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

- *SOD1*-ALS is a devastating, uniformly fatal, and ultra-rare genetic form of ALS estimated to affect less than 1,000 people in Europe¹
- 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

Biogen 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 Reviere, 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.

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.

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.

Source: **Biogen**

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