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SAGE Therapeutics Announces Positive End-of-Phase 2 Meeting With FDA and Planned Initiation of SAGE-547 Global Phase 3 Trial in Mid-2015

Final SAGE-547 Phase 1/2 Clinical Data to be Presented at Annual Antiepileptic Drug and Device Trials Conference

CAMBRIDGE, Mass., April 2, 2015 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-threatening, rare central nervous system (CNS) disorders, today announced details of its planned SAGE-547 global Phase 3 development program for the treatment of patients with super-refractory status epilepticus (SRSE). SRSE is a rare and life-threatening seizure disorder for which there are no approved therapies. At a recent End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA), there was general agreement on the design and key elements of a Phase 3 clinical program for SAGE-547. SAGE believes the results from the planned Phase 3 clinical trial, together with other clinical data obtained from the SAGE-547 development program, could form the basis of a New Drug Application (NDA) submission for SAGE-547.

"We are very pleased with the outcome of the End-of-Phase 2 meeting, and we look forward to initiating our Phase 3 clinical trial for SAGE-547 as potentially the first approved treatment for patients with SRSE," said Jeff Jonas, M.D., chief executive officer of SAGE. "Our Phase 3 program will be an important milestone for SAGE and, we hope, for patients suffering from SRSE. Our team has made rapid progress in advancing SAGE-547 in this indication and in furthering our $GABA_A$ modulation platform. This progress brings us one step closer to our goal of developing a family of molecules offering potential new treatment options for other forms of epilepsy and CNS disorders."

"There is a pressing need for new drugs to treat patients with SRSE, a devastating seizure disorder for which current treatment options are severely limited," said Andrew J. Cole, M.D., F.R.C.P.(C.), director of the Massachusetts General Hospital Epilepsy Service and professor of neurology at Harvard Medical School. "The combined safety and clinical activity data from SAGE's Phase 1/2 clinical trial and emergency-use cases suggest that SAGE-547 has the potential to improve the therapeutic approach for patients with SRSE."

The Phase 3 clinical trial is planned as a randomized, double-blind, placebo-controlled Phase 3 trial designed to assess the efficacy and safety of SAGE-547 in approximately 126 patients with SRSE, aged two years or older, at up to 150 sites in the U.S. and Europe. Patients will be randomized 1:1 to receive either SAGE-547 or placebo in addition to standard-of-care third-line anti-seizure agents for a total of six days. Based on data from the ongoing Phase 1/2 clinical trial, the planned Phase 3 clinical trial is designed to provide 90 percent statistical power. SAGE plans to begin enrollment of the Phase 3 clinical trial mid-year, following submission and review by the FDA of the final clinical trial protocol and updated chemistry, manufacturing and controls information.

The planned primary endpoint of the Phase 3 clinical trial will be successful resolution of status epilepticus (SE) after weaning the patient off all third-line anti-seizure agents, and SAGE-547 or placebo, without resumption of SE within 24 hours after completion of blinded SAGE-547 or placebo administration. Secondary endpoints are expected to explore the rate of recovery, regaining of consciousness, mental status and functional outcome. Patients who fail to respond to initial blinded treatment (SAGE-547 or placebo) may be eligible to be treated with an open-label, higher dose regimen of SAGE-547.

"Our planned Phase 3 randomized clinical trial of SAGE-547 is a pioneering and first-of-its-kind trial for SRSE. It marks an important step in developing new treatment options for patients affected with SRSE," said Steve Kanes, M.D., Ph.D., chief medical officer of SAGE. "Our clinical and operations teams have executed aggressively to advance SAGE-547 through to late-stage development. Building off SAGE-547's safety and clinical activity observed to date, we believe we have designed a highly efficient Phase 3 development program that, if successful, positions us to bring a first-in-class targeted treatment for patients with SRSE."

In conjunction with its planned Phase 3 clinical trial, SAGE also plans to initiate an open-label, expanded access protocol designed to offer SAGE-547 to patients affected with SRSE with limited treatment options. Dose regimen, trial procedures and assessment of patient outcomes in the expanded access protocol will be consistent with the planned Phase 3 clinical trial.

