Biogen's QALSODY® (tofersen) Approved in the UK as the First Therapy to Treat a Rare, Genetic Form of Motor Neurone Disease

- *SOD1*-ALS is a devastating, uniformly fatal, and ultra-rare genetic form of amyotrophic lateral sclerosis (ALS), also known as motor neurone disease (MND)[1]
- 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[2]
- Tofersen is the first treatment to be approved in the UK to target a genetic cause of ALS
- With tofersen, Biogen has helped advance neurofilament as an *in vitro* tool to optimise clinical trial design in ALS, offering the potential to expedite further breakthroughs in the field

Maidenhead, UK. – 28 July, 2025 – Biogen UK today announced the United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA) has granted marketing authorisation for QALSODY® (tofersen) through the International Recognition Procedure (IRP) for the treatment of adults with amyotrophic lateral sclerosis (ALS) associated with a mutation in the superoxide dismutase 1 gene (*SOD1*-ALS).[3] The decision follows the European Commission granting marketing authorisation under exceptional circumstances for tofersen in May 2024.[4]

Despite decades of research, ALS, also known as motor neurone disease (MND), remains an exceptionally difficult condition to treat due to its biological complexity, variability in progression, and the lack of reliable biomarkers or effective models.[1,2] These obstacles, coupled with the rarity of the disease and previous clinical trial setbacks, have historically hindered drug development. Tofersen is the first treatment that has been granted marketing authorisation by the MHRA in the UK to target a genetic cause of ALS.

The three main UK MND charities - MND Scotland, MND Association and My Name'5 Doddie Foundation - welcome the MHRA's decision to approve tofersen in the UK. They said: "As the first targeted gene therapy to prolong survival, tofersen is a genuine breakthrough for people with a type of MND that arises from an alteration in the *SOD1* gene. This is a significant milestone for the MND community as it's the first new treatment to receive marketing authorisation in the UK in almost 30 years. This news gives hope to the whole community that, with research investment, treatments for MND will be found."

"The MND community have been waiting for a long time for significant progress in the development of effective treatments that help slow disease progression. This authorisation stands as both a major scientific achievement and a clear indication of the advances being made for those affected by this condition," said Professor Ammar Al-Chalabi, Professor of Neurology and Complex Disease Genetics, King's College London. "Until now there have been no treatment options specifically for people with *SOD1*-ALS, which is an ultra-rare condition that sadly leads to the loss of everyday functions and ultimately death. The approval of tofersen means that we may be able to access a therapeutic option that has the potential to improve the lives of people living with this devastating disease."

The approval of tofersen is based on the totality of evidence, including the targeted mechanism of action, biomarker, and clinical data. It is supported by data from the Phase 3 VALOR study and 12-

month integrated results from VALOR and its open-label extension (OLE), comparing earlier initiation of tofersen (at the start of VALOR) to delayed initiation of tofersen (six months later, in the OLE).[5]

"We are incredibly proud to announce the MHRA approval of tofersen in the UK which is a major milestone in our mission to improve the lives of those living with rare diseases," said Dr. Kylie Bromley, General Manager, Biogen UK & Ireland. "This approval represents not only a significant scientific and regulatory achievement, but more importantly, a moment of real hope for the MND community. This progress would not have been possible without the dedication of the researchers, clinicians, and trial participants here in the UK who worked tirelessly to bring tofersen to this point.

“The next step for tofersen is reimbursement on the National Health Service (NHS) to ensure this treatment is made available to patients as quickly as possible. In the UK, rigid cost-effectiveness thresholds are applied which present challenges for the reimbursement of rare disease medicines. These are medicines that demonstrate potential efficacy and promise for patients but, due to the rarity of the conditions, are invariably supported by limited data and high levels of uncertainty. We are calling for flexibility from the National Institute for Health and Care Excellence (NICE), Scottish Medicines Consortium (SMC) and NHS England to secure long-term and sustainable access for tofersen through a collaborative reimbursement process.”

