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SAGE Therapeutics Reports Positive Top-Line Phase 2 Data of SAGE-547 in Patients With Super-Refractory Status Epilepticus

SAGE-547 Met Primary and Secondary Efficacy and Safety Endpoint Targets

Overall Response Rate of 73 Percent Reported with No Drug-Related SAEs

CAMBRIDGE, Mass., Nov. 10, 2014 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE) today announced that in a Phase 1/2 clinical trial of SAGE-547, an allosteric modulator of both synaptic and extra-synaptic $GABA_A$ receptors, all primary and secondary endpoint targets were achieved in patients with super-refractory status epilepticus (SRSE), a critical condition in which the brain is in a state of persistent seizure. In 73 percent of patients, treatment with SAGE-547 allowed for patients to be successfully weaned off their anesthetic agent.

"We believe SAGE-547 has the potential to dramatically improve the therapeutic approach for patients with SRSE, and the efficacy and safety results from this trial support our continued development of SAGE-547 as a treatment for this disorder," said Jeff Jonas, M.D., chief executive officer of SAGE. "We look forward to working with the U.S. Food and Drug Administration (FDA) on the appropriate design of a pivotal trial, which we anticipate initiating in the first half of 2015 pending our discussions with the FDA. We believe SAGE-547 has the potential to be the first therapy intended specifically for the treatment of SRSE, and that is very exciting for patients and clinicians managing this life-threatening disease."

Top-line data reported from 12 patients, eight males and four females with a mean age of 54, enrolled in the study show that all 12 patients met the primary endpoint, safety and tolerability. Of the 11 patients evaluable for efficacy, eight patients met the key efficacy endpoint of being successfully weaned off their anesthetic agents while SAGE-547 was being administered, and eight patients were successfully weaned off SAGE-547 without recurrence of SRSE. The mean duration of status epilepticus prior to treatment with SAGE-547 was 11 days. With an overall response rate of 73 percent, SAGE-547 was generally well tolerated and no drug-related serious adverse events, as determined by the Safety Review Committee, were reported in treated patients. Mean exposure levels of SAGE-547 were approximately 200nm.

The Phase 1/2 open-label trial of SAGE-547 as an adjunctive therapy was designed to provide clear data around safety, exposure and the ability of SAGE-547 to effectively halt SRSE. The trial enrolled adult patients with SRSE who have not responded to conventional therapy with continuous intravenous antiepileptic agents and who remain in a state of persistent seizure following one or more weaning attempts from general anesthesia. In the trial, patients are administered SAGE-547 intravenously for five days while weaning from anesthesia is attempted and are monitored for four weeks following treatment with SAGE-547.

Trial Will Continue Enrollment Under Protocol Amendment

The FDA recently approved a protocol amendment for the Phase 1/2 trial submitted by SAGE that will enable the company to treat pediatric patients as young as two years old and to increase the dose of SAGE-547 being administered to patients. SAGE is continuing to enroll patients as an expansion cohort in this trial, and this enrollment will proceed in parallel with SAGE's regulatory initiatives.

"We are pleased that we were able to complete this portion of our development plan ahead of our projected timelines and would like to thank all of our investigators, patients and their families involved in this trial," commented Steve Kanes, M.D., Ph.D., chief medical officer of SAGE. "We are also pleased that the approved protocol amendment to our Phase 1/2 trial will enable us to explore the potential of SAGE-547 in a broader population, particularly in very young children affected with this disorder that have no other treatment options."

Updated SAGE-547 Emergency-Use Results

In addition to the top-line Phase 1/2 trial results, SAGE reported that seven patients, four males and three females with a mean age of 12.5, have been treated with SAGE-547 by independent centers under emergency-use Investigational New Drug (IND) Applications. Five of these patients treated with SAGE-547 achieved resolution of SRSE either during the course of or soon after SAGE-547 treatment. The overall response rate was 71 percent, similar to the observed response rate in the Phase 1/2 clinical trial.

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 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 SRSE, as well as in an exploratory Phase 2 clinical trial for the treatment of essential tremor. 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.

About Status Epilepticus (SE)

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.[1] 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 (Nasdaq:SAGE) is a clinical-stage biopharmaceutical company committed to developing and commercializing novel medicines to treat life-threatening, rare central nervous system, or CNS disorders. SAGE's lead program, SAGE-547, is in clinical development for super-refractory status epilepticus, or 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

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 and essential tremor, the expected development pathway for its other drug candidates and its expectations with respect to the timing and success of its clinical trials, in particular a new clinical trial for SAGE-547 as a treatment for SRSE and whether such trial will be deemed by FDA to be a pivotal trial, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. 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 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, 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.

[1] 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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