Sage Therapeutics and Biogen Announce SAGE-324 Phase 2 Placebo-Controlled KINETIC Study in Essential Tremor Met Primary Endpoint

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Statistically significant reduction in tremor score compared to placebo at Day 29 in adults with essential tremor

SAGE-324 demonstrated a 36% reduction in upper limb tremor amplitude from baseline at Day 29 in the total studied population; in a more severe population (baseline TETRAS Upper Limb Item 4 >12), SAGE-324 demonstrated a 41% reduction in upper limb tremor amplitude compared to baseline

SAGE-324 demonstrated a safety profile generally consistent with previously reported data

Sage Therapeutics to host conference call today at 8 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 12, 2021-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) today reported topline results from the Phase 2 KINETIC Study evaluating SAGE-324 in the treatment of people with essential tremor (ET). The study (n=67 full analysis set) achieved its primary endpoint of a statistically significant reduction from baseline compared to placebo in The Essential Tremor Rating Assessment Scale (TETRAS) Performance Subscale Item 4 upper limb tremor score on Day 29 (P=0.049), which corresponded to a 36% reduction from baseline in upper limb tremor amplitude in patients receiving SAGE-324 compared to a 21% reduction in patients receiving placebo. Activities of daily living (ADL) scores showed a statistically significant correlation with upper limb tremor score at all timepoints. While not powered to fully examine TETRAS ADL, SAGE-324 was numerically superior to placebo at all time points. Reported treatment-emergent adverse events (TEAEs) were generally consistent with the safety profile of SAGE-324 to date.

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In the KINETIC Study, patients (n=47) with a more severe tremor at baseline (at or above the median TETRAS Performance Subscale upper limb tremor Item 4 score of 12) who received SAGE-324, demonstrated a statistically significant reduction (P=0.007) from baseline in TETRAS Performance Subscale Item 4 upper limb tremor score compared to placebo at Day 29, corresponding to a 41% reduction from baseline in upper limb tremor amplitude in patients receiving SAGE-324 compared to an 18% reduction for placebo. Study patients were not taking other medications for ET during the 28-day treatment period.

The collaboration partners are pleased with the progress to date and are planning next steps for development of SAGE-324.

“In the design of the KINETIC Study, we set a high bar and believe we exceeded it. SAGE-324 met the primary endpoint in the trial and demonstrated a safety profile generally consistent with previously reported data. The strong correlation observed in this study between TETRAS performance scale – measuring reduction of upper limb tremor, a disabling symptom experienced by more than 90% of people suffering from essential tremor -- and improvement on the ADL score provides suggestive evidence that these findings have the potential to be truly impactful for people with essential tremor,” said Barry Greene, chief executive officer at Sage Therapeutics. “We believe the data announced today provide clear support and insights for the continued development of SAGE-324 in an area of significant unmet medical need. People with brain health disorders have been conditioned to accept the status quo due to limited innovation or the lack of truly transformative medicines in recent years – and that’s certainly been the case with essential tremor. However, at Sage, we believe that people suffering from brain health disorders deserve better and we aim to help achieve that.”

“We are encouraged by the positive results of the KINETIC Study, which indicate that SAGE-324 may provide relief in people suffering with essential tremor, a movement disorder that affects an estimated 6.4 million people – and is one of the most common movement disorders – in the United States,” said Alfred Sandrock, Jr., M.D., Ph.D., Head of Research and Development at Biogen. “For people with essential tremor, uncontrollable shaking of the hands, head, voice, or legs can create difficulty eating, dressing, writing, and pursuing other day-to-day tasks. It is our hope that, in collaboration with Sage, we will be able to deliver an innovative and meaningful new treatment option for these patients. The positive results of the KINETIC Study represent one step further towards that goal, and also underscore Biogen’s commitment to delivering new therapeutic options to patients living with movement disorders that have high medical unmet need, including essential tremor.”

