Sage Therapeutics and Biogen Announce Positive, One-Year Zuranolone 50 mg Data in the Ongoing Open-Label SHORELINE Study in Patients with MDD

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In the zuranolone 50 mg cohort, the majority of patients who responded to an initial 14-day course received only one two-week course of treatment during the study and nearly 80% received only one or two treatment courses in total

Zuranolone 50 mg was generally well-tolerated with an overall adverse event profile consistent with data reported earlier and 6.5% of patients discontinuing study drug due to adverse events

Across the LANDSCAPE clinical program to date, zuranolone has consistently demonstrated rapid and sustained improvements in depressive symptoms and a well-tolerated safety profile

CAMBRIDGE, Mass. – December 1, 2021 – Sage Therapeutics, Inc. (Nasdaq: SAGE), and Biogen Inc. (Nasdaq: BIIB) today announced 12-month data for the cohort of patients (n=199), who received zuranolone 50 mg once nightly for 14-days as their initial dose in the ongoing Phase 3 open-label SHORELINE Study and had the opportunity to be followed for 12-months. The SHORELINE Study, part of the LANDSCAPE clinical program, was designed to naturalistically follow adult patients with major depressive disorder (MDD) and evaluate the safety and tolerability of zuranolone as well as the need for repeat dosing for up to one year. For the primary endpoint of safety and tolerability, the data analyzed to date show zuranolone was generally well-tolerated, with no new safety findings or trends identified in the long-term safety data available regardless of the number of courses of zuranolone a patient received. Zuranolone has consistently demonstrated rapid and sustained improvements in depressive symptoms and a well-tolerated safety profile throughout the LANDSCAPE clinical program.

Secondary endpoints included the percentage of patients who received repeat dosing with zuranolone as well as response and remission as evaluated by the 17-item Hamilton Rating Scale for Depression (HAMD-17). In the zuranolone 50 mg cohort, nearly 75% of patients responded to the initial 2-week treatment course. Of those who responded to the initial course and continued in the study, approximately 80% of those patients received at most one additional zuranolone treatment during their time in the study.

The SHORELINE Study, with nearly 1,000 patients enrolled to date, is comprised of multiple cohorts, including a completed cohort with zuranolone 30 mg as a starting dose (data previously reported in 2020 and earlier in 2021) and an ongoing cohort with zuranolone 50 mg as a starting dose; both cohorts are administered zuranolone once nightly for 14 days. Enrollment of an anticipated 300 additional patients in the 50 mg cohort is ongoing. The study provides real-world insight into the potential use of zuranolone, if approved, as an as-needed treatment for MDD and builds on the data assembled in the LANDSCAPE clinical program to date. Data from the LANDSCAPE clinical program has been presented at numerous medical and scientific conferences and the Companies plan to present additional data from the ongoing SHORELINE Study in future scientific forums.

“We believe zuranolone has the potential to offer an innovative treatment approach that may enable patients with MDD to experience reductions in depressive symptoms quickly, achieve related improvements in functioning and well-being, and maintain long treatment free intervals without the types of burdensome side effects that are often associated with discontinuation of standard of care antidepressants. The SHORELINE Study helps provide important information on how zuranolone, if approved, could be used to treat people with MDD,” said Barry Greene, Chief Executive Officer at Sage Therapeutics. “We are pleased by the progress made with zuranolone throughout 2021 and the data we have generated in clinical development to date supports our belief in the overall profile of zuranolone, and its potential to make a profound difference in the lives of many patients living with MDD.”

“In the SHORELINE Study, zuranolone was generally well-tolerated by participants regardless of the number of treatment courses received during the one-year study,” said Priya Singhal, M.D., M.P.H., Head of Global Safety and Regulatory Sciences and Interim Head of R&D at Biogen. “These new data further reinforce positive findings from multiple late-stage studies of zuranolone and underscore the potential of zuranolone as a well-tolerated, rapid-acting and durable treatment option for depression.”

Zuranolone 50 mg: Summary of One-Year Results

This cohort of the ongoing Phase 3 SHORELINE Study is evaluating the safety and tolerability of zuranolone 50 mg in adults 18-75 who have MDD.