Biogen is committed to working closely with stakeholders including NICE, the SMC and the NHS but is encouraging collaboration from all sides. Tofersen is also approved for use in the United States and European Union and Biogen is engaging with regulatory authorities in other regions.[4,6]

Ends

Notes to the Editors

About QALSODY® (tofersen)
QALSODY® (tofersen) is an antisense oligonucleotide (ASO) designed to bind to *SOD1* mRNA to reduce SOD1 protein production.[7] In April 2023, The U.S. Food and Drug Administration granted accelerated approval for tofersen to treat amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene.[6] This indication is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with tofersen.[6] Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).[6,7] In May 2024, the European Commission granted marketing authorisation under exceptional circumstances and orphan designation for tofersen.[4]

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

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.[1,2] 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.[1,2] 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.[1,2] 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.[1,2] Mutations in the *SOD1* gene are responsible for approximately 2% of the estimated 168,000 people who have ALS globally (*SOD1*-ALS).[1,5] More than 15% of people with ALS are thought to have a genetic form of the disease;[8,9] however, they may not have a known family history of the disease.[1] *SOD1*-ALS is estimated to affect less than 60 people in the UK.[1,9]

In people with *SOD1*-ALS, mutations in their *SOD1* gene cause their bodies to create a toxic misfolded form of SOD1 protein.[5,8] This toxic protein causes motor neurons to degenerate, resulting in progressive muscle weakness, loss of function, and eventually, death.[8]

About the VALOR Study[5]

In the randomised, double-blind, placebo-controlled Phase 3 VALOR study (n=108), patients were randomised 2:1 to receive treatment with either tofersen 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 favoured 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 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 tofersen-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.[5,7]

Biogen's Continuous Commitment to ALS

For nearly two decades, Biogen has been committed to advancing ALS research to provide a deeper understanding of all forms of the disease. Despite setbacks and disappointments[10,11], the company has continued to invest in and pioneer research. 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 tofersen, 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 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.

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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.
2. 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: July 2025.
3. Qalsody. Summary of Product Characteristics.
4. Biogen. Biogen Receives European Commission Approval for QALSODY® (tofersen), the First Therapy to Treat a Rare, Genetic Form of ALS. Biogen Press Release, 30 May 2024. Available at: https://investors.biogen.com/news-releases/news-release-details/biogen-receives-european-commission-approval-qalsodyr-tofersen. Last accessed: July 2025.
5. Miller TM., *et al*. Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS. *N Engl J Med*. 2022;387(12):1099-1110.
6. Biogen. FDA Grants Accelerated Approval for QALSODY™ (tofersen) for SOD1-ALS, a Major Scientific Advancement as the First Treatment to Target a Genetic Cause of ALS. Biogen Press Release, 25 April 2023. Available at: https://investors.biogen.com/news-releases/news-release-details/fda-grants-accelerated-approval-qalsodytm-tofersen-sod1-als. Last accessed: July 2025.
7. QALSODY U.S. Prescribing Information, Cambridge, MA: Biogen.
8. Akçimen F, Lopez ER, Landers JE, *et al*. Amyotrophic lateral sclerosis: translating genetic discoveries into therapies. *Nat Rev Genet*. 2023;24(9):642-658.
9. National Institute for Health and Care Excellence. Highly Specialised Technologies (HST) criteria checklist Tofersen for treating amyotrophic lateral sclerosis caused by SOD1 gene mutations. Available at: https://www.nice.org.uk/guidance/gid-hst10062/documents/h-s-t-checklist. Last accessed: July 2025.
10. Biogen. Biogen Idec Reports Top-Line Results From Phase 3 Trial Investigating Dexpramipexole In People With Amyotrophic Lateral Sclerosis (ALS). Biogen Press Release, 3 January 2013. Available at: https://investors.biogen.com/news-releases/news-release-details/biogen-idec-reports-top-line-results-phase-3-trial-investigating. Last accessed: July 2025.
11. Biogen. Biogen Announces Topline Results From The Tofersen Phase 3 Study And Its Open-Label Extension In SOD1-ALS. Biogen Press Release, 17 October 2021. Available at: https://investors.biogen.com/news-releases/news-release-details/biogen-announces-topline-results-tofersen-phase-3-study-and-its. Last accessed: July 2025.

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