Biogen Receives European Commission Approval for QALSODY® (tofersen), the First Therapy to Treat a Rare, Genetic Form of ALS

May 30, 2024

- *SOD1*-ALS is a devastating, uniformly fatal, and ultra-rare genetic form of ALS estimated to affect less than 1,000 people in Europe[1]
- QALSODY is Biogen's third rare disease therapy to be approved in the EU, demonstrating the company's commitment to addressing diseases with a high unmet need
- With QALSODY, Biogen has helped advance neurofilament as a tool to optimize clinical trial design in ALS, offering the potential to expedite further breakthroughs in the field

CAMBRIDGE, Mass., May 30, 2024 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) announced the European Commission (EC) has granted marketing authorization under exceptional circumstances and maintained orphan designation for QALSODY® (tofersen) for the treatment of adults with amyotrophic lateral sclerosis (ALS) associated with a mutation in the superoxide dismutase 1 gene (*SOD1*-ALS). QALSODY is the first treatment approved in the European Union to target a genetic cause of ALS, also known as motor neuron disease (MND).

"The European Commission's approval of QALSODY is a testament to the unwavering dedication of the ALS community – people living with ALS and their loved ones, scientists, clinicians, and advocates – who have worked together over the past two decades to bring forward this important new treatment for the *SOD1*-ALS community," said Stephanie Fradette, Pharm.D., Head of the Neuromuscular Development Unit at Biogen. "We are working with the medical community and local authorities to bring QALSODY to people living with *SOD1*-ALS across the region as quickly as possible."

The marketing authorization for QALSODY is granted under exceptional circumstances, which is recommended when the benefit/risk assessment of a treatment 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 European Medicines Agency (EMA) recommended QALSODY's designation as an orphan medicinal product be maintained.

"QALSODY's approval represents a paradigm shift in the treatment of *SOD1*-ALS, offering hope to patients and loved ones who have long awaited a breakthrough," 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. "The European Academy of Neurology has confirmed new treatment guidelines for ALS that recognize QALSODY should be offered as first-line treatment for patients with *SOD1*-ALS."

The approval of QALSODY is based on the totality of evidence, including the targeted mechanism of action, biomarker, and clinical data. In the randomized, double-blind, placebo-controlled Phase 3 VALOR study (n=108), patients were randomized 2:1 to receive treatment with either QALSODY 100 mg (n=72) or placebo (n=36) for 24 weeks. The primary efficacy endpoint was the change from baseline to Week 28 in the ALS Functional Ratings Scale-Revised total score. The results numerically favored tofersen, but were not statistically significant (ITT population: tofersen-placebo adjusted mean difference [95% CI]: 1.4 [-1.3, 4.1]). At Week 28, mean plasma neurofilament light chain (NfL), a marker of axonal injury and neurodegeneration, was reduced by 55% (geometric mean ratio to baseline) in the tofersen-treated participants (ITT), compared to a 12% increase with placebo (difference in geometric mean ratios for tofersen to placebo: 60% (95% CI: 51%, 67%)). Very common adverse reactions (may affect more than 1 in 10 people) reported in QALSODY-treated participants were pain (back pain, pain in arms or legs), feeling tired, muscle and joint pain, fever, and an increase in protein and/or white blood cell count occurring in the fluid that surrounds the brain and spinal cord.

"At EUpALS, we are excited that people with *SOD1*-ALS in Europe will have access to QALSODY, the first treatment targeting a genetic cause of ALS. This is a major milestone for the ALS community, showing that ALS is a treatable disease," said Evy Reviers, Chairwoman of the European Organisation for Professionals and People living with ALS (EUpALS). "As a representative of the European ALS community, I am excited to enter a new evolution in the common fight against ALS. We thank Biogen for the many years of scientific and clinical pioneering efforts that led to this medical success."

Biogen is committed to working closely with all stakeholders to enable access to this treatment for eligible European patients. Through the Biogen early access program, about 330 people with *SOD1*-ALS have received QALSODY across 18 EU countries. QALSODY is also approved for use in the United States and Biogen is engaging with regulatory authorities in other regions.

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] The European Commission granted marketing authorization under exceptional circumstances and orphan designation for QALSODY.

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% of the estimated 168,000 people who have ALS globally (*SOD1*-ALS).[1] More than 15% 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 robust discovery pipeline including efforts to address TDP43 pathology for the broad ALS population. TDP43 pathology is seen in 97% of ALS cases and is considered a hallmark of the disease.

About Biogen
Founded in 1978, Biogen is a leading biotechnology company that pioneers innovative science to deliver new medicines to transform patients' 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 QALSODY; 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 QALSODY; 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:

1. Brown CA, Lally C, Kupelian V, Flanders WD. Estimated Prevalence and Incidence of Amyotrophic Lateral Sclerosis and SOD1 and C9orf72 Genetic Variants. Neuroepidemiology. 2021;55(5):342-353. doi: 10.1159/000516752. Epub 2021 Jul 9.
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 2024.
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

MEDIA CONTACT:
Biogen
Jack Cox
+ 1 781 464 3260
public.affairs@biogen.com

INVESTOR CONTACT:
Biogen
Chuck Triano
+1 781 464 2442
IR@biogen.com