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First Evaluation of SAGE-547 to Treat Super-Refractory Status Epilepticus in Children Published in Annals of Neurology

Use of SAGE-547 Resolved Status Epilepticus With No Serious Adverse Events

CAMBRIDGE, Mass., Nov. 3, 2014 (GLOBE NEWSWIRE) -- SAGE Therapeutics (Nasdaq:SAGE) today announced that SAGE-547, an allosteric modulator of $GABA_A$ receptors, was used to treat super-refractory status epilepticus (SRSE) in two pediatric patients. The research, published online in the *Annals of Neurology*, is the first report of SAGE-547 treatment in children. Following treatment with SAGE-547, resolution of status epilepticus (SE) was demonstrated in both patients after weaning from general anesthetic infusions with no drug-related serious adverse effects. Both patients were treated with SAGE-547 under emergency-use Investigational New Drug Applications.

"Refractory status epilepticus is a medical emergency with high risk for poor outcome. In both of these cases, the patient had been put in a medically induced coma to control seizures, and there were multiple unsuccessful attempts to wean the patient from anesthetic agents prior to treatment," said Mark Wainwright, M.D., Ph.D, director of the pediatric neurocritical care program at Northwestern University Feinberg School of Medicine and senior author of the study. "There are no truly effective treatments for refractory status epilepticus - it is incredibly exciting to work with a new therapy that may help both pediatric and adult patients affected by this disorder."

The first patient, who was treated at Ann & Robert H. Lurie Children's Hospital of Chicago, was an otherwise healthy 11-year-old girl who presented with SE caused by an autoimmune disorder with antithyroid and anti-glutamic acid decarboxylase antibodies. She received an infusion of SAGE-547 over five days, after which pentobarbital sedation was weaned and discontinued. Over the remainder of the hospitalization she had intermittent, controllable seizures. She was transferred for inpatient rehabilitation, regained her ability to walk, and is now back at home, continuing to show cognitive improvement, reading, doing arithmetic and playing the piano.

The second patient, a two-year-old girl, presented with SE associated with a febrile illness. SAGE-547 was infused over four days and tapered off between 96 and 120 hours. SE resolved after SAGE-547 treatment and 12 days following the completion of treatment with SAGE-547 all anti-seizure therapies were discontinued. She was transferred to inpatient rehabilitation and is now able to walk and speak. In both patients, there were no drug-related serious adverse effects detected by any of the laboratory tests used.

"Mortality in refractory status epilepticus can be as high as 35 percent, and previously, pediatric patients have not participated in studies to test the effectiveness of SAGE-547," said Stephen Kanes, M.D., Ph.D., chief medical officer of SAGE and co-author of the study. "Our ongoing Phase1/2 clinical trial has yielded promising results in adult patients with super-refractory status epilepticus, and we are excited about the possibility of delivering this treatment to children, as well."

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

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 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

This release contains forward-looking statements and information, including statements concerning SAGE's expectations regarding the potential safety, pharmacological effect and efficacy of SAGE-547, the expected development pathway for SAGE-547 and other product candidates and its expectations with respect to the timing and success of its clinical trials concerning its product candidates, and the applicability of the results from emergency-use cases to the population at large. These and other statements concerning SAGE's future expectations, plans and prospects 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 are preliminary in nature and that the 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 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 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 discussions of potential risks, uncertainties, and other important factors in SAGE's most recent quarterly report on Form 10-Q filed with the Securities and Exchange Commission, as well any 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.

CONTACT: Media Contact:

Dan Budwick, Pure Communications

dan@purecommunicationsinc.com

973-271-6085

Investor Contact:

Monique Allaire, Pure Communications

monique@purecommunicationsinc.com

781-631-0759

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