Biogen's QALSODY® (tofersen), the First Therapy to Treat Rare, Genetic Form of ALS, Received Positive Opinion from CHMP

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- *SOD1*-ALS is a devastating, uniformly fatal, and ultra-rare genetic form of ALS affecting less than 1,000 people in Europe[1]
- With QALSODY, Biogen has advanced the role of neurofilament in the development of new medicines for ALS, with the potential to accelerate further discovery in the field

CAMBRIDGE, Mass., Feb. 23, 2024 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending a marketing authorization under exceptional circumstances for QALSODY® (tofersen) for the treatment of adults with amyotrophic lateral sclerosis (ALS), associated with a mutation in the superoxide dismutase 1 (*SOD1*) gene. If authorized by the European Commission (EC), QALSODY will be the first treatment approved in the European Union to target a genetic cause of ALS, also known as motor neuron disease (MND).

"The CHMP's positive opinion reinforces the impact QALSODY can have in *SOD1*-ALS and further demonstrates Biogen's commitment to address the unmet needs of people living with ALS and neuromuscular diseases," said Priya Singhal, M.D., M.P.H., Head of Development at Biogen. "We are proud to help pioneer the role of neurofilament in *SOD1*-ALS clinical trials and are deeply grateful to the people living with *SOD1*-ALS, their loved ones and study care teams for their dedication to furthering research for the ALS community."

The CHMP's recommendation for QALSODY is based on the totality of evidence, including the targeted mechanism of action, biomarker and clinical data. In the 28-week Phase 3 VALOR study, reductions of 60% in plasma neurofilament light chain (NfL) were observed in participants who received QALSODY compared to the placebo group, suggesting reduced neuronal injury. Trends towards improvement in the physical abilities of participants who received QALSODY were seen compared to those who received placebo, as measured by the ALS Functional Ratings Scale-Revised (ALSFRS-R). The most common side effects that occurred in ≥10% of QALSODY treated participants and more than the placebo arm were pain, fatigue, fever, joint pain, muscle pain and increased levels of white blood cells and proteins in the cerebrospinal fluid. Serious neurologic events, including myelitis and/or radiculitis; papilledema and elevated intracranial pressure; and aseptic meningitis have also been reported.

"The CHMP's recommendation in support of QALSODY approval provides new hope for the ALS community in Europe," said Philip Van Damme, M.D., Ph.D., professor of neurology and director of the Neuromuscular Reference Center at the University Hospital Leuven in Belgium. "This is a significant milestone for the entire ALS community - for the first time we have a treatment that led to sustained reductions in neurofilament, a marker of axonal injury and neurodegeneration. The QALSODY development program has provided critical learnings on clinical trial design and the use of biomarkers that is advancing the entire field."

A marketing authorization under exceptional circumstances is recommended when the benefit/risk assessment is determined to be positive but due to the rarity of the disease, it is unlikely that comprehensive data can be obtained under normal conditions of use. The CHMP's recommendation for QALSODY will now be reviewed by the EC for a decision on a marketing authorization in the European Union, with a decision expected in the second quarter of 2024.

About QALSODY® (tofersen)

QALSODY® (tofersen) is an antisense oligonucleotide (ASO) designed to bind to *SOD1* mRNA to reduce SOD1 protein production. The U.S. Food and Drug Administration granted accelerated approval for QALSODY to treat amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene. This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with QALSODY. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).[2]

Biogen licensed QALSODY from Ionis Pharmaceuticals, Inc. under a collaborative development and license agreement. QALSODY was discovered by Ionis.

In addition to the ongoing open label extension (OLE) of the Phase 3 VALOR study, QALSODY is being studied in the Phase 3, randomized, placebo-controlled ATLAS study to evaluate whether QALSODY can delay clinical onset when initiated in presymptomatic individuals with a *SOD1* genetic mutation and biomarker evidence of disease activity (elevated plasma NfL). More details about ATLAS (NCT04856982) can be found at clinicaltrials.gov.

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.[3]

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 known family history of the disease. Mutations in the *SOD1* gene are responsible for approximately 2 percent of the estimated 168,000 people who have ALS globally (*SOD1*-ALS).[1] More than 15 percent of people with ALS are thought to have a genetic form of the disease; [4] however, they may not have a known family history of the disease.[1]

In people with *SOD1*-ALS, mutations in their *SOD1* gene cause their bodies to create a toxic misfolded form of SOD1 protein. This toxic protein causes motor neurons to degenerate, resulting in progressive muscle weakness, loss of function, and eventually, death.[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. In addition to QALSODY, the company has a pipeline of investigational drugs being evaluated in ALS, including BIIB105.

About Biogen
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patient's lives and to create value for shareholders and our communities. We apply deep understanding of human biology and leverage different modalities to advance first-in-class treatments or therapies that deliver superior outcomes. Our approach is to take bold risks, balanced with return on investment to deliver long-term growth.

We routinely post information that may be important to investors on our website at www.biogen.com. Follow us on social media - Facebook, LinkedIn, X, YouTube.

Biogen Safe Harbor
This news release contains forward-looking statements, the potential clinical effects of QALSODY; the potential benefits, safety and efficacy of QALSODY; the clinical development program for QALSODY; 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 QALSODY; 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 our forward-looking statements.

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; 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 speak only as of the date of this news release.

We do not undertake any obligation to publicly update any forward-looking statements.

References:

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2. QALSODY Prescribing Information, Cambridge, MA: Biogen.
3. National Institute of Neurological Disorders and Stroke. Amyotrophic Lateral Sclerosis (ALS). Available at: https://www.ninds.nih.gov/health-information/disorders/amyotrophic-lateral-sclerosis-als. Accessed: April 2023.
4. Akcimen F, Lopez ER, Landers JE, et al. Amyotrophic lateral sclerosis: translating genetic discoveries into therapies. Nat Rev Genet. 2023. https://doi.org/10.1038/s41576-023-00592-y

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