Sage Therapeutics and Biogen Announce New Analyses from the LANDSCAPE Clinical Development Program of Zuranolone in MDD Presented at the American College of Neuropsychopharmacology (ACNP) Congress

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Patients receiving zuranolone 50 mg in the WATERFALL Study demonstrated rapid improvements in depressive and anxiety symptoms, as early as the first measured timepoint (Day 3 for HAMD-17 and Day 8 for HAM-A), with average improvements maintained through the end of the study (Day 42)

Safety data from the WATERFALL Study was consistent with the zuranolone safety profile seen to date across the LANDSCAPE program

Zuranolone was generally well-tolerated in a subgroup of patients aged 65 years and older in the SHORELINE Study, showing similar efficacy and safety results in the datasets analyzed to that observed in the general study population

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Dec. 8, 2021-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) today announced new data from the LANDSCAPE clinical program evaluating the efficacy and safety of zuranolone for the treatment of major depressive disorder (MDD) presented at the American College of Neuropsychopharmacology (ACNP) Congress taking place December 5-8 in San Juan, Puerto Rico. Data from the SHORELINE and WATERFALL Studies in the LANDSCAPE clinical program further the understanding of the potential efficacy and safety profile of zuranolone for the treatment of MDD. Across the studies, zuranolone treatment led to improvements in depressive symptoms as well as in symptoms of elevated anxiety as assessed by multiple scales (HAMD-17, MADRS and HAM-A, respectively). In the WATERFALL Study, a rapid onset of effect in HAMD-17 was observed compared to placebo as early as Day 3, reaching statistical significance, followed by a stabilization of depressive symptoms through the follow-up period.

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Zuranolone has demonstrated a consistent safety profile in the totality of clinical data to date, with no increased incidence of adverse events (AEs) of weight gain, sexual dysfunction, or sleep disruption relative to placebo, symptoms that are often the cause of standard of care antidepressant discontinuation. In an analysis of a subgroup of patients (N=96) over the age of 65 in the SHORELINE Study, zuranolone efficacy and safety results for the initial 2-week dose treatment course were similar to that of the general study population. At the time of the analysis, retreatment data were only available for the zuranolone 30 mg cohort of the SHORELINE Study. In a subgroup of patients 65 years and older who responded to the initial 2-week treatment course of zuranolone 30 mg, and were followed for up to one year in the SHORELINE Study, more than half did not receive a second course of treatment during their time in the study.

“The data shared at ACNP continue to provide insight to help us better understand how zuranolone could impact the treatment of depression and potentially differentiate further from current antidepressants, if approved,” said Barry Greene, Chief Executive Officer at Sage Therapeutics. “The analysis conducted evaluating zuranolone’s effects on measures of anxiety in patients with MDD is critical. Symptoms of anxiety are highly present in patients with depression, which can pose unique challenges to care. We are also pleased with the data for those 65 and older, who can struggle with current therapies to treat their depression. Zuranolone has consistently demonstrated rapid and sustained improvements in depressive symptoms and a well-tolerated safety profile in our clinical trials to date without the adverse events that are often associated with discontinuation of standard of care antidepressants.”

ACNP presentations included data from the WATERFALL Study, a Phase 3 placebo-controlled trial that evaluated the efficacy and safety of zuranolone 50 mg in adults 18 to 64 years old with MDD as well as the ongoing open-label SHORELINE Study in MDD. In an oral session, an analysis from the WATERFALL Study assessing zuranolone (50 mg) on symptoms of anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A) showed improvements in symptoms of anxiety compared with placebo at Days 8 and 15. Additional data presented provided an efficacy analysis from the WATERFALL Study as measured by the Montgomery-Åsberg Depression Rating Scale (MADRS) total score, which addresses core mood symptoms such as sadness, lack of energy, and suicidal thoughts. The group of patients receiving zuranolone (50 mg) showed rapid improvements in depressive symptoms and anxiety symptoms, as early as the first measured timepoint (Day 3 for HAMD-17 and Day 8 for HAM-A). Similar results have been observed across the LANDSCAPE program. Additionally, data from the SHORELINE Study support the potential of zuranolone as an oral, as-needed treatment for patients with MDD, including those age 65 and older

“The new data shared at ACNP further our confidence in the potential of zuranolone to help rapidly mitigate various symptoms associated with depression, including elevated anxiety,” said Priya Singhal, M.D., M.P.H., Head of Global Safety and Regulatory Sciences and Interim Head of Research and Development at Biogen. “As we continue to evaluate the totality of the data from the LANDSCAPE clinical develop program – which includes the Phase 3 WATERFALL and SHORELINE Studies – we aim to gain a more comprehensive understanding of how zuranolone may one day be a valuable option for people worldwide who seek a new way to treat depression.”

Data presented at ACNP:

- **Oral Presentation & Poster:** Improvement in Symptoms of Depression and Anxiety With Zuranolone Treatment in Patients With Major Depressive Disorder: HAM-A Analysis From the Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled WATERFALL Study
- **Poster Presentation:** Improvement in Severity and Symptoms of Major Depressive Disorder With Zuranolone Assessed by

MADRS: Results From the Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled WATERFALL Study
- **Poster Presentation:** Zuranolone in Major Depressive Disorder: Safety and Tolerability Results From the Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled WATERFALL Study
- **Poster Presentation:** Zuranolone in Major Depressive Disorder: Results From the Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, WATERFALL Study
- **Poster Presentation:** Zuranolone in the Treatment of Major Depressive Disorder in Patients ≥65 Years of Age: Outcomes From the Phase 3, Naturalistic SHORELINE Study

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 NEST and LANDSCAPE 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 MDD in Japan.

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

As pioneers in neuroscience, Biogen discovers, develops, and delivers worldwide innovative therapies for people living with serious neurological 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, Sir 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, and is providing the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing the industry's most diversified pipeline in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

In 2020, Biogen launched a bold 20-year, $250 million initiative to address the deeply interrelated issues of climate, health, and equity. Healthy Climate, Healthy Lives™ aims to eliminate fossil fuels across the company's operations, build collaborations with renowned institutions to advance the science to improve human health outcomes, and support underserved communities.

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.

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 future regulatory approval and commercialization of zuranolone; the potential profile and benefit of zuranolone in MDD; planned next steps for the program; our estimates as to the number of patients with MDD; and the goals, opportunity and potential for zuranolone and 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 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 filing or approval of zuranolone 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 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 our efforts; 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 development, 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 and increase our costs; decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, progress

and cost of clinical trials or may impair the potential for successful development; if approved, zuranolone may not have the same profile in clinical practice as observed in clinical trials, and the profile may not meet our expectations or the expectations of patients, prescribers or payors; the number of patients with MDD, the unmet need for additional treatment options and the potential market for zuranolone may be significantly smaller than we expect; and we may encounter technical and other unexpected hurdles in the development and manufacture of our zuranolone and our other product candidates or the commercialization of our marketed product which may delay our timing or change our plans, increase our costs 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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