- 199 people with MDD (HAMD-17 ≥20 and Montgomery Asberg Depression Rating Scale (MADRS) ≥28) were treated with an initial dose of zuranolone 50 mg once nightly for 14 days and had the opportunity to be followed for up to one year.
- The mean baseline HAMD-17 score (± SD) at entry into the study was 25.1 ± 3.29 (n=199).
- At baseline, 81 (40.7%) patients were on pre-existing antidepressant therapy (ADT) that was continued, while 118 (59.3%) were not on ADT.

Safety and tolerability of zuranolone 50 mg:

- Zuranolone 50 mg was generally well-tolerated with no new safety finding or trend identified in the long-term safety data available to date on patients followed up to one year who received a single or repeat dosing courses. Safety was assessed during treatment and in between treatment courses and over multiple treatment courses to inform tolerability over time and long-term.
- Over the entire study, 137 of 199 (68.8%) patients who initiated treatment with zuranolone 50 mg reported at least one adverse event, similar to the previously reported 30 mg cohort (68.0%). The majority of patients reported treatment emergent adverse events (TEAEs) with maximum severity of mild to moderate.
- The most common TEAEs reported >5% (N, % with TEAE) were somnolence (32; 16.1%), dizziness (30; 15.1%), headache (25; 12.7%), sedation (20; 10.1%), insomnia (14; 7.0%), nausea (13; 6.5%), and tremor (11; 5.5%).

- The types of TEAEs reported by patients receiving zuranolone 50 mg were similar to those previously reported for zuranolone 30 mg. The frequency of adverse drug reactions known to be associated with zuranolone, such as somnolence, dizziness, sedation, and tremor, were higher in the 50 mg cohort; however, the severity and outcome of events remained consistent with the 30 mg cohort and the overall safety profile of zuranolone.
- The percent of patients reporting TEAEs leading to discontinuation of study drug and withdrawal from study, respectively, were 6.5% (13/199) and 8.0% (16/199).
- There was no signal for increased suicidal ideation or suicidal behavior compared to baseline in any study period or dose cohort, as measured by the Columbia-Suicide Severity Rating Scale (C-SSRS).
- The overall adverse event profile from this zuranolone 50 mg cohort is generally consistent with the previously reported SHORELINE Study data, and the types of TEAEs reported are similar to what has been reported across the LANDSCAPE clinical program.

Efficacy of zuranolone 50 mg:

- At Day 15 following the initial 2-week treatment, the HAMD-17 mean change from baseline was -16.0 ± 6.04 (n=185).
    - 149 (74.9%) patients achieved response (at least 50% reduction from baseline) and 80 (40.2%) achieved remission (HAMD ≤7).
    - Of the 149 responders, 3 withdrew from the study prior to Day 28, leaving 146 beyond Day 28.
- 79.5% of the 146 patients who responded to the initial 2-week treatment received at most one additional zuranolone treatment course during their time in the study.
    - 54.8% (N=80) received 1 treatment course in total.
    - 24.7% (N=36) received 2 treatment courses in total.
    - 10.3% (N=15) received 3 treatment courses in total.
    - 6.8% (N=10) received 4 treatment courses in total.
    - 3.4% (N=5) received 5 treatment courses in total.
- The proportion of patients receiving zero or at most 1 additional treatment course was similar regardless of use of antidepressant therapy at baseline.

About the SHORELINE Study

The SHORELINE Study (217-MDD-303) is an ongoing Phase 3, open-label, 1-year longitudinal study evaluating the safety, tolerability, and need for repeat dosing with zuranolone in adults with MDD. The study is comprised of multiple cohorts, including a completed cohort with zuranolone 30 mg as a starting dose and an ongoing cohort with zuranolone 50 mg as a starting dose; both cohorts are administered zuranolone once nightly for 14 days. Enrollment of an additional 300 patients in the 50 mg cohort is ongoing. Patients who achieve a response after the first treatment course are eligible to remain on study with the opportunity to receive additional treatment courses as needed. The need for repeated dosing is assessed every 14 days based on the results of a patient-reported PHQ-9 (≥10) and HAMD-17 (≥20) assessment. There is a minimum of 56 days between zuranolone 14-day courses, to allow for a maximum of five courses over the 12-month study period. The complete 12-month data from the zuranolone 30 mg cohort and initial interim data from the zuranolone 50 mg cohort read out in early 2021.