SAGE-547 has been investigated for its safety and activity in two groups of patients with SRSE to date. Data reported in January 2015 from the ongoing Phase 1/2 open-label clinical trial in patients with SRSE showed that 71 percent of 17 evaluable

patients met the key efficacy endpoints of being successfully weaned off their anesthetic agents while SAGE-547 was being administered and being weaned off SAGE-547 without recurrence of SRSE. These clinical trial data are consistent with the level of activity observed in emergency-use cases, in which an overall response rate of 78 percent in nine cases has been observed. Independent of treatment response, five patient deaths occurred within the trial period, all driven by underlying conditions. Although 13 patients (65 percent) reported serious adverse events, none were considered drug-related.

The Phase 1/2 clinical trial is continuing to enroll patients in an expansion cohort under a protocol amendment, allowing treatment of pediatric patients as young as two years old and investigating a higher dose regimen of SAGE-547. SAGE anticipates reporting clinical data from the Phase 1/2 open-label clinical trial of SAGE-547 at the Antiepileptic Drug and Device Trials XIII Conference, which is taking place May 13-15.

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 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 well as in exploratory Phase 2a clinical trials for the treatment of essential tremor and as an adjunctive therapy for the treatment of severe postpartum depression. In 2014, the U.S. Food and Drug Administration (FDA) granted both Fast Track and orphan drug designation to SAGE-547 for the treatment of SRSE. The active pharmaceutical ingredient, treatment IND and support for emergency-use patients have been contributed under agreement by the Regents of the University of California and the University of California Davis.

About Status Epilepticus

Status epilepticus (SE) is a life-threatening seizure condition that occurs in approximately 150,000 people each year in the U.S., of which 30,000 SE patients die.[i] We estimate that there are 35,000 patients with SE in the U.S. that are hospitalized in the intensive care unit (ICU) each year. An SE patient is first treated with benzodiazepines, and if no response, is then treated with other, second-line, anti-seizure drugs. If the seizure persists after the second-line therapy, the patient is diagnosed as having refractory SE (RSE), admitted to the ICU and placed into a medically induced coma.

Currently, there are no therapies that have been specifically approved for RSE; however, physicians typically use anesthetic agents to induce the coma and stop the seizure immediately. After a period of 24 hours, an attempt is made to wean the patient from the anesthetic agents to evaluate whether or not the seizure condition has resolved. Unfortunately, not all patients respond to weaning attempts, in which case the patient must be maintained in the medically induced coma. At this point, the patient is diagnosed as having SRSE. Currently, there are no therapies specifically approved for SRSE.

About SAGE Therapeutics

SAGE Therapeutics is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system (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 anti-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

Various statements in this release concerning SAGE's future expectations, plans and prospects, including without limitation, SAGE's expectations regarding SAGE-547 as a treatment for SRSE, essential tremor and postpartum depression, statements concerning the potential safety and efficacy of SAGE-547 and durability of response, the final protocol design, statistical power and timing of a planned Phase 3 clinical trial and an open-label, expanded access protocol for SAGE-547, and whether the results from the planned Phase 3 clinical trial together with other available clinical data for SAGE-547 will be sufficient to support submission of an NDA for this product candidate, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. In particular, it should be noted that FDA typically requires at least two well-controlled studies be completed prior to submission of an NDA. Whether a single Phase 3 trial of SAGE-547 will be sufficient to support submission of an NDA is typically a review issue to be discussed with FDA following completion of the trial. In addition, it should be noted that the data reported above for SAGE-547 are preliminary in nature. The Phase 1/2 clinical trial has not been completed and the emergency use cases are not part of that clinical trial. There is limited data concerning the safety and efficacy of SAGE-547. These data may not be repeated or observed in ongoing or future studies involving SAGE-547 or SAGE's 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 drug 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 SAGE's annual report on Form 10-K for the fiscal year ended December 31, 2014, 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.

[i] DeLorenzo, Robert J., Pellock, John M., Towne, Alan R., Boggs, Jane G. Epidemiology of Status Epilepticus. *J Clin Neuro* 1995; 12(4): 316-325.

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