Sage Therapeutics Announces Phase 2 SURVEYOR Study Reinforces Cognitive Impact of Huntington's Disease

June 11, 2024

The SURVEYOR Study met its primary endpoint demonstrating a statistically significant difference as measured by the HD-Cognitive Assessment Battery (HD-CAB) composite score at baseline between healthy participants and participants with Huntington's Disease (HD) prior to any treatment with dalzanemdor (SAGE-718) or placebo; further underscoring the cognitive impact of HD

For participants with HD that received dalzanemdor or placebo, dalzanemdor was generally well-tolerated with no new safety signals observed

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 11, 2024-- Sage Therapeutics announced today topline results from the Phase 2 SURVEYOR Study. The study met its primary endpoint demonstrating a statistically significant difference as measured by the HD-Cognitive Assessment Battery (HD-CAB) composite score at baseline between healthy participants and participants with Huntington's Disease (HD) prior to any treatment with dalzanemdor (SAGE-718) or placebo.

"Huntington's Disease is a rare, genetic, neurodegenerative condition that greatly impacts the ability of individuals to function independently. While symptoms of cognitive impairment can precede motor symptoms by up to 15 years, it is a historically underrecognized aspect of HD and there are no approved treatments for cognitive impairment in HD," said Laura Gault, Chief Medical Officer, Sage Therapeutics. *"The findings from the SURVEYOR Study highlight the extent of cognitive impairment associated with HD and enhance our collective understanding of this devastating disease. This finding further underscores the importance of developing treatments that can address this critical unmet need for people living with HD."*

SURVEYOR (NCT05358821) was a small study with three objectives: to determine the magnitude of cognitive impairment in HD compared to healthy participants; to evaluate the safety of dalzanemdor in participants with HD; and to better understand the relationship between changes in cognition and changes in function. A total of 40 participants with HD and 29 healthy participants were enrolled. The HD-CAB, a composite battery comprised of six individual tests to assess various domains of cognition relevant to HD, was used to evaluate cognition in all study participants.

SURVEYOR Study Results:

The study met its primary endpoint demonstrating a statistically significant difference as measured by the HD-CAB composite score at baseline between healthy participants and participants with Huntington's Disease (HD) prior to any treatment with dalzanemdor or placebo. The baseline composite score for participants with HD was markedly lower ($p < 0.0001$) compared to healthy participants, further underscoring the extent of cognitive impairment associated with HD and the significant unmet need for treatment options.

In the second part of the study, participants with HD were randomly assigned to receive dalzanemdor or placebo for a 28-day treatment period. The study was **not** designed or powered to demonstrate a statistically significant difference between dalzanemdor and placebo.

- In this part of the study, the safety and tolerability of dalzanemdor was evaluated as a secondary objective, and exploratory analyses included measures of cognition and function.
- Dalzanemdor was generally well-tolerated and no new safety signals were observed. A total of 11 participants with HD experienced treatment emergent adverse events (TEAEs), the vast majority of which were mild to moderate in severity. There were no discontinuations related to TEAEs.
- There was a small numerical difference observed between dalzanemdor and placebo on the HD-CAB composite score at Day 28. Other prespecified analyses suggested the potential for directionally positive signals in a number of individual component tests of the HD-CAB and in some functional assessments. Additional work is ongoing to further analyze and understand the data including the relationship of changes in cognition to changes in function.

As the Company continues to evaluate the SURVEYOR Study data, it plans to apply relevant learnings to ongoing work on the dalzanemdor program. The Company expects the following dalzanemdor program milestones in late 2024:

- Report topline data from LIGHTWAVE Study in mild cognitive impairment and mild dementia in Alzheimer's Disease
- Report topline data from DIMENSION Study in cognitive impairment associated with HD

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 mild cognitive impairment and mild dementia 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 belief in the potential profile and benefit of dalzanemdor; the potential impact of findings from the SURVEYOR Study; our plans for further development of dalzanemdor; 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 cognitive impairment in HD; the potential utility of the HD-CAB and other functional assessments of cognition in HD; the potential for positive results from ongoing studies of dalzanemdor in HD and AD; our statements as to the potential for dalzanemdor in the treatment of cognitive impairment in HD and other 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; the ongoing studies of dalzanemdor may not meet their primary or key secondary endpoints; potentially directionally positive signals in certain measures of the treatment phase of the SURVEYOR study may not prove to be actual signals or meaningful to the development program; positive signals or results from earlier open-label trials 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 or other regulatory authorities 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 authorities 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 or other regulatory authorities 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 to file for or receive 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; even if dalzanemdor is approved for any indication, it may only be approved or used to treat a subset of the relevant patient population and may not achieve market acceptance; 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 or impact our results; 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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