Sage Therapeutics and Biogen Initiate Rolling Submission of New Drug Application (NDA) to U.S. Food and Drug Administration for Zuranolone for the Potential Treatment of Major Depressive Disorder (MDD)

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The companies expect to complete submission of the NDA for treatment of MDD in the second half of 2022; associated filing for postpartum depression anticipated in the first half of 2023

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 2, 2022-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) initiated a rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for zuranolone in the treatment of major depressive disorder (MDD). Zuranolone is an investigational two-week, once-daily oral drug being developed for MDD and postpartum depression (PPD). The companies have submitted the nonclinical module of the NDA to the FDA and plan to submit the remaining components for the MDD filing in the second half of 2022.

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Data from the completed studies of zuranolone in the LANDSCAPE and NEST clinical development programs, including data from the ongoing open-label SHORELINE Study in MDD, as well as data from the completed clinical pharmacology studies, will comprise the full submission package. The rolling submission process allows completed sections of an NDA to be submitted to the FDA for review on an ongoing basis.

“There are millions of people living with depression and the initiation of the rolling NDA submission brings us one step closer to our goal of offering zuranolone as a potential new treatment option,” said Barry Greene, Chief Executive Officer at Sage. “We believe the results from the LANDSCAPE and NEST programs, in which zuranolone demonstrated rapid and sustained effects and a well-tolerated safety profile in clinical trials, support zuranolone as a potential novel treatment option for MDD, if approved. We look forward to providing an update when the rolling submission for zuranolone in MDD is complete, which we expect to occur in the second half of this year.”

“Zuranolone has the potential to help address a significant unmet medical need in depression as an innovative option in a therapeutic area where little has changed in the past 30 years,” said Priya Singhal, M.D., M.P.H., Head of Global Safety and Regulatory Sciences and Interim Head of R&D at Biogen. “We are committed to advancing the science and developing new approaches to treating mental health, a major public health challenge that was exacerbated by the COVID-19 pandemic.”

Zuranolone was granted Fast Track Designation by the FDA in 2017 in MDD and Breakthrough Therapy Designation in 2018. Sage and Biogen plan to submit an associated NDA filing for PPD in the first half of 2023.

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 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 people with PPD (ROBIN and SKYLARK Studies). Additionally, Shionogi completed a Phase 2 study of zuranolone in Japan in people with MDD.

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 more than 21 million adults[1] in the U.S. and approximately 280 million people[2] worldwide suffer from depression. While antidepressants are widely used to treat MDD, large-scale studies have demonstrated the need for additional therapies with a differentiated profile.

About Postpartum Depression (PPD)

Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy. 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[3] women annually.

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 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: plans for completing the NDA filing for zuranolone in MDD and for submitting an associated NDA filing in PPD, and the anticipated timing of such activities; our belief in the potential profile and benefit of zuranolone in the treatment of depression; our belief that the data from our clinical programs support the potential of zuranolone in the treatment of depression; our plan to request priority review for our NDA; our goal of making zuranolone available as a new treatment option in the treatment of depression; the potential for approval of zuranolone in the treatment of depression; 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 to make the associated filing in PPD, and we may not be able to complete such activities 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 grant priority review for our NDA; 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; we may experience negative results in the ongoing SKYLARK Study in PPD that negatively affect our ability to file the associated NDA for approval of zuranolone in PPD; 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 that negatively impact further development 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 MDD and PPD, the unmet need for additional treatment options and the potential market for zuranolone in the treatment of depression, 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 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 annual/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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3. Bauman BL, Ko JY, Cox S, D'Angelo Mph DV, Warner L, Folger S, Tevendale HD, Coy KC, Harrison L, Barfield WD. Vital Signs: Postpartum Depressive Symptoms and Provider Discussions About Perinatal Depression—United States *Morb Mortal Wkly Rep.* 2020; 69(19):575-581.

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