Sage Therapeutics and Biogen Announce FDA Accepts Filing of New Drug Application and Grants Priority Review of Zuranolone in the Treatment of Major Depressive Disorder and Postpartum Depression

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Zuranolone is being evaluated as a potential 14-day, rapid-acting, once-daily, oral medication to treat major depressive disorder (MDD) and postpartum depression (PPD)

Depression is a public health issue with significant unmet medical need

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 6, 2023-- Sage Therapeutics, Inc. (Nasdaq: SAGE) and Biogen Inc. (Nasdaq: BIIB) announced the U.S. Food and Drug Administration (FDA) has accepted the filing of a New Drug Application (NDA) for zuranolone in the treatment of major depressive disorder (MDD) and postpartum depression (PPD). Zuranolone is an investigational drug being evaluated as a 14-day, rapid-acting, once-daily, oral treatment in adults with MDD and PPD. The application has been granted priority review and the FDA has assigned a Prescription Drug User Fee Act (PDUFA) action date of August 5, 2023.

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“We see potential for zuranolone, if approved, to be a meaningful new option that can help address the serious unmet need faced by the diverse populations struggling with MDD and PPD,” said Priya Singhal, M.D., M.P.H., Executive Vice President, Head of Development and Interim Head of Research and Global Safety and Regulatory Sciences at Biogen. “The FDA filing acceptance and granting of priority review are important milestones in the mission Biogen and our collaboration partner Sage share to advance the understanding and treatment of depression.”

Depression is one of the leading contributors to disability worldwide.[1] It is estimated that more than 21 million adults in the U.S. experienced at least one major depressive episode in 2020, with nearly 14 million people diagnosed with major depressive disorder,[2] and an estimated 500,000 cases of PPD annually.[3] Symptoms of MDD and PPD have been shown to have an impact on a person’s overall quality of life, functioning and well-being. In 2018, the incremental economic burden of MDD was an estimated $326 billion in the U.S. alone.[4]

The zuranolone NDA includes data from the LANDSCAPE and NEST clinical development programs as well as a Phase 2 study of zuranolone completed by Shionogi in Japan in adults with MDD. The LANDSCAPE program includes five studies of zuranolone in adults with MDD (MDD-201B, MOUNTAIN, SHORELINE, WATERFALL, and CORAL). The NEST program includes two studies of zuranolone in adult women with PPD (ROBIN and SKYLARK).

“We feel a tremendous responsibility to patients with MDD and PPD to deliver a potential new treatment option, which is so desperately needed. Most current approved therapies may take weeks or months to work. We are committed to advancing treatments that could help physicians and patients by addressing depression symptoms quickly,” said Laura Gault, M.D., Ph.D., Chief Medical Officer at Sage. “We believe zuranolone, if approved, could offer a new way for physicians to support patients.”

Zuranolone, a neuroactive steroid, has a novel mechanism of action as a positive allosteric modulator of GABA-A receptors. In people with depression, it is thought to work by rapidly rebalancing dysregulated neuronal networks to help reset brain function. Zuranolone targets brain networks responsible for functions such as mood, arousal, behavior, and cognition.

Priority Review is granted by the FDA to applications for medicines that, if approved, would provide significant improvements in the effectiveness or safety of the treatment, diagnosis, or prevention of serious conditions.

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 in 2020, more than 21 million adults in the U.S. experienced at least one major depressive episode in the past year with nearly 14 million people diagnosed with major depressive disorder.[2] There were approximately 190 million cases of MDD worldwide in 2020.[5]

About Postpartum Depression (PPD)

Postpartum depression (PPD) is one of the most common medical complications during and after pregnancy.[6] 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.[3]

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 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 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 pipelines in neuroscience that will transform the standard of care for patients in several areas of high unmet need.

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 for approval of zuranolone in the treatment of MDD and PPD and the potential benefit of zuranolone, if approved, as a new treatment option in the treatment of MDD and PPD; our expectations regarding the PDUFA date for our NDA; our estimates as to the number of people with MDD and PPD and the need for new treatment options; and other statements as to our mission, goals and plans. 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 find that the data included in our NDA for zuranolone are not sufficient for approval and may not approve the NDA or may grant a more narrow or limited approval than we are seeking; 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 or there may be other delays in such timelines; an Advisory Committee of the FDA, if convened, may not recommend approval of our NDA or may recommend a more narrow approval than we are seeking; other decisions or actions of the FDA 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 that negatively impact further development or that require additional nonclinical and clinical work which may not yield positive results; the number of patients with MDD and PPD, the unmet need for additional treatment options and the potential profile and market for zuranolone in the treatment of MDD and 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:

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.
2. SAMHSA: 2020 NSDUH Detailed Tables.
3. Bauman BL, et al. Morbidity and Mortality Weekly Report, 2020;69(19):575-581.
4. Greenberg PE, Fournier AA, Sisitsky T, et al. The economic burden of adults with major depressive disorder in the United States (2010 and 2018). Pharmacoeconomics. 2021;39(6):653-665.
5. Santomauro DF, Mantilla Herrera AM, Shadid J, et al. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. Lancet. 2021;398(10312):1700-1712.
6. "ACOG Committee Opinion No. 757: Screening for Perinatal Depression." Obstetrics and gynecology vol. 132,5 (2018): e208-e212. doi:10.1097/AOG.0000000000002927.

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