Sage Therapeutics and Biogen Present New Analyses at Psych Congress Further Evaluating the Efficacy and Safety of Zuranolone

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CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 19, 2022-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) today announced new analyses from across the development program for zuranolone, an investigational, oral, once-daily, 14-day treatment in clinical development for adult patients with major depressive disorder (MDD) and postpartum depression. The 11 new analyses are being presented at the 2022 Psych Congress in New Orleans, September 17 to 20.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20220918005062/en/

An analysis from the ongoing open-label, longitudinal SHORELINE Study in MDD (30 mg cohort n=725, 50 mg cohort n=199) found the median time to the first repeat treatment course for those patients who responded to the initial 14-day treatment course was 135 days for the completed 30 mg cohort (n=489) and 249 days for the ongoing 50 mg cohort (n=146). These data further support zuranolone as a potential episodic treatment for people with MDD.

Key findings from the completed 30 mg cohort of the SHORELINE Study, other clinical data and health economics and outcomes research (HEOR), and patient survey data being presented include:

- In an analysis of patients in the 30 mg cohort of the SHORELINE Study with elevated anxiety (n=569) and without elevated anxiety (n=156), there was a mean reduction in the 17-item Hamilton Rating Scale for Depression (HAMD-17) total score from baseline to Day 15; for those patients who had a HAMD-17 response at Day 15 and continued in the study beyond Day 28, scores remained below baseline through Day 70 independent of the presence of elevated anxiety at baseline.
- Among patients with and without elevated anxiety in the 30 mg cohort of the SHORELINE Study who responded to the initial 14-day treatment at Day 15 (≥ 50% reduction in HAMD-17 total score), approximately 70% of patients received 1 or 2 total treatment courses through their time in the study. Patients had the opportunity for follow-up for up to 1 year.
- In patients who completed 1 year of follow-up in both cohorts of the SHORELINE Study (n=407), most had minimal or mild depressive symptoms at study exit as assessed by the Clinical Global Impressions-Severity scale.
- Zuranolone was generally well-tolerated with a safety profile consistent with prior clinical studies. The most common adverse events associated with zuranolone included headache, somnolence, dizziness and sedation.
- Data from a post-hoc analysis of 4 studies in the LANDSCAPE program demonstrated that improvements in depressive symptoms with zuranolone at Day 15 were sustained beyond the end of treatment.
- A post-hoc analysis of the WATERFALL Study in MDD evaluated the statistically significant reduction in depressive symptoms as measured by HAMD-17 at Day 15 as well as rapid onset observed at Day 3 and Day 8 with zuranolone 50 mg compared to placebo suggested that the differences were clinically meaningful according to estimates of minimal important difference.
- Results from a cross-sectional survey of U.S. adults with depression (n=715), highlighted unmet needs in the treatment of MDD. The characteristics rated as either very or extremely important by the majority of participants were the prevention of depression symptoms returning, fewer side effects, a treatment supported by a body of research on safety and efficacy, the ability to discontinue drug without withdrawal symptoms, works quickly, and can be repeated if symptoms recur.
- Health economics data showed that patients with MDD who also received a prescription for anxiety medication incurred over twice the annual all-cause healthcare costs than those without an anxiety prescription medication.

“The data presented at Psych Congress highlight the rapid and sustained improvement in depressive symptoms seen with zuranolone in clinical trials and reinforce its potential to be an as-needed treatment in MDD,” said Dr. Greg Mattingly, Associate Clinical Professor, Washington University. “Depression is a leading contributor of disability worldwide and importantly awareness has grown during the past few years of the global pandemic. We can and must do more to help people living with MDD and those that care about them overcome the challenges of this disease.”

