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SAGE Therapeutics Reports Updated Data From Ongoing Clinical Trial and Emergency Use Program of SAGE-547 in Patients With Super-Refractory Status Epilepticus

Greater Than 70 Percent Response Rate Observed in Two Patient Groups

Data Reinforce Clinical Activity and Safety Profile Demonstrated by SAGE-547

Phase 3 Pivotal Trial Expected to Begin by Mid-2015

CAMBRIDGE, Mass., Jan. 9, 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 reported updated data from the ongoing Phase 1/2 clinical trial and emergency use program of SAGE-547 in patients with super-refractory status epilepticus (SRSE). SRSE is a critical condition in which the brain is in a state of persistent seizure, where patients are placed in a medically induced coma in an attempt to stabilize them and where conventional and approved therapies fail to awaken the patients. The clinical data encompass a total of 20 enrolled patients and include 30-day follow-up from the 12 previously enrolled patients, as well as preliminary data on eight additional patients. SAGE is also reporting results from nine of ten emergency use cases.

Consistent with topline data announced in November, the primary endpoint, safety and tolerability, was achieved in all patients. Of the 20 patients enrolled in the ongoing Phase 1/2 clinical trial, 17 patients were evaluable for efficacy. Seventy-one percent of evaluable patients met the key efficacy endpoint of being successfully weaned off their anesthetic agents while SAGE-547 was being administered. In addition, 71 percent of evaluable patients were successfully weaned off SAGE-547 without recurrence of SRSE. As a group, patients who responded to SAGE-547 generally demonstrated rapid improvement over the first five days following treatment. Patients who responded also continued to improve over the 30-day follow-up period as assessed by several measures. Consistent with the level of activity observed in the ongoing Phase 1/2 clinical trial, a response rate of 78 percent was observed in emergency-use cases.

As of December 11, 2014, the Phase 1/2 clinical trial of SAGE-547 had enrolled 20 patients - 12 males and eight females with a mean age of 51. In the ongoing trial, patients are administered SAGE-547 intravenously for five days while weaning from anesthesia. Patients are then monitored for 30 days from treatment initiation. The mean duration of status epilepticus prior to treatment with SAGE-547 was 11 days.

"SAGE-547 has continued to show the potential for significant benefit for patients facing SRSE, a devastating and life-threatening disorder, which supports our continued development of SAGE-547 for the treatment of this disorder," said Jeff Jonas, M.D., chief executive officer of SAGE. "In the past year, we've achieved many important milestones in the development of SAGE-547. We believe these data, combined with the emergency use data, support the initiation of a pivotal study and look forward to discussing this with the FDA."

At baseline, all patients were measured by the Clinical Global Impression of Severity (CGI-S) scale, which tracks patient progress and treatment response over time, as well as the Glasgow Coma Scale, which helps gauge the severity of an acute brain injury. At baseline, 19 patients were classified as "most extremely ill" as measured by CGI-S, the remaining patient was described as "severely ill." By day 30, the group of patients who responded to SAGE-547 had improved to "mildly ill," which represents a three-step improvement in the severity of their illness. In contrast, the group of patients who did not respond to SAGE-547 did not improve beyond "severely ill" throughout the study period. As measured by the Glasgow Coma Scale, the group of patients who responded to SAGE-547 showed rapid improvement in the first five days following treatment and continued improvement throughout the complete study period.

The underlying etiology was explored in the 20 patients enrolled. SRSE was attributed to brain hemorrhage in four patients, infections in four patients, worsening of seizures in two patients, primary or metastatic brain tumors in two patients and to unknown causes in three patients. SRSE was caused by each of the following in one case: stroke, sickle cell anemia, Lupus, PRES and toxic ingestion.

Independent of treatment response, five patient deaths occurred within the study period, all driven by underlying conditions. Although 13 patients (65 percent) reported serious adverse events, none were considered drug-related. Mean exposure levels of SAGE-547 were approximately 200 nM.

"The SAGE-547 clinical program may give hope to families searching for a treatment. With the support of many researchers, health care professionals, patients and families, we have made remarkable progress in the development of SAGE-547 as a potential treatment for patients suffering from SRSE," said Steve Kanes, M.D., Ph.D., chief medical officer of SAGE. "Data from the Phase 1/2 trial continue to show promise for further development of SAGE-547, and we look forward to advancing this medicine for patients in need."

Updated SAGE-547 Emergency Use Results

In addition to the updated Phase 1/2 trial results, SAGE reported that ten patients, six males and four females with a mean age of 17, have been treated with SAGE-547 by independent centers under emergency use Investigational New Drug (IND) applications. Seven of nine evaluable patients treated with SAGE-547 achieved resolution of SRSE either during the course of or soon after SAGE-547 treatment, resulting in an overall response rate of 78 percent, similar to the observed response rate in the Phase 1/2 clinical trial. The outcome of the tenth patient is pending.

About the Phase 1/2 Clinical Trial

The Phase 1/2 open-label trial of SAGE-547 as an adjunctive therapy was designed to provide data around safety, exposure and ability of SAGE-547 to effectively halt SRSE. The trial, under protocol amendment, is enrolling patients aged two and older 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.

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 SE.

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 (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. The active pharmaceutical ingredient has been contributed under agreement by the Regents of the University of California and the University of California, Davis. 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, statements concerning the potential safety and efficacy of SAGE-547 and durability of response, the timing of discussions with FDA and the outcome of any such discussions, the expected development pathway for SAGE-547 or 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. In particular, 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 most recent quarterly report on Form 10-Q, 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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