October 23, 2014

SAGE Therapeutics Initiates Exploratory Study of SAGE-547 in Essential Tremor

Study to Further Evaluate SAGE-547 Mechanism of Action

CAMBRIDGE, Mass., Oct. 23, 2014 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE) today announced dose initiation of the first patient in a single-center Phase 2a clinical trial of SAGE-547, an allosteric modulator of $GABA_A$ receptors, in patients with essential tremor. This trial is designed to evaluate the safety, tolerability, pharmacokinetics and activity of SAGE-547 in patients with essential tremor, a neurological disorder that causes involuntary, rhythmic shaking with no known cause. The trial is being conducted under a newly accepted Investigational New Drug filing.

"SAGE-547 is a molecule with an attractive, acute therapeutic profile well-suited for exploring the impact of its mechanism on many GABA-related disorders, including essential tremor," said Jeffrey Jonas, M.D., chief executive officer of SAGE Therapeutics. "There is clinical and preclinical evidence that GABA receptor dysfunction in the brain may be a factor in essential tremor. We plan to use data from this exploratory study, if positive, to help model and guide the design of a second-generation molecule for the chronic treatment of this debilitating disease."

This Phase 2a trial is a double blind, proof-of-concept study of SAGE-547 in patients who have a diagnosis of essential tremor with symptoms clearly present in at least one upper limb. The trial is expected to enroll 24 adult patients with essential tremor for at least 2 years, a score of ≥ 2 for at least one upper limb maneuver as measured by The Essential Tremor Rating Scale (TETRAS) performance subscale, and who are not currently taking medication for their tremor or are on a stable dose of medication for at least 28 days prior to enrollment. This trial is designed to provide clear data regarding the safety and tolerability of SAGE-547 using ratings and mechanical measures of motor activity designed to rapidly yield unambiguous endpoints. The activity of SAGE-547 will be assessed via physician examination, transducer measurement of tremor amplitude and full TETRAS and TETRAS performance subscale measurements. Patients will be administered either SAGE-547 or placebo intravenously for 12 hours on Day 1 and Day 10 in a double blind cross-over manner. Patients will be monitored for up to 30 days following treatment.

"Current treatments for essential tremor are only moderately effective, as most reduce but do not resolve tremor levels in the majority of treated patients," said Stephen Kanes, M.D., Ph.D., chief medical officer of SAGE Therapeutics. "There remains a dire need for new therapies for these patients with persistent, visible tremor that significantly impacts their daily life."

About SAGE-547

SAGE-547 is an allosteric modulator of both synaptic and extra-synaptic $GABA_A$ receptors. $GABA_A$ receptors are widely regarded as validated drug targets for a variety of CNS disorders, with decades of research and multiple approved drugs targeting these receptor systems. SAGE-547 is an intravenous agent in Phase 1/2 clinical development as an adjunctive therapy, a therapy combined with current therapeutic approaches, for the treatment of super-refractory status epilepticus (SRSE), as a treatment for essential tremor.

About Essential Tremor

Essential tremor (ET) is a common neurological condition that affects an estimated 10 million Americans and millions more worldwide. ET 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. All current treatments for ET are only moderately effective, reducing, though not resolving, tremor amplitudes in about 50% of the patients. In addition, one out of three patients abandons treatment due to side effects or poor efficacy.

About SAGE Therapeutics

SAGE Therapeutics is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare CNS disorders. SAGE's lead program, SAGE-547, is in clinical development for super-refractory status epilepticus (SRSE) and is the first of several compounds the company is developing in its portfolio of potential seizure medicines. SAGE's proprietary chemistry platform has generated multiple new compounds that target $GABA_A$ and NMDA receptors, which are broadly accepted as impacting many psychiatric and neurological disorders. For more information, please

visit www.sagerx.com.

Forward-Looking Statements

This release contains forward-looking statements and information. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward looking statements. For example SAGE's future expectations, plans and prospects, including without limitation, SAGE's expectations regarding the potential safety, pharmacological effect and efficacy of SAGE-547 as a treatment for SRSE and essential tremor, the expected development pathway for its other product candidates and its expectations with respect to the timing and success of its clinical trials, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995 and other federal securities laws. In particular it should be noted that the initial data reported from the ongoing Phase 1/2 clinical trial of SAGE-547 for SRSE are preliminary in nature and that this SAGE-547 clinical trial has not been completed. The preliminary data may change as additional data is released and such preliminary data may not be repeated or observed in ongoing or future studies involving SAGE-547 or our other product candidates. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including, without limitation, SAGE's ability to successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not support further development of product candidates, actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials, obtaining, maintaining and protecting intellectual property, SAGE's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties, competition from others developing products for similar uses, SAGE's ability to manage operating expenses, SAGE's ability to obtain additional funding to support its business activities and establish and maintain strategic business alliances and new business initiatives, SAGE's dependence on third parties for development, manufacture, marketing, sales and distribution of products, the outcome of litigation, and unexpected expenditures, as well as those risks more fully discussed in the section entitled "Risk Factors" in the final prospectus related to SAGE's initial public offering filed with the Securities and Exchange Commission pursuant to Rule 424(b) of the Securities Act of 1933, as amended, as well as discussions of potential risks, uncertainties, and other important factors in SAGE's subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent SAGE's views only as of today and should not be relied upon as representing its views as of any subsequent date. SAGE explicitly disclaims any obligation to update any forward-looking statements.

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Source: SAGE Therapeutics