The 11 Sage and Biogen data presentations at Psych Congress were:

SHORELINE Study Presentations:

- Assessing the Need for Repeat Treatment Courses with Zuranolone in Adult Patients With Major Depressive Disorder With Elevated Anxiety: An Analysis of the Open-Label, Phase 3 SHORELINE Study
- Safety, Tolerability, and Efficacy of Zuranolone Repeat Treatment Courses in Adult Patients With Major Depressive Disorder–An Analysis of the Open-Label, Phase 3 SHORELINE Study

- Safety and Efficacy of Zuranolone 50 mg and Need for Repeat Treatment Courses in the Open-label, Phase 3 SHORELINE Study of Adult Patients With Major Depressive Disorder
- Safety and Efficacy of Zuranolone in Young Adults With Major Depressive Disorder: A Subgroup Analysis of the Open-Label, Long-Term, Phase 3 SHORELINE Study
- Depressive Symptom Severity in Patients with Major Depressive Disorder (MDD) at Study Exit in the One-Year SHORELINE Study of Episodic Treatment with Zuranolone

LANDSCAPE Program Cross-Study Presentations:

- Sustained Benefits of Zuranolone in Patients With Major Depressive Disorder: Results From the LANDSCAPE Clinical Development Program
- Efficacy and Safety of Zuranolone in Adults With Major Depressive Disorder With and Without Use of Standard-of-Care Antidepressants at Baseline in the LANDSCAPE Clinical Development Program

Health Economics and Outcomes Research Presentations:

- Perspectives on the Desirable Attributes Associated With a New Pharmacotherapy for Major Depressive Disorder: Results From a Patient Survey
- Zuranolone in Major Depressive Disorder (MDD): Minimal Important Difference (MID) and Meaningful Change Threshold (MCT) on the 17-item Hamilton Rating Scale for Depression (HAMD-17)
- Economic Burden Among Individuals with Major Depressive Disorder Utilizing Anti-Anxiety Medications in the United States
- Healthcare Resource Utilization in 6 Weeks Post-Diagnosis Among Individuals with Major Depressive Disorder in the United States

About Zuranolone
Zuranolone (SAGE-217/BIIB125) is a once-daily, 14-day, investigational drug in development for the treatment of major depressive disorder (MDD) and postpartum depression (PPD). Zuranolone is an 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 Fast Track and Breakthrough Therapy Designation for MDD and Fast Track Designation for PPD by the U.S. Food & Drug Administration.

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

About Sage Therapeutics
Sage Therapeutics is a biopharmaceutical company fearlessly leading the way to create a world with better brain health. Our mission is to pioneer solutions to deliver life-changing brain health medicines, so every person can thrive. 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 a leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for spinal muscular atrophy, and developed the first and only approved treatment to address a defining pathology of Alzheimer's disease. Biogen is also commercializing biosimilars and focusing on advancing one of 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.

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 profile and benefit of zuranolone in the treatment of MDD and PPD; our belief that the data from our clinical programs support the potential of zuranolone in the treatment of MDD and PPD; the potential for zuranolone to become a new treatment option in the treatment of MDD and PPD; and other statements as to our mission and goals. 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 never gain regulatory approval of zuranolone as a treatment for MDD or PPD; we may not be successful in filing a new drug application (NDA) for zuranolone in these indications; even if we complete the NDA filing, the FDA may find that the data included in the NDA are not sufficient for acceptance of the filing for review or 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; results of ongoing or future studies may impact our ability to obtain approval of zuranolone or impair the potential profile of zuranolone; 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 or use of zuranolone that negatively impact further development or the potential for approval or impair the potential profile of zuranolone, and such events may require additional nonclinical and clinical work which may not yield positive results; the profile and potential benefits of zuranolone in the treatment of MDD and PPD, if approved, may be different than the results seen in our clinical trials and may not meet our current expectations; the unmet need for additional treatment options in MDD and PPD and the potential market and market acceptance for zuranolone in the treatment of these indications, if approved, may be significantly smaller than we expect; and we may encounter technical and other unexpected hurdles which may negatively impact our efforts to gain approval of zuranolone and to make it available as a treatment option for depression or to accomplish other aspects of our mission and goals; as well as those risks more fully discussed in the section entitled "Risk Factors" in our most recent quarterly report with the Securities and Exchange Commission (SEC), as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the SEC. 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 and PPD; 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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