Sage Therapeutics and Biogen Present Further Analyses from Phase 3 SKYLARK Study of Zuranolone in Postpartum Depression at the European College of Neuropsychopharmacology (ECNP) Congress

October 17, 2022

Zuranolone 50 mg demonstrated a clinically meaningful and statistically significant improvement in depressive symptoms at Day 15, the primary endpoint, and at Days 3, 28, and 45, key secondary endpoints as previously reported

Newly presented data offered additional insight into the SKYLARK Study and further demonstrated the rapid improvements in depressive symptoms observed in the clinical trial

Zuranolone was generally well-tolerated, with a safety profile consistent with previous clinical trials; most treatment-emergent adverse events (TEAEs) were mild or moderate in severity in the SKYLARK Study

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 17, 2022-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) today presented additional data from the Phase 3 SKYLARK Study of zuranolone in adult women with postpartum depression (PPD), at the 35th European College of Neuropsychopharmacology (ECNP) Congress, taking place October 15-18, 2022, in Vienna, Austria. This was the first time the SKYLARK Study was presented at a medical congress. Zuranolone is an investigational therapy being evaluated as a once-daily, 14-day oral short course treatment in adults with major depressive disorder (MDD) and PPD.

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The SKYLARK Study, as previously reported, achieved the primary and all key secondary endpoints, with study participants demonstrating rapid and significant improvements in depressive symptoms as early as Day 3 that were sustained through Day 45. Women with PPD who were treated with zuranolone 50 mg (n=98) showed a statistically significant and clinically meaningful improvement in depressive symptoms at Day 15, the primary endpoint, compared to placebo (n=97) as measured by a change from baseline (CFB) in the 17-item Hamilton Rating Scale for Depression (HAMD-17) total score (least-squares mean ±SE: zuranolone 50 mg −15.6 ±0.82 vs. placebo −11.6 ±0.82; [p=0.0007]). The study population was diverse, including approximately 22% Black or African American women and 38% identifying ethnically as Hispanic or Latina women.

In the presentation at ECNP, additional secondary endpoint data demonstrated that a higher proportion of patients in the zuranolone 50 mg arm achieved a HAMD-17 response (≥ 50% decrease from baseline HAMD-17 total score) as compared with the placebo arm at Days 3, 8, 15, 21, and 28 ($p<0.05$, at all time points). Data also showed that a higher proportion of patients in the zuranolone arm achieved HAMD-17 remission (HAMD-17 total score ≤ 7) than in the placebo arm from Day 3 through Day 45 (Day 45 $p<0.05$).

“The results of the SKYLARK Study are incredibly encouraging and show the potential positive impact zuranolone could have for women with PPD. Rapid symptom relief is critical for women with PPD, because delays in treatment efficacy can negatively impact resolving depressive symptoms and overall clinical outcomes for mother and baby,” said Dr. Kristina Deligiannidis, Principal Investigator of the study and Professor, the Feinstein Institutes for Medical Research in Manhasset, New York. “I’ve seen the consequences PPD can have on a mother’s ability to care for herself, her baby, and her family in a way that can have a generational impact. There are currently no oral therapies approved for PPD and we desperately need new treatment options to help women get well as soon as possible and stay well.”

Additional secondary endpoints showed further evidence of the potential impact of zuranolone on the reduction of other PPD related symptoms, including anxiety in these patients. Treatment with zuranolone was shown to significantly improve symptoms of anxiety at Days 3, 8, 15, and 45 ($p<0.05$, at all time points) when compared to placebo as measured by the Hamilton Anxiety Rating Scale (HAM-A).

In the SKYLARK Study, zuranolone was generally well-tolerated, with a safety profile consistent with that observed in the clinical development program to date. The majority of treatment-emergent adverse events (TEAEs) experienced by women in both treatment groups were mild to moderate in severity. A total of two participants (all in the zuranolone group) experienced four serious adverse events all of which were assessed by the investigator as unrelated to the therapy. Common TEAEs (>5% in the zuranolone 50 mg arm) were somnolence, dizziness, sedation, headache, diarrhea, nausea, urinary tract infection and COVID-19.

Sage Therapeutics and Biogen have initiated a rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration for zuranolone in the treatment of MDD and PPD, and plan to complete the NDA filing in the second half of 2022.

About Postpartum Depression (PPD)

Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy.[1] PPD can have a serious negative impact on a woman, including significant functional impairment, depressed mood and/or loss of interest in her newborn, and associated symptoms of depression such as loss of appetite, difficulty sleeping, motor challenges, lack of concentration, loss of energy and poor self-esteem. PPD is estimated to affect approximately one in eight women who have given birth in the U.S. or approximately 500,000 women annually.[2]

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.

Sage Therapeutics and Biogen have initiated a rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration for zuranolone in the treatment of MDD and PPD, and plan to complete the NDA filing in the second half of 2022. If approved, zuranolone would be the first oral medication specifically indicated to treat PPD.

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.

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Sage Therapeutics Safe Harbor

Various statements in this release concern Sage's future expectations, plans and prospects, including without limitation our statements regarding: plans for completing the NDA filing for zuranolone in MDD and PPD, and the anticipated timing of such filing; the potential profile and benefit of zuranolone in the treatment of PPD; our belief that the data from the SKYLARK Study support the potential of zuranolone in the treatment of 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 experience delays or unexpected hurdles in our efforts to complete the NDA submission for zuranolone in MDD and PPD, and we may not be able to complete such filing on the timelines we expect or at all; the FDA may find inadequacies and deficiencies in our NDA for zuranolone, including in the data we submit, despite prior discussions, and may decide not to accept the NDA for filing; even if the FDA accepts the NDA for filing, 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; the FDA may not meet expected review timelines for our NDA; 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 that negatively impact further development or the potential or scope of approval or that require additional nonclinical and clinical work which may not yield positive results; the need to align with our collaborators may hamper or delay our development and commercialization efforts or increase our costs; the number of patients with PPD, the unmet need for additional treatment options and the potential market for zuranolone in the treatment of PPD, if approved, may be significantly smaller than we expect; and we may encounter technical and other unexpected hurdles which may delay our timing or change our plans, increase our costs or otherwise negatively impact our efforts to gain approval of zuranolone and to make it available as a treatment option for MDD and PPD 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.

References*:*

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