“There is an extraordinary unmet need for people suffering with essential tremor, a condition that can cause significant disability in patients,” said Dr. Rodger Elble, M.D., a neurologist at the Southern Illinois University School of Medicine. “The only approved medicine was developed more than 50 years ago, and most medicines used for ET were developed for other conditions, and their benefits to people with ET were only discovered serendipitously. Current investigational drugs like SAGE-324, if successful, may offer potential for new treatment options for tremor management, as more than 50% of people with ET do not respond optimally to the current standard of care.”

Full data from the KINETIC Study will be shared at future scientific forums and in publications.

Summary of Topline Results from KINETIC Study

In the KINETIC Study, SAGE-324 taken orally, once daily in the morning, showed a statistically significant reduction from baseline in upper limb tremor score as measured by Item 4 of TETRAS Performance Subscale on Day 29 compared to placebo. TETRAS Scale includes two subscales: the Performance Subscale and the Activities of Daily Living (ADL) Subscale. The TETRAS Performance Subscale is a validated, physician-administered scale designed to provide an accurate, comprehensive assessment of ET motor symptoms and has been shown to correlate with TETRAS ADL. The Performance Subscale includes Item 4, which measures upper limb tremor.

Primary Endpoint
Patients receiving SAGE-324 experienced a statistically significant reduction from baseline in TETRAS Performance Subscale Item 4 compared to placebo at Day 29 (P=0.049), corresponding to a 36% reduction in upper limb tremor amplitude from baseline in the SAGE-324 group compared to a 21% reduction in the placebo group. The analysis is based on the prespecified Full Analysis Set.

Safety and Tolerability

Patients were randomized 1:1 to receive SAGE-324 (60 mg) or matched placebo once daily in the morning. The trial evaluated treatment of SAGE-324 at the higher end of the dose range and the daily dose could be down-titrated to 45 mg or 30 mg if 60 mg was not well tolerated. Down-titration of dose occurred in 62% of patients who received SAGE-324 and discontinuations were noted in 38% of patients receiving SAGE-324. Adverse events were generally consistent with the safety profile of SAGE-324 seen to date. The most common TEAEs that occurred in ≥10% of patients in the SAGE-324 treatment group and at a rate at least twice as high as that of patients in the placebo group were: somnolence 68%; dizziness 38%; balance disorder 15%; diplopia 12%; dysarthria 12%; and gait disturbance 12%.

Sage Therapeutics Conference Call Information
Sage will host a conference call and webcast today, Monday, April 12, at 8:00 a.m. ET to discuss the KINETIC Study topline 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 approximately two hours after the completion of the event and will be archived for up to 30 days.

About the KINETIC Study
The KINETIC Study is a Phase 2 study that evaluated the efficacy, safety, and tolerability of SAGE-324 60 mg in 69 patients with essential tremor aged 18 to 80 years old. The primary endpoint of the multicenter, randomized, double-blind, placebo-controlled study was change from baseline compared to placebo on Day 29 in upper limb tremor score as measured by Item 4 of the TETRAS Performance Subscale.

About Essential Tremor
Essential Tremor (ET) is one of the most common movement disorders in the United States, affecting an estimated 6.4 million Americans. For ET patients, uncontrollable shaking of the hands, head, voice, or legs creates difficulty eating, dressing, writing, and pursuing other day-to-day tasks. While ET is often associated with aging populations, ET can begin much earlier in life, with a progressive disease course that can eventually necessitate a care partner. Social anxiety and depressive symptoms can manifest in patients with ET as tremor severity increases and may negatively impact a patient's ability to work and engage in hobbies. The only U.S. Food and Drug Administration (FDA) approved pharmacological treatment for ET was approved more than 50 years ago, and more than 50% of patients with ET experience a sub-optimal response with standard-of-care treatments, highlighting a significant unmet need in care.

About SAGE-324
SAGE-324 is an investigational oral neuroactive steroid (NAS) $GABA_A$ receptor positive allosteric modulator (PAM). NAS $GABA_A$ receptor PAMs bind to both synaptic and extrasynaptic $GABA_A$ receptors, enhancing inhibitory activity of the GABAergic system, the major inhibitory neurotransmission system in the brain. GABA is the primary inhibitory neurotransmitter in the central nervous system and plays a critical role in maintaining balanced neuronal activity in the brain. GABA dysregulation has been implicated in the pathophysiology of ET.