About Major Depressive Disorder (MDD)

Major depressive disorder (MDD) is a common but serious mood disorder in which people experience depressive symptoms that impair their social, occupational, educational, or other important functioning, such as a depressed mood or loss of interest or pleasure in daily activities, consistently for at least a two-week period. It is estimated that approximately 19 million people in the U.S. and more than 250 million people worldwide suffer from MDD each year. While antidepressants are widely used to treat MDD, large-scale studies have demonstrated the need for additional therapies with a differentiated profile.

About Zuranolone

Zuranolone (SAGE-217/BIIB125) is a once-daily, two-week, investigational drug in development for the treatment of major depressive disorder (MDD) and postpartum depression (PPD). Zuranolone is an investigational oral neuroactive steroid (NAS) GABA-A receptor positive allosteric modulator (PAM). The GABA system is the major inhibitory signaling pathway of the brain and central nervous system and contributes to regulating brain function. Zuranolone has been granted Breakthrough Therapy Designation by the U.S. Food & Drug Administration.

Zuranolone is being evaluated in the LANDSCAPE and NEST clinical trial programs. The two development programs include multiple studies examining use of zuranolone in several thousand patients with a variety of dosing, clinical endpoints, and treatment paradigms. The LANDSCAPE program includes five studies of zuranolone in patients with MDD (MDD-201B, MOUNTAIN, SHORELINE, WATERFALL, and CORAL Studies). The NEST program includes two placebo-controlled studies of zuranolone in patients with PPD (ROBIN and SKYLARK Studies). Additionally, Shionogi recently completed a Phase 2 study of zuranolone in Japan in patients with MDD.

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.

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Forward-Looking Statements

Sage Therapeutics Safe Harbor

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: the potential for approval of zuranolone and our belief in its potential profile, benefit and impact in the treatment of MDD, if approved; our estimates as to the number of people with MDD; our future plans and expected activities; 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: we may experience delays or unexpected hurdles in our efforts to seek approval for zuranolone in the treatment of MDD or PPD; even if we are successful in our efforts to file a new drug application (NDA) for zuranolone, the FDA may find that the data included in the NDA are not sufficient for approval and may not approve the NDA; the FDA may decide that the design, conduct or results of our completed and ongoing clinical trials for zuranolone, even if positive, are not sufficient for approval in MDD or PPD and may require additional trials or data which may significantly delay and put at risk our efforts to obtain approval and may not be successful; other decisions or actions of the FDA or other regulatory agencies may affect our efforts with respect to zuranolone and our plans, progress or results; we may experience negative results in ongoing or future studies of zuranolone that negatively affect our ability to obtain approval of zuranolone or that impair the potential profile of zuranolone; success in earlier clinical trials of zuranolone or any of our other product candidates may not be repeated or observed in ongoing or future studies, and ongoing and future clinical trials may not meet their primary or key secondary endpoints which may substantially impair development or our future plans or potential for success; unexpected concerns may arise from additional data, analysis or results from any of our completed studies; we may encounter 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 our ongoing and planned clinical trials, including as a result of slower than expected site initiation or enrollment, the need or decision to expand the trials or other changes, that may impact our ability to meet our expected timelines; the number of people with MDD and potential market for zuranolone as a treatment for MDD, if approved, may be substantially smaller than our estimates; the unmet need for additional treatment options in MDD and the potential benefit for zuranolone may not be as significant as we expect; and we may encounter technical and other unexpected hurdles in the development and manufacture of zuranolone or any of our other product candidates which may delay our timing or change our plans or prospects, or otherwise negatively impact our business; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent Quarterly Report on Form 10-Q, as well as 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. We explicitly disclaim 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 zuranolone; the potential clinical effects of zuranolone; the clinical development program for zuranolone; clinical development programs, clinical trials and data readouts and presentations for zuranolone; the potential treatment of MDD; the potential of Biogen's commercial business and pipeline programs, including zuranolone; the anticipated benefits and potential of Biogen's collaboration arrangement 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," "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 zuranolone; unexpected concerns may arise from additional data, analysis or results of clinical studies of zuranolone; 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 zuranolone; the occurrence of adverse safety events; the risks of other unexpected hurdles, costs or delays; failure to protect and enforce data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; third party collaboration risks; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, results of operations and financial condition. 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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