Sage Therapeutics Announces Topline Results from Phase 2 PRECEDENT Study of Dalzanemdor (SAGE-718) in the Treatment of Mild Cognitive Impairment in Parkinson's Disease

April 17, 2024

- In the Phase 2 PRECEDENT Study, dalzanemdor (SAGE-718) did not show statistically significant differences versus placebo on the primary endpoint in patients with mild cognitive impairment in Parkinson's disease

- Dalzanemdor (SAGE-718) was generally well-tolerated and there were no new safety signals observed

- Topline data readouts from the Phase 2 studies in Huntington's disease and Alzheimer's disease are expected later this year

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 17, 2024-- Sage Therapeutics, Inc. (Nasdaq: SAGE) announced today topline results from PRECEDENT, a double-blind, placebo-controlled Phase 2 study of the investigational oral medicine dalzanemdor (SAGE-718) in people with mild cognitive impairment (MCI) in Parkinson's Disease (PD). The PRECEDENT Study did not meet its primary endpoint of demonstrating statistically significant difference from baseline in participants treated with once-daily dalzanemdor versus placebo on the Wechsler Adult Intelligence Scale Fourth Edition-IV (WAIS-IV) Coding Test score at Day 42. Dalzanemdor (SAGE-718) was generally well-tolerated, and there were no new safety signals observed.

"*We are disappointed by the results of the Phase 2 PRECEDENT study given the significant burden of mild cognitive impairment on people and families affected by Parkinson's Disease* ," said Barry Greene, Chief Executive Officer at Sage Therapeutics. "*We are thankful for the patients and healthcare professionals who participated in this research. Although cognitive impairment is common in neurodegenerative disorders, the underlying pathophysiology and symptomatology in Parkinson's disease is distinctive, and these results do not necessarily predict results with dalzanemdor in other neurodegenerative conditions. We look forward to the topline data readouts from the Phase 2 studies in Huntington's disease and Alzheimer's disease expected later this year*."

PRECEDENT Study Results

The PRECEDENT Study was a double-blind, placebo-controlled Phase 2 study in people with MCI in PD. The study is designed to evaluate the safety and efficacy of dalzanemdor (SAGE-718) dosed over 6 weeks. A total of 86 participants were enrolled and randomized.

- The PRECEDENT Study did not meet its primary endpoint of demonstrating statistically significant difference from baseline in participants treated with once-daily dalzanemdor versus placebo on the Wechsler Adult Intelligence Scale Fourth Edition-IV (WAIS-IV) Coding Test score at Day 42.
- Dalzanemdor (SAGE-718) was generally well-tolerated, and there were no new safety signals observed. A total of 48 participants experienced treatment emergent adverse events (TEAEs). The vast majority of TEAES were mild to moderate in severity.
- Analyses did not suggest any meaningful differences versus placebo in the other exploratory endpoints such as SCOPA-Cog.

Based on the data, the Company does not plan any further development of dalzanemdor (SAGE-718) in PD. The Company expects the following milestones for the dalzanemdor (SAGE-718) Phase 2 clinical development program in 2024:

- Mid-2024:
  - Report topline data from SURVEYOR Study in people with HD cognitive impairment
- Late 2024:
  - Report topline data from LIGHTWAVE Study in people with MCI and mild dementia in AD
  - Report topline data from DIMENSION Study in people with HD cognitive impairment

Conference Call Information

Sage will host a conference call and webcast today, Wednesday, April 17 at 8:00 a.m. ET to review the PRECEDENT study results. The live webcast can be accessed on the investor page of Sage's website at investor.sagerx.com. A replay of the webcast will be available on Sage's website following the completion of the event and will be archived for up to 30 days.

About dalzanemdor (SAGE-718)

Dalzanemdor (SAGE-718), a first-in-class investigational NMDA receptor positive allosteric modulator (PAM), is in development as a potential oral therapy for cognitive disorders associated with NMDA receptor dysfunction, including Huntington's disease (HD) and Alzheimer's disease (AD). Sage is advancing a clinical program for dalzanemdor (SAGE-718) with multiple ongoing placebo-controlled Phase 2 studies across multiple disease areas, including its potential lead indication, cognitive impairment associated with HD, as well as cognitive impairment in AD. The Company is also

conducting an open-label safety study in HD cognitive impairment.

About Sage Therapeutics

Sage Therapeutics (Nasdaq: SAGE) is a biopharmaceutical company committed to our mission of pioneering solutions to deliver life-changing brain health medicines, so every person can thrive. Sage developed the only two FDA-approved treatments indicated for postpartum depression and is advancing a robust pipeline to target unmet needs in brain health. Sage was founded in 2010 and is headquartered in Cambridge, Mass. Find out more at www.sagerx.com or engage with us on Facebook, LinkedIn, Instagram, and X.

Forward-Looking Statements

Various statements in this release concern future expectations, plans and prospects, including without limitation statements regarding: our expectations with respect to the timing of reporting of results from ongoing clinical trials of dalzanemdor; our belief in the unmet need for new treatment options for brain health disorders; the potential for positive results from ongoing studies of dalzanemdor in HD and AD, despite negative results from the PRECEDENT study in PD; our views regarding possible distinctions among indications as a result of the underlying pathophysiology and symptomatology in PD; our statements as to the potential for dalzanemdor in the treatment of cognitive impairment due to certain neurodegenerative diseases; and the mission, goals, opportunity and potential 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 results of our ongoing clinical studies of dalzanemdor in HD and AD may be negative like the results we announced today from the PRECEDENT study in MCI in PD; the possible distinctions among indications as a result of the underlying pathophysiology and symptomatology in PD may not prove to be relevant in the context of clinical trials of dalzanemdor; the ongoing studies of dalzanemdor may not meet their primary or key secondary endpoints; results of earlier trials in HD and AD may not be replicated in ongoing or future trials; clinical and nonclinical data we generate in the course of the dalzanemdor development program may not be sufficient to move to the next phase of development for an indication 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 or reporting of clinical trial results, including as the result of the need to meet with regulatory authorities, or as a result of actions arising from those meetings, 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 or the regulatory pathway for dalzanemdor in an indication or our ability to proceed with further development; the FDA may ultimately decide that the design or results of completed, ongoing and planned clinical trials, even if positive, are not sufficient for the next phase of development or ultimately for regulatory approval of dalzanemdor in any indication or of any of our other product candidates in any indications that are the focus of our development programs and plans; we may encounter technical and other unexpected hurdles in the development and manufacture of dalzanemdor 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 Quarterly Report on Form 10-Q, 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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MEDIA:
Sage Therapeutics
Matthew Henson
+1 917 930 7147
Matthew.Henson@sagerx.com

INVESTOR:
Sage Therapeutics
Ashley Kaplowitz
+1 786 252 1419
Ashley.Kaplowitz@sagerx.com

Source: Sage Therapeutics, Inc.