About Sage Therapeutics
Sage Therapeutics is a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating disorders of the brain. We are pursuing new pathways with the goal of improving brain health, and our depression, neurology and neuropsychiatry franchise programs aim to change how brain disorders are thought about and treated. Our mission is to make medicines that matter so people can get better, sooner. For more information, please visit www.sagerx.com.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases as well as related therapeutic adjacencies. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, neuropsychiatry, immunology, acute neurology and neuropathic pain.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Sage Therapeutics Safe Harbor
Various statements in this release concern future expectations, plans and prospects, including without limitation statements regarding: Sage's belief and confidence in the potential profile and benefit of SAGE-324 and the potential impact of the findings from the KINETIC Study; our goals and plans for further development of SAGE-324 and the potential for successful development; estimates as to the number of patients with ET; Sage's belief in the need for new treatment options for ET; and the goals, opportunity and potential for the SAGE-324 program and for Sage's 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 of the KINETIC Study may not be repeated in future studies, and future clinical results may not meet their primary or key secondary endpoints; clinical and nonclinical data we generate may not be sufficient to file for or gain regulatory approval to market SAGE-324 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 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 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-324 in ET or of any of our product candidates in any indications that are the focus of our development programs and plans; the actual size of the ET patient population and unmet need may be significantly lower than our estimates and, even if SAGE-324 is approved to treat ET, 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-324 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 Sage's 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 Sage's views only as of today, and should not be relied upon as representing Sage's views as of any subsequent date. Sage explicitly disclaims any obligation to update any forward-looking statements.

Biogen Safe Harbor
This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, relating to the potential, benefits, safety and efficacy of SAGE-324; the potential clinical effects of SAGE-324; results from the Phase 1/2 studies of SAGE-324; the clinical development program, clinical trials, data readouts and presentations related to SAGE-324; the treatment of essential tremor; the potential of Biogen's commercial business and pipeline programs, including SAGE-324; the anticipated benefits and potential of Biogen's collaboration arrangements with Sage; and risks and uncertainties associated with drug development and commercialization.

These forward-looking statements may be accompanied by words such as “aim,” “anticipate,” “believe,” “could,” “estimate,” “expect,” “forecast,” “hope,” “intend,” “may,” “plan,” “potential,” “possible,” “will,” “would” and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk and only a small number of research and development programs result in commercialization of a product. Results in early-stage clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements, or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation, uncertainty of success in the development and potential commercialization of SAGE-324; unexpected concerns may arise from additional data, analysis or results obtained during the KINETIC Study; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of Biogen’s drug candidates, including SAGE-324; the occurrence of adverse safety events; the risks of other unexpected hurdles, costs or delays; uncertainty of success in the development of SAGE-324; failure to protect and enforce data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; the direct and indirect impacts of the ongoing COVID-19 pandemic on Biogen’s business, results of operations and financial condition; product liability claims; and third party collaboration risks. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen’s expectations in any forward-looking statement. Investors should consider this cautionary statement as well as the risk factors identified in Biogen’s most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission. These statements are based on Biogen’s current beliefs and expectations and speak only as of the date of this news release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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SAGE MEDIA CONTACT:
Maureen L. Suda
Sage Therapeutics
Tel: (617) 949-4289
Email: Maureen.Suda@sagerx.com

SAGE INVESTOR CONTACT:
Jeff Boyle
Sage Therapeutics
Tel: (617) 949-4256
Email: Jeff.Boyle@sagerx.com

BIOGEN MEDIA CONTACT:
David Caouette
Tel: +1 (617) 679-4945
public.affairs@biogen.com

BIOGEN INVESTOR CONTACT:
Mike Hencke
Tel: +1 (781) 464-2442
IR@biogen.com

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