Sage Therapeutics Receives FDA Breakthrough Therapy Designation for SAGE-217 for the Treatment of Major Depressive Disorder

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– Designation offers potential for expedited development and review, and highlights the urgent need for additional treatment options for patients suffering from depression –

– Sage has received two Breakthrough Therapy designations for separate psychiatric drug candidates, reinforcing the Company's distinct approach to developing therapeutics to treat serious brain disorders –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 7, 2018-- 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 U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation to SAGE-217 for the treatment of major depressive disorder (MDD). This is the second Breakthrough Therapy designation granted to Sage since 2016.

The Breakthrough Therapy designation is intended to offer a potentially expedited development path and review for promising drug candidates, which includes increased interaction and guidance from the FDA. This regulatory decision was based primarily on the recent positive results from the Phase 2, placebo-controlled trial of SAGE-217 in 89 adult patients with moderate to severe MDD. In the trial, SAGE-217 met the primary endpoint with a statistically significant mean reduction in the Hamilton Rating Scale for Depression (HAM-D) 17-item total score from baseline at Day 15 in the SAGE-217 group, compared to placebo ($p<0.0001$). Statistically significant improvements were observed in the HAM-D score compared to placebo by the morning following the first dose through Week 4 and the effects of SAGE-217 remained numerically greater than placebo through the end of follow-up at Week 6. SAGE-217 was generally well-tolerated. The most common adverse events in the SAGE-217 group were headache, dizziness, nausea, and somnolence.

Detailed results of the Phase 2, placebo-controlled trial will be presented at an upcoming medical meeting.

About FDA Breakthrough Therapy Designation

The FDA's Breakthrough Therapy designation is intended to expedite the development and review of a drug candidate that is planned for use, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy designation include the same benefits as Fast Track designation, plus an organizational commitment involving the FDA's senior managers with more intensive guidance from the FDA. Breakthrough Therapy designation does not change the standards for approval.

About Major Depressive Disorder

Major depressive 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. It is estimated that 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 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 in clinical research to rate the severity of a patient's depression by probing mood, feelings of guilt, suicidal ideation, insomnia, agitation, anxiety, weight loss, and somatic symptoms.

About SAGE-217

SAGE-217 is a next generation positive allosteric modulator that targets synaptic and extrasynaptic GABA receptors and has 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. SAGE-217 is currently being developed in the treatment of MDD and certain other affective disorders, Parkinson's disease and sleep disorders.

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, a proprietary IV formulation of brexanolone (SAGE-547), has completed two Phase 3 clinical trials in 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.

Forward-Looking Statements

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation: our statements as to the potential for expedited development and review for SAGE-217 in MDD as a result of the Breakthrough Therapy designation; our statements regarding the potential for SAGE-217 and Sage's other product candidates, and our development plans; our views as to the unmet need for additional treatment options in MDD and the potential of SAGE-217 to meet the unmet need, and our estimates as to the 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 achieve expedited development or review of SAGE-217 as a result of the Breakthrough Therapy designation; we may not be able to successfully demonstrate the efficacy and safety of SAGE-217 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 SAGE-217 or any of our other product candidates; ongoing and future clinical results may not support further development or be sufficient to gain regulatory approval to market SAGE-217 or any of our other product candidates; we may decide that a development pathway for one of our product candidates in one or more indications is no longer feasible or advisable; the unmet need for new products in an indication may change while we are developing our product candidates; 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 encounter unexpected safety or tolerability issues with SAGE-217 or any of our other product candidates in ongoing or future development; the actual size of the MDD patient population may be significantly lower than our estimates and, even if SAGE-217 is successfully developed and approved for MDD, it may only be approved or used to treat a subset of the MDD population; and we may encounter technical and other unexpected hurdles in the development and manufacture of SAGE-217 or any of our other 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, and 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.

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