Sage Therapeutics Announces Presentation of Encouraging Results from the Phase 2 PARADIGM Study (Part A) of SAGE-718 in Patients with Mild Cognitive Impairment due to Parkinson's Disease

March 15, 2022

Data Presented at the AD/PD 2022 Advances in Science & Therapy International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders

The PARADIGM Study is a Phase 2, open-label study evaluating the safety, tolerability, and efficacy of SAGE-718 once daily in individuals with mild cognitive impairment due to Parkinson's disease

Patients who received SAGE-718 in the study experienced improvement in performance of cognitive tests of executive functioning and learning and memory

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 15, 2022-- Sage Therapeutics, Inc. (Nasdaq: SAGE), a biopharmaceutical company leading the way to create a world with better brain health, announced today the presentation of data that showed SAGE-718, a first-in-class, oral, positive allosteric modulator of the NMDA receptor, was associated with improvements on multiple tests of executive functioning and learning and memory in patients with mild cognitive impairment (MCI) due to Parkinson's disease (PD) in the open label Phase 2 PARADIGM Study. The PARADIGM Study (Part A) is part of CogNEXT, Sage's early-stage trial platform designed to evaluate the therapeutic potential of SAGE-718 to treat cognitive deficits across a range of brain health disorders. The data were presented as a virtual oral presentation at the AD/PD 2022 Advances in Science & Therapy International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders taking place from March 15-20 both in-person in Barcelona, Spain, and virtually.

"Improving cognitive function is an area of significant unmet need in the management of Parkinson's disease as it is estimated that up to 50 percent of people living with PD are affected by cognitive changes, including mild cognitive impairment, that can result in loss of independence for patients," said Jim Doherty, Ph.D., Chief Development Officer at Sage. "We are encouraged by these preliminary data as they support our belief in the potential of SAGE-718 for the treatment of MCI in patients with PD, and we look forward to learning more from our multiple, ongoing or planned placebo-controlled clinical trials in patients with PD and other brain health disorders."

In the PARADIGM Study (Part A), a comprehensive battery of tests was used to assess multiple domains of cognitive performance in eleven patients receiving SAGE-718 3 mg once daily. Tests included the Digital Symbol Substitution Test, spatial working memory, stockings of Cambridge, the 2-Back Test and the Multitasking Test. SAGE-718 was associated with improved performance at Day 14, compared to baseline, on tests of executive functioning, and an emerging signal suggests improved performance on tests of learning and memory (paired associates, pattern recognition, and verbal memory). Sustained effects and improving trends were seen out to Day 28 for assessments completed at the follow-up visit. As expected, no appreciable effect was observed on measures of simple attention/psychomotor speed, in keeping with the profile of SAGE-718 based on data to date. These data support the further development of SAGE-718 in PD-MCI, suggesting improved performance on executive functioning, as well as promising signals on learning and memory.

SAGE-718 was generally well tolerated in the PARADIGM Study (Part A); there were no serious adverse events and no treatment emergent adverse events were determined to be related to SAGE-718.

About the PARADIGM Study (Part A)

The PARADIGM Study (Part A) was a Phase 2, open-label study with a primary objective to evaluate the safety, tolerability, and efficacy of SAGE-718 in patients with MCI due to PD. During the 2-week screening period, patients were assessed for the prespecified inclusion and exclusion criteria. Eligible patients were aged 50 to 75 years, had a diagnosis of idiopathic PD and MCI per the 2015 Movement Disorder Society criteria, and Montreal Cognitive Assessment or MoCA of 20-25 at screening. After the 1-week baseline period, eligible patients entered a 2-week treatment period during which they received a 3 mg oral dose of SAGE-718 once daily. The final period was a 2-week, off-treatment follow-up period. A 4-week dosing cohort, PARADIGM Part B, is ongoing.

About SAGE-718

SAGE-718, Sage's first-in-class NMDA receptor PAM and lead neuropsychiatric drug candidate, is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, potentially including Huntington's disease (HD), Parkinson's disease (PD) and Alzheimer's disease (AD). Ongoing and planned studies aim to evaluate whether SAGE-718 may have the potential to improve cognitive symptoms for these difficult-to-treat disorders. SAGE-718 is currently being studied in the ongoing Phase 2 DIMENSION Study, a double-blind placebo-controlled study in people with early to moderate HD cognitive impairment that is designed to evaluate the efficacy of once-daily dosed SAGE-718 over three months. Sage expects to initiate additional Phase 2 studies evaluating SAGE-718 in HD, PD and AD in 2022. In 2021, SAGE-718 received Fast Track Designation from the FDA for development of SAGE-718 as a potential treatment for HD.

About Sage Therapeutics

Sage Therapeutics is a biopharmaceutical company fearlessly leading the way to create a world with better brain health. Our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. For more information, please visit www.sagerx.com.

Forward-Looking Statements

Various statements in this release concern future expectations, plans and prospects, including without limitation statements regarding: Sage's belief in the potential profile and benefit of SAGE-718 and the potential impact of the findings from the PARADIGM Study; our goals and plans for further development of SAGE-718 and the potential for successful development; our estimates as to the number of patients with Parkinson's Disease who are affected by cognitive changes; our belief in the need for new treatment options for this indication; the goals, opportunity and potential for the SAGE-718 program; and the mission and goals for our business. These statements constitute forward-looking statements as that term is defined in 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: the positive results from the PARADIGM Study may not be repeated in future studies in Parkinson's Disease cognitive impairment or in other indications we are studying or may study in the future with SAGE-718, and future clinical results may not meet their primary or key secondary endpoints; clinical and nonclinical data we generate in the course of our development program may not be sufficient to file for or gain regulatory approval to market SAGE-718 without further development work or may not support further development at all; we may encounter adverse results or adverse events at any stage of development that negatively impact further development or that require additional nonclinical and clinical work which may not yield positive results; we may encounter delays in initiation, conduct or completion of ongoing or future clinical trials that may impact our ability to meet our expected time-lines; the FDA may not agree with our view of the data we generate from our development efforts at any stage; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, or progress of ongoing or future clinical trials and our ability to proceed with further development; the FDA may ultimately decide that the design or results of completed and planned clinical trials, even if positive, are not sufficient for regulatory approval of SAGE-718 in any indication or of any of our other product candidates in any indications that are the focus of our development programs and plans; the actual size of the patient population in Parkinson's Disease cognitive impairment or in any other indication we study and the unmet need for new treatment options may be significantly lower than our estimates and, even if SAGE-718 is approved for any indication, it may only be approved or used to treat a subset of the relevant patient population; we may encounter technical and other unexpected hurdles in the development and manufacture of SAGE-718 or our other product candidates which may delay our timing or change our plans; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K, and 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. Sage explicitly disclaims any obligation to update any forward-looking statements.

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