Sage Therapeutics Announces Presentation of Promising Results from the Phase 2 LUMINARY Study of SAGE-718 in Patients with Mild Cognitive Impairment and Mild Dementia due to Alzheimer's Disease

April 1, 2022

Data to be Presented During the Emerging Science Session at the American Academy of Neurology's 74th Annual Meeting

The LUMINARY 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 and mild dementia due to Alzheimer's disease

SAGE-718 demonstrated improvement across multiple tests of executive performance as well as improvement on key tests of learning and memory in the LUMINARY Study

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 1, 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 from the Phase 2 LUMINARY Study that showed SAGE-718, a first-in-class, oral, positive allosteric modulator of the NMDA receptor, was generally well-tolerated and associated with improvement on multiple tests of executive performance and learning and memory in patients with mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD). The LUMINARY Study 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 will be presented during the Emerging Science Session on Tuesday, April 5, at the 74th Annual Meeting of the American Academy of Neurology (AAN) in Seattle.

"Alzheimer's disease is one of the greatest areas of unmet patient need, with an estimated global prevalence of more than 134 million people and few, if any, treatment options to specifically address mild cognitive impairment and mild dementia," said Jim Doherty, Ph.D., Chief Development Officer at Sage. "We are encouraged by the positive results shared from the LUMINARY Study, which are consistent with signals suggesting improvement in cognitive performance seen across the SAGE-718 program, including in people with Parkinson's and Huntington's disease. We look forward to learning more about the potential of SAGE-718 as we continue to advance our program with multiple ongoing or planned Phase 2 studies."

In the LUMINARY Study, a comprehensive battery of tests was used to assess multiple domains of cognitive performance in 26 patients receiving SAGE-718 3 mg once daily for 14 days. At Day 14, improvements from baseline were observed on multiple tests of executive functioning (Digit Symbol Substitution, Multitasking, One Touch Stockings, Spatial Working Memory, and 2-Back tests) and learning and memory (Pattern Recognition Memory and Verbal Recognition Memory tests).

Statistically significant improvement in the Montreal Cognitive Assessment (MoCA) (+2.3 points vs baseline) was observed at Day 28. 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. Functional assessments also captured notable improvement in some patients (Clinical Global Impressions Scales and Amsterdam Instrumental Activities of Daily Living Questionnaire), particularly on items measuring aspects of complex/higher order activities.

SAGE-718 was generally well-tolerated in the LUMINARY Study. Eight mild/moderate treatment-emergent adverse events (TEAE) were reported in seven patients. No serious adverse events or deaths were reported.

About the LUMINARY Study

The LUMINARY Study was an open-label, Phase 2 study evaluating SAGE-718, 3mg once daily for 14 days in patients with mild cognitive impairment and mild dementia due to AD. Patients aged 50–80 years with MoCA scores of 15-24 were included. Treatment-emergent adverse event incidence through Day 28 (primary endpoint), other safety outcomes (secondary endpoints) and cognitive and functional assessments were analyzed.

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, Parkinson's disease and Alzheimer's disease. Ongoing 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 cognitive impairment due to Huntington's disease 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 Huntington's, Parkinson's and Alzheimer's diseases in 2022. In 2021, SAGE-718 received Fast Track Designation from the FDA for development of SAGE-718 as a potential treatment for Huntington's disease.

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 findings from the LUMINARY 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 Alzheimer's disease; 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 LUMINARY Study or from other studies we have conducted with SAGE-718 may not be repeated in future studies in the indications we have studied to date or in other indications we 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 Alzheimer's disease 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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