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Sage Therapeutics Announces Initiation of Phase 1 Development and First Dosing of SAGE-718

Lead compound from novel NMDA modulator product development platform

Top-line results from single ascending dose trial expected in 2H 2017

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Sage Therapeutics (NASDAQ:SAGE), a clinical-stage biopharmaceutical company developing novel medicines to treat life-altering central nervous system (CNS) disorders, today announced it has initiated a Phase 1 single ascending dose (SAD) trial of SAGE-718 in healthy volunteers. Top-line results from the SAD study are expected in the second half of 2017.

"Advancing SAGE-718 into Phase 1 clinical development represents a significant achievement in broadening our clinical pipeline beyond GABA, with a new product development platform focused on a novel mechanism to modulate the NMDA receptor system," said Jeff Jonas, M.D., Chief Executive Officer of Sage. "Loss of NMDA function may have significant impact in many neuropsych disorders, and SAGE-718 and our novel follow-on compounds have the potential to further extend our pipeline into a broad array of CNS indications."

SAGE-718 is a novel, oral, first-in-class oxysterol-based positive allosteric modulator (PAM) of the N-methyl-D-aspartate (NMDA) receptor, acting in a similar manner as 24(S)-hydroxycholesterol (cerebrosterol), an endogenous modulator of NMDA receptor function. Positive modulation of NMDA receptors may have potential in the treatment of a range of neurological disorders associated with a variety of cognitive, neurological and behavioral symptoms.

SAGE-718 may also have potential in the treatment of CNS disorders associated with a high prevalence of anti-NMDA antibodies or reduced levels of plasma cerebrosterol. In preclinical studies, SAGE-718 improved social behavior in an animal model of NMDA hypofunction, and ameliorated both behavioral and electrophysiological deficits in a model of compromised cholesterol regulation. The effects of NMDA PAMs on cerebrosterol deficit preclinical models were presented at the 2016 annual meetings of the Society of Biological Psychiatry and the Society for Neuroscience.

"SAGE-718 is our lead NMDA PAM candidate, and was selected from over 800 novel compounds in our NMDA modulator library. SAGE-718 is designed for once-daily dosing, good oral bioavailability, and high selectivity for the NMDA receptors," said Albert Robichaud, Ph.D., Chief Scientific Officer of Sage. "The NMDA receptor system plays a critical role in brain network balance and plasticity. Sage has discovered a novel platform and approach to modulating NMDA receptors by enhancing receptor response without the direct activation which may contribute to the limitations of prior NMDA-targeted compounds."

The Phase 1 single ascending dose study of SAGE-718 is a double-blind, placebo-controlled trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamic effects of SAGE-718 administered orally in healthy adult volunteers.

About SAGE-718 and NMDA Receptors

SAGE-718 is a novel, oral, first-in-class, oxysterol-based positive allosteric modulator (PAM) of N-methyl-D-aspartate (NMDA) receptors. SAGE-718 is the lead compound from Sage's NMDA modulator platform.

NMDA receptors are glutamate-gated cation channels that play a critical role in the health and regulation of neurons, and are involved in learning, memory and neuroplasticity. Positive modulation of NMDA receptors may have potential in the treatment of conditions associated with NMDA hypofunction and disorders associated with a high prevalence of anti-NMDA antibodies, such as anti-NMDA receptor encephalitis, as well as in disorders associated with reductions in plasma cerebrosterol, such as Huntington's disease and Alzheimer's disease.

About Sage Therapeutics

Sage Therapeutics is a clinical-stage biopharmaceutical company committed to developing novel medicines to transform the lives of patients with life-altering central nervous system (CNS) disorders. Sage has a portfolio of novel product candidates targeting critical CNS receptor systems, GABA and NMDA. Sage's lead program, brexanolone (SAGE-547), is in Phase 3

clinical development for super-refractory status epilepticus, a rare and severe seizure disorder, and for postpartum depression. Sage is developing its next generation modulators, including SAGE-217 and SAGE-718, in various CNS 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, our expectations regarding development of SAGE-718 and the potential of SAGE-718 and positive modulation of NMDA receptors in the treatment of various CNS disorders; the expected timing of availability of data from the Phase 1 study of SAGE-718; and the potential for our other product candidates, constitute forward-looking statements for the purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those contemplated in these forward-looking statements, including the risks that: we may encounter unexpected adverse events in healthy volunteers that causes us to discontinue further development of SAGE-718; we may not be able to successfully demonstrate the safety and efficacy of SAGE-718, or any of our other product candidates, at each stage of development; success in pre-clinical studies or in early stage clinical trials may not be repeated or observed in ongoing or future studies involving the same compound or other product candidates, and ongoing or future pre-clinical and clinical results may not support further development of product candidates or a class of product candidates or be sufficient to gain regulatory approval to market any product; decisions or actions of regulatory agencies may negatively affect the initiation, timing and progress of clinical trials, and our ability to proceed with further clinical studies of a product candidate or to obtain marketing approval; we may not be able to obtain or maintain adequate intellectual property protection and other forms of marketing and data exclusivity for our product candidates; and we may encounter technical and other unexpected hurdles in the manufacture and development of our products, as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent annual report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We explicitly disclaim any obligation to update any forward-looking statements.

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