Sage Therapeutics Inc Logo

Sage Therapeutics Announces the New England Journal of Medicine Publishes Data from Phase 2 Trial with SAGE-217 in Major Depressive Disorder

September 4, 2019

Results from pivotal trial showed treatment with SAGE-217 resulted in rapid, clinically meaningful improvement in major depressive disorder (MDD) symptoms across multiple measures and time points

SAGE-217 is currently being investigated in the Phase 3 MOUNTAIN trial for the treatment of MDD, with results expected in Q4 2019 or Q1 2020

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 4, 2019-- Sage Therapeutics (NASDAQ: SAGE), a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating brain disorders, today announcedthat the *New England Journal of Medicine (NEJM)* published full results from the double-blind, randomized, placebo-controlled Phase 2 study evaluating SAGE-217 as a treatment for major depressive disorder (MDD). In the study, SAGE-217, taken orally, once daily, showed a rapid, statistically significant reduction in Hamilton Rating Scale for Depression (HAM-D) total scores versus placebo beginning the morning following the first dose (Day 2) and sustained through the primary endpoint of Day 15 (-7.1 difference, $p<0.001$). At Day 15, 64% of patients who received SAGE-217 achieved remission, defined as a score of 7 or less on the HAM-D scale, compared with 26% of patients who received placebo. Additionally, at Day 15 the HAM-D response rates were 78.6% versus 40.5% in the SAGE-217 and placebo groups, respectively.

Results published in *NEJM* also include additional data from multiple secondary endpoints, all of which generally favored SAGE-217 at the end of treatment (Day 15). In the study, SAGE-217 was generally well tolerated with a safety profile consistent with that seen in earlier SAGE-217 trials. Overall reports of treatment emergent adverse events (TEAEs) were 53.3% in the SAGE-217 group and 45.5% in the placebo group. No serious adverse events or deaths occurred during the trial.

“The findings published in the *New England Journal of Medicine* suggest the potential for SAGE-217 to be developed as a novel treatment option for people living with major depressive disorder,” said Anthony J. Rothschild, M.D., Irving S. and Betty Brudnick Endowed Chair of Psychiatry, professor of psychiatry and psychiatry department vice chair for research at the University of Massachusetts Medical School and an author on the manuscript. “Current treatments can take many weeks to work yet patients often experience side effects almost immediately. The significant and rapid improvements in depression and anxiety symptoms observed with SAGE-217 in this trial, combined with the response, remission and safety data, are extremely encouraging for a clinical disorder that can have such debilitating effects on people’s lives.”

Major depressive disorder causes a persistent feeling of sadness and loss of interest in daily activities, often affecting how a person feels, thinks and behaves, and can lead to a variety of emotional and physical problems. It affects more than 17 million American adults, or about 6.8% of the U.S. population age 18 and older in a given year, and is one of the most common, but serious, mood disorders impacting people of all ages, races, and socioeconomic status.

“Our ongoing research into the treatment and management of depression, and other mood disorders, is driven by an ultimate goal of transforming the lives of people suffering from these conditions,” said Steve Kanes, M.D., Ph.D., chief medical officer of Sage Therapeutics. “The Phase 2 results suggest SAGE-217, if successfully developed, may offer a rapid-acting, well-tolerated, and durable therapy, which could change the way depression is treated. The ongoing clinical program for SAGE-217 in major depressive disorder and postpartum depression is intended to generate key efficacy and safety information needed to support a submission for regulatory approval and to further inform use if the drug is approved.”

About the placebo-controlled pivotal Phase 2 trial of SAGE-217 in MDD
In the randomized, double-blind, parallel-group, placebo-controlled trial, 89 eligible patients (with a minimum total score of 22 on the Hamilton Rating Scale for Depression at baseline) were randomized in a 1:1 ratio to receive SAGE-217 capsules (30 mg) (n=45) or matching placebo (n=44). All doses of study drug were administered at night with food. The study consisted of a 14-day treatment period and a 4-week follow-up period. The mean HAM-D total scores at baseline were 25.2 for the SAGE-217 group and 25.7 for the placebo group (overall range 22-33), representing patients with moderate to severe MDD. Approximately 90% of patients in each group completed the study. The most common treatment emergent adverse events (≥5%) in the SAGE-217 group included headache (17.8%), nausea (11.1%), dizziness (11.1%), and somnolence (6.7%).

About Major Depressive Disorder
Major depressive disorder (MDD) is a common but serious mood disorder in which people experience depressive symptoms that impair their social, occupational, educational or other important functioning, such as a depressed mood or loss of interest or pleasure in daily activities, consistently for at least a two-week period. It is estimated that approximately 17 million people in the U.S. suffer from MDD each year. While antidepressants are widely used to treat MDD, large-scale studies have demonstrated the need for additional therapies.

About SAGE-217
SAGE-217 is a next generation positive allosteric modulator that has been optimized for selectivity to synaptic and extrasynaptic $GABA_A$ receptors and has a pharmacokinetic profile intended for periods of daily oral dosing. The GABA system is the major inhibitory signaling pathway of the brain and central nervous system (CNS), and contributes significantly to regulating CNS function. SAGE-217 is currently being developed for major depressive disorder, postpartum depression, and certain other mood disorders.

About Sage Therapeutics
Sage Therapeutics is a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain. We are pursuing new pathways with the goal of improving brain health and our depression, neurology and neuropsychiatry franchise programs aim to change how brain disorders are thought about and treated. Our mission is to make medicines that matter so people can get better, sooner. 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 views, statements and expectations regarding: the potential timing for reporting results from the MOUNTAIN study; the goals of our development program for SAGE-217, and the potential to generate data sufficient to file for regulatory approval; the potential of SAGE-217 as a future treatment option in the treatment of MDD and PPD, and the potential to change treatment paradigms and benefit patients, if SAGE-217 is successfully developed and approved; our estimates as to the number of people in the U.S. who suffer from MDD; and the goals and vision for our programs and potential of our business. These statements constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. 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 successful in our development of SAGE-217 or any of our other current or future product candidates in any indication we are currently pursuing or may in the future pursue; success in earlier clinical trials or nonclinical studies may not be repeated or observed in ongoing or future studies; ongoing and future clinical or nonclinical results may generate negative results or results that are otherwise different than we expect which may cause a delay or curtailment of future development efforts or may not support further development or be sufficient to file for or gain regulatory approval; we may decide

that a development pathway in one or more indications is no longer feasible or advisable or that the unmet need no longer exists; the FDA may decide that a development program, even if positive, is not sufficient for a new drug application filing or approval; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress and cost of clinical trials and our ability to proceed with further development; we may experience slower than expected initiation or enrollment in ongoing or future clinical trials or issues with sites or data collection or generation; we may encounter unexpected safety or tolerability issues; the number of people suffering from MDD or the unmet need for additional treatment options may be significantly smaller than we expect and our results may not be sufficient to meet the unmet need or to change treatment paradigms, even if we are successful in our development efforts; the internal and external costs required for our ongoing and planned activities, and to build our organization in connection with such activities, and the resulting use of cash, may be higher than expected which may cause us to change or curtail some of our plans; and we may encounter technical and other unexpected hurdles in our development efforts; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent quarterly report filed with the Securities and Exchange Commission (SEC), and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. 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.

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Source: Sage Therapeutics

Investor Contact:
Matt Calistri, 617-914-2635
matthew.calistri@sagerx.com

Media Contact:
Jeff Boyle, 617-949-4256
jeff.boyle@sagerx.com