FDA Accepts Biogen's New Drug Application and Grants Priority Review of Tofersen for a Rare, Genetic Form of ALS

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- SOD1-ALS is a rare genetic form of ALS that affects approximately 330 people in the U.S.,[1] it is progressive, leads to the loss of everyday functions and is uniformly fatal
- If approved, tofersen would be the first treatment to target a genetic cause of ALS
- 12-month data included in the filing show that earlier initiation of tofersen slowed decline across measures of clinical and respiratory function, strength, and quality of life

CAMBRIDGE, Mass., July 26, 2022 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced that the U.S. Food and Drug Administration (FDA) has accepted a New Drug Application (NDA) for tofersen, an investigational drug for superoxide dismutase 1 (SOD1) amyotrophic lateral sclerosis (ALS). The application has been granted priority review and given a Prescription Drug User Fee Act action date of January 25, 2023. The FDA has noted that it is currently planning to hold an Advisory Committee meeting for this application, on a yet-to-be determined date. The average life expectancy for people with ALS is three to five years from time of symptom onset. There is currently no treatment targeted for SOD1-ALS.[2]

"The available data show that tofersen has the potential to make a meaningful difference for people with SOD1-ALS," said Priya Singhal, M.D., M.P.H., Head of Global Safety and Regulatory Sciences and Interim Head of R&D at Biogen. "Pursuing the FDA's accelerated approval pathway offers the potential to make tofersen available to people living with this fatal, neurodegenerative disease as quickly as possible. If approved, tofersen will be the first treatment to target a genetic cause of ALS and we hope this will pave the way for further advances in this relentless disease."

Biogen is seeking approval of tofersen under the FDA's accelerated approval pathway, based on the use of neurofilament as a surrogate biomarker that is reasonably likely to predict clinical benefit. Neurofilaments are normal proteins found in healthy neurons, that are increased in blood and cerebrospinal fluid when damage has been done to neurons or their axons and are a marker of neurodegeneration. In ALS, higher levels of neurofilaments have been found to predict more rapid decline in clinical function and shortened survival.[3] Tofersen study results suggest reductions in neurofilament preceded and predicted slowing of decline in measures of clinical and respiratory function, strength, and quality of life. Biogen is committed to ongoing data generation and finalizing the confirmatory data package with the FDA.

"The 12-month results showed that individuals with SOD1-ALS who started tofersen earlier experienced a slower rate of decline in clinical and respiratory function, strength and quality of life. These are critical measures for people living with this devastating disease," said Timothy Miller, M.D., Ph.D., principal investigator of VALOR and ALS Center co-Director at Washington University School of Medicine, St. Louis. "For people in my clinic living with SOD1-ALS, tofersen may meaningfully slow the rapid progression of their disease and the impact it has on their lives."

The tofersen NDA included results from a Phase 1 study in healthy volunteers, a Phase 1/2 study evaluating ascending dose levels, the Phase 3 VALOR study, and the open label extension (OLE) study. Also included are the most current 12-month integrated results from VALOR and the OLE study, recently presented at the European Network to Cure ALS (ENCALS) annual meeting.

As previously reported in October 2021, VALOR, a six-month Phase 3 randomized study, did not meet the primary endpoint of change from baseline to week 28 in the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale. However, trends of reduced disease progression across multiple secondary and exploratory endpoints were observed. The 12-month integrated data showed that earlier initiation of tofersen led to sustained reductions in neurofilament, a marker of neurodegeneration and slowed decline across multiple efficacy endpoints.

In the 12-month data, the most common adverse events (AEs) in participants receiving tofersen in VALOR and the OLE study were headache, procedural pain, fall, back pain and pain in extremities. Most AEs in both VALOR and the OLE were mild to moderate in severity. Serious neurologic events including myelitis, radiculitis, aseptic meningitis, and papilledema, were reported in 6.7 percent of participants receiving tofersen in VALOR and its OLE.

During the FDA review period Biogen will maintain its early access program for tofersen, now with participants in over a dozen countries. The open-label extension and Phase 3 ATLAS study in presymptomatic individuals with a SOD1 genetic mutation remain ongoing. Biogen is actively engaging with other regulators around the world and will provide updates when appropriate.

About Tofersen
Tofersen is an antisense drug being evaluated for the potential treatment of SOD1-ALS. Tofersen binds to SOD1 mRNA, allowing for its degradation by RNase-H in an effort to reduce synthesis of SOD1 protein production. In addition to the ongoing open label extension of VALOR, tofersen is being studied in the Phase 3 ATLAS study designed to evaluate whether tofersen can delay clinical onset when initiated in presymptomatic individuals with a SOD1 genetic mutation and biomarker evidence of disease activity. Biogen licensed tofersen from Ionis Pharmaceuticals, Inc. under a collaborative development and license agreement.

About Amyotrophic Lateral Sclerosis and SOD1-ALS
Amyotrophic lateral sclerosis (ALS) is a rare, progressive and fatal neurodegenerative disease that results in the loss of motor neurons in the brain and the spinal cord that are responsible for controlling voluntary muscle movement. People with ALS experience muscle weakness and atrophy, causing them to lose independence as they steadily lose the ability to move, speak, eat, and eventually breathe. Average life expectancy for people with ALS is three to five years from time of symptom onset.[2]

Multiple genes have been implicated in ALS. Genetic testing helps determine if a person's ALS is associated with a genetic mutation, even in individuals without a family history of the disease. Currently, there are no genetically targeted treatment options for ALS. Mutations in the SOD1 gene are responsible for approximately 2 percent of the estimated 168,000 people who have ALS globally (SOD1-ALS).[1] Life expectancy in SOD1-ALS varies widely with some patients surviving less than a year.[4]

Biogen's Continuous Commitment to ALS
For over a decade, Biogen has been committed to advancing ALS research to provide a deeper understanding of all forms of the disease. The company has continued to invest in and pioneer research despite making the difficult decision to discontinue a late-stage ALS asset in 2013. Biogen has applied important learnings to its portfolio of assets for genetic and other forms of ALS, with the goal of increasing the probability of bringing a potential therapy to patients in need. These applied learnings include evaluating genetically validated targets in defined patient populations, pursuing the most appropriate modality for each target and employing sensitive clinical endpoints. Today, the company has a pipeline of investigational drugs being evaluated in ALS, including tofersen and BIIB105.

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 pipelines 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.

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, including statements about results from the Phase 3 VALOR study of tofersen or its OLE; the potential clinical effects of tofersen; the potential benefits, safety and efficacy of tofersen; the clinical development program for tofersen; the potential approval of tofersen; the identification and treatment of ALS; our research and development program for the treatment of ALS; the potential of our commercial business and pipeline programs, including tofersen; 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 tofersen; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; unexpected concerns may arise from additional data, analysis or results obtained during our clinical trials; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including tofersen; the occurrence of adverse safety events; the risks of unexpected hurdles, costs or delays; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; product liability claims; 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 our expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this news release.

We do 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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