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Sage Therapeutics Announces Initiation of Phase 2 Clinical Development for SAGE-217 in Movement Disorders

First patient dosed in Phase 2 proof-of-concept trial of SAGE-217 in Parkinson's disease

Trial sites are open and screening patients for the Phase 2a trial in essential tremor; patients expected to be dosed imminently

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 the initiation of Phase 2 clinical development of SAGE-217, a novel, internally-developed, next generation oral $GABA_A$ receptor modulator that Sage is developing in both mood and movement disorders. Dosing has now been initiated in the first of two movement disorder indications. Patients are receiving SAGE-217 in a Phase 2 proof-of-concept trial in Parkinson's disease. In addition, trial sites are open and screening patients for a Phase 2a trial in essential tremor. Patients in this trial are expected to be dosed imminently. Top-line results from the Part A open-label study in Parkinson's disease are expected in the first half of 2017 and the essential tremor study is anticipated to report results in the second half of 2017. The Company also plans to initiate Phase 2 clinical trials of SAGE-217 in two mood disorders - major depressive disorder (MDD) and postpartum depression (PPD).

"Sage continues to pioneer innovative approaches to neuroscience drug development in CNS indications with high unmet need where we can redefine treatment paradigms," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "The SAGE-217 clinical program is an excellent example of this approach. The initiation of mid-stage trials of our novel, proprietary oral compound is a significant corporate milestone and a credit to our talented team of translational chemists, and clinical and regulatory leaders."

"Administering the first dose of SAGE-217 in a proof-of-concept study in Parkinson's disease and the initiation of SAGE-217 in essential tremor illustrate major progress in Sage's effort to address the serious need for additional effective treatments for these movement disorders and in building our multi-product, neuropsych portfolio," said Steve Kanes, M.D., Ph.D., Chief Medical Officer of Sage. "SAGE-217 is one of several product candidates that Sage is developing to target the $GABA_A$ receptor system. Dysfunction in this system is thought to be at the core of numerous psychiatric and neurological disorders including essential tremor and both the motor and non-motor symptoms in Parkinson's disease."

The essential tremor study is a Phase 2a double-blind, placebo-controlled, randomized withdrawal study that will evaluate the efficacy, safety, tolerability and pharmacokinetics of SAGE-217 in approximately 60 patients with essential tremor. The primary endpoint of the study is to compare the effect of one week of SAGE-217 on overall kinetic tremor symptoms. Secondary endpoints include additional accelerometer-derived and clinician-rated rating scales.

The Parkinson's disease program is a two-part Phase 2 clinical trial evaluating the safety, tolerability, pharmacokinetics and efficacy of SAGE-217 in moderate Parkinson's disease patients. Part A of the Phase 2 trial will be an open-label, proof-of-concept study evaluating SAGE-217 in approximately 18 patients which, if promising, may lead to a randomized, placebo-controlled Phase 2 trial. The primary endpoint for the Part A study will be to evaluate the safety and tolerability of SAGE-217. The secondary endpoint will be to evaluate improvement in motor symptoms as assessed by the change from baseline after one week in the Movement Disorder Society - Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Part 3 (Motor Examination) total score.

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 well-tolerated 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. A Phase 2 clinical trial in Parkinson's disease is ongoing and initiation of dosing in the essential tremor study is pending. Phase 2 clinical trials in postpartum depression and major depressive disorder are planned.

About Essential Tremor

Essential tremor is a common neurological condition that affects an estimated 6 to 7 million in the U.S.[1] Essential tremor causes a rhythmic trembling of the hands, head, voice, legs or trunk. Symptoms generally evolve over time and are both visible and persistent following onset, which commonly occurs either between 15-20 or 50-70 years of age. First-line treatments for essential tremor include the anticonvulsant primidone and the β-adrenergic blocker propranolol. Current treatments for essential tremor are only moderately effective, reducing, though not resolving, tremor amplitudes in about 50% of patients. In addition, one out of three patients abandons treatment due to side effects or poor efficacy.

About Parkinson's Disease

Parkinson's disease is a progressive neurodegenerative disorder that affects an estimated 700,000 patients in the U.S.[2] and causes impairment of motor function, including impaired movement, muscle stiffness and tremors as well as non-motor symptoms including anxiety, depression, sleep difficulties and gastrointestinal disorders. Symptoms generally become more pronounced over time, and the average age of Parkinson's diagnosis is 60 years of age. First-line treatments for Parkinson's disease include combination levodopa/carbidopa therapy. Current treatments for Parkinson's disease are only moderately effective in reducing symptoms in the early stages of the disease, and patients become less responsive to treatment as the disease progresses. Thus, there is a growing need for innovative new treatments to prevent, delay onset or alleviate symptoms of Parkinson's disease.

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 development of SAGE-217 and our other product candidates and their potential in the treatment of various CNS disorders; the expected initiation and timing of clinical trials and anticipated availability and announcement of data and results; our estimates as to the number of patients with essential tremor and Parkinson's disease and our belief as to unmet need in these populations. 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 experience slower than expected clinical site initiation or enrollment in our clinical trials, or the potential need for additional analysis or data or the need to enroll additional patients, leading to possible delays in completion of trials or in the availability of data; we may not be able to generate supportive non-clinical data or to successfully demonstrate the efficacy and safety of our product candidates at each stage of development; success in our non-clinical studies or in earlier 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 pre-clinical and clinical results may not support further development of 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 and cost of clinical trials, and our ability to proceed with further clinical studies of a product candidate or to obtain marketing approval; we may encounter adverse events at any stage of development that negatively impact further development; the actual size of the essential tremor and Parkinson's disease patient populations may be significantly lower than our estimates; 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; and we may encounter technical and other unexpected hurdles in the development and manufacture of our products which may delay our timing or increase our expenses and use of cash, 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.

[1] Louis ED, Ottman R. How many people in the USA have essential tremor? Deriving a population estimate based on epidemiological data. *Tremor Other Hyperkinet Mov.* 2014; 4. doi: 10.7916/D8TT4P4B

[2] Willis et al, Neuroepidemiology. 2010;34:143-151

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