind, placebo-controlled study (Part B).

"Understanding the caveats associated with open-label data, we are highly encouraged by the strong signal we achieved in this study, which met our internal criteria for achieving a positive signal and thus supported our plan to proceed to the double-blind, placebo-controlled part of the Phase 2 trial," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "These initial results in MDD were achieved utilizing our data-driven approach to CNS drug development - employing efficient human proof-of-concept studies to both uncover activity signals and help understand future trial methodology, before investing in larger clinical programs."

“Our novel, orally-administered molecule, SAGE-217, was designed to reproduce the important GABA-related pharmacology of our intravenous agent SAGE-547, and is an example of our translational approach to drug development. The positive results from this clinical trial, along with the outcomes observed with SAGE-547 in postpartum depression, further validate studying this mechanism as a potential broad therapy for the treatment of mood disorders," said Steve Kanes, M.D., Ph.D., Chief Medical Officer of Sage. "SAGE-217 has the potential to be a rapid-acting, once-daily oral therapy for MDD, with a novel mechanism of action."

The major depressive disorder program is a two-part Phase 2 clinical trial evaluating the safety, tolerability, pharmacokinetics and efficacy of SAGE-217 in moderate to severe MDD patients. Part A of the Phase 2 trial was an open-label study evaluating SAGE-217 in 13 patients. The primary endpoint for the Part A study was to evaluate the safety and tolerability of SAGE-217. The secondary endpoint was to evaluate the effect of SAGE-217 compared to baseline following two weeks of once-daily treatment as measured by the HAM-D total score. The Part B phase of the trial will be a randomized, double-blind, parallel-group, placebo-controlled study evaluating SAGE-217 as a treatment for MDD. The design of this study will be finalized after analyses of the Part A data set are complete.

Summary of Top-Line Results from Part A of Phase 2 Study

Safety and Tolerability (Primary Endpoint):

- SAGE-217 was generally well tolerated in Part A of the study. There were no deaths, serious adverse events or discontinuations.
- The most common adverse events were sedation/somnolence, headache, dizziness, and myalgia.

Effect on Depressive Symptoms at Day 15:

- SAGE-217 reduced depressive symptoms as assessed by the HAM-D total score, with patients experiencing a 19.9 mean reduction in their HAM-D total score at Day 15, a decrease from a mean total score of 27.2 at baseline to 7.3 at Day 15.
At least a 50% reduction in HAM-D total score was demonstrated in 11 of 13 patients (85%).

Remission from depression, as determined by a HAM-D total score less than or equal to 7, was seen in 8 of 13 patients (62%).

About SAGE-217

SAGE-217 is a next generation positive allosteric modulator that has been optimized for selectivity to synaptic and extrasynaptic GABA receptors and a pharmacokinetic profile intended for daily oral dosing. The GABA system is the major inhibitory signaling pathway of the brain and CNS, and contributes significantly to regulating CNS function. In a Phase 1 clinical program, SAGE-217 was studied in single and multiple ascending doses and the results were consistent with the predicted pharmacokinetic and pharmacologic profile. SAGE-217 is currently being developed for certain mood and movement disorders.

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 the patient's depression by probing mood, feelings of guilt, suicide ideation, insomnia, agitation, anxiety, weight loss, and somatic symptoms.

About Major Depressive Disorder

Major depression disorder (MDD) is a common but serious mood disorder in which patients exhibit depressive symptoms, such as a depressed mood or a loss of interest or pleasure in daily activities consistently for at least a two-week period, and demonstrate impaired social, occupational, educational or other important functioning. Approximately 16 million people in the U.S. suffer from MDD each year. While antidepressants are widely used for treatment, large scale studies have demonstrated the need for additional therapies.

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 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 expectations regarding further development and the potential of SAGE-217 in the treatment of MDD; our plans to commence additional clinical trials, and the potential timing of such efforts; our view of the potential of the GABA mechanism and our product candidates in the treatment of CNS diseases and disorders; and our views as to the unmet need for additional treatment options in MDD and estimated number of patients with MDD. 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 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; decisions or actions of regulatory agencies may affect the initiation, timing, progress 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 one of our product candidates in one or more indications is no longer feasible or advisable or that the unmet need no longer exists; 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.


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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