The Journal of the American Medical Association (JAMA) Neurology Publishes Long Term Results from the QALSODY Phase 3 VALOR Study and its Open-Label Extension in SOD1-ALS

December 22, 2025

- Long-term data published in *JAMA Neurology* further illustrate the effects of Biogen's QALSODY on function, strength, and survival in *SOD1*-ALS
- Over 3 years, a subset of QALSODY-treated participants regained previously lost function and strength, something not previously reported in the natural history of *SOD1*-ALS
- Biogen is committed to advancing additional ALS research, including the ongoing QALSODY ATLAS study in pre-symptomatic *SOD1*-ALS and a robust discovery pipeline in ALS

CAMBRIDGE, Mass., Dec. 22, 2025 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) – today announced that *The Journal of the American Medical Association (JAMA) Neurology* has published final results from the completed Phase 3 VALOR study and its open-label extension (OLE) study evaluating QALSODY® (tofersen) for the treatment of superoxide dismutase 1 (*SOD1*) amyotrophic lateral sclerosis (ALS) with over 3.5 years of follow-up. These results show that early initiation of QALSODY was associated with numerically slower decline in measures of clinical function, breathing and strength, as well as reduction in the risk of death or permanent ventilation. Sustained reductions in neurofilament, a marker of neurodegeneration, further validate the clinical results and demonstrate QALSODY's impact on the underlying biology of *SOD1*-ALS.

"The final VALOR/OLE data further emphasize that, with the right target paired with the right therapeutic approach, we have the potential to meaningfully impact the course of ALS and improve the outlook for people living with this devastating disease. Supported by these data, treatment-driven reductions in neurofilament are now being used as an early decision-making endpoint to accelerate future research," said Stephanie Fradette, Pharm.D., Head of the Neuromuscular Development Unit at Biogen. "We are excited to share this progress which would not have been possible without the study participants and their caregivers, investigators and site staff, and all who have contributed to the development of QALSODY over many years."

QALSODY 100 mg/15mL injection is approved for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (*SOD1*) gene. In the United States, QALSODY received 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).

QALSODY has received approval in 44 countries around the world, including accelerated approval in the US and conditional or standard approval in other countries.

About VALOR and the OLE
VALOR was a six-month Phase 3, randomized, double-blind, placebo-controlled study to evaluate the effects of tofersen 100 mg in adults with ALS associated with a *SOD1* mutation. In total, 108 participants were randomized in VALOR (n=72 to tofersen 100 mg and n=36 to placebo). Of these participants, 95 enrolled in the OLE. At the completion of the OLE, the median opportunity for follow-up was 4.9 years (range 3.6-5.4).

"For people living with ALS, irreversible loss of muscle strength is a foundational symptom of the disease. In the QALSODY study, 27% of study participants in the early-start group experienced improvements in muscle strength over ~3 years," said Timothy Miller, M.D., Ph.D., principal investigator of VALOR and ALS Center Director at Washington University School of Medicine in St. Louis. "This just does not happen in ALS: In the past, conversations with people living with *SOD1*-ALS were about how best to manage the progression of the disease, today these conversations include the potential for how to maximize improvement."

At the conclusion of VALOR and the OLE, the most common adverse events (AEs) were headache, procedural pain, fall, back pain and extremity pain. Serious neurological AEs of myelitis or radiculitis, papilledema and/or increased intracranial pressure, and chemical or aseptic meningitis were reported in nine participants (8.7%). These events were manageable with standard of care and resolved. One myelitis event and one chemical meningitis event led to treatment discontinuation. Safety findings are consistent with previously reported results.

"These final results illustrate what is possible with early initiation of QALSODY," said Merit Cudkowicz, M.D., co-principal investigator of the VALOR trial and co-founder of the Northeast ALS Consortium, Director of the Healey & AMG Center for ALS and Executive Director Mass General Brigham Neuroscience Institute and the Julieanne Dorn Professor of Neurology at Harvard Medical School. "In the faster-progressing participants, initiation of QALSODY just 6 months earlier was associated with a 3.4-year extension of event-free-survival. This makes all of us very excited about what we will learn from the presymptomatic ATLAS study where there is a possibility we could delay the onset of disease."

About QALSODY™(tofersen)
QALSODY is an antisense oligonucleotide (ASO) designed to bind to *SOD1* mRNA to reduce *SOD1* protein production. In the U.S., QALSODY is indicated for the treatment of ALS in adults who have a mutation in the *SOD1* gene. This indication is approved under accelerated approval based on reduction in plasma NfL observed in patients treated with QALSODY. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s). QALSODY is administered intrathecally as three loading doses administered at 14-day intervals followed by maintenance doses administered once every 28 days thereafter.[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.[2]

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

In addition to the ongoing OLE of VALOR, QALSODY is being studied in the Phase 3, randomized, placebo-controlled ATLAS study to evaluate

whether QALSODY can delay clinical onset of ALS when initiated in presymptomatic individuals with a *SOD1* genetic mutation and biomarker evidence of disease activity (elevated plasma NfL). The primary efficacy endpoint is the proportion of participants with emergence of clinically manifest ALS. 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. *SOD1*-ALS is diagnosed in approximately 2 percent of all ALS cases, with about 330 people in the United States living with the disease.[4] More than 15 percent of people with ALS are thought to have a genetic form of the disease;[2] however, they may not have a known family history of the disease.[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.[5]

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; advancing ALS research and the 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 such words as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "estimate," "expect," "forecast," "goal," "guidance," "hope," "intend," "may," "objective," "outlook," "plan," "possible," "potential," "predict," "project," "prospect," "should," "target," "will," "would" or the negative of these words or 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. Given their forward-looking nature, these statements involve substantial risks and uncertainties that may be based on inaccurate assumptions and could cause actual results to differ materially from those reflected in such statements.

These forward-looking statements are based on management's current beliefs and assumptions and on information currently available to management. Given their nature, we cannot assure that any outcome expressed in these forward-looking statements will be realized in whole or in part. We caution that these statements are subject to risks and uncertainties, many of which are outside of our control and could cause future events or results to differ materially from those stated or implied in this document, including, among others, uncertainty of our long-term success in developing, licensing, or acquiring other product candidates or additional indications for existing products; expectations, plans, prospects and timing of actions relating to product approvals, approvals of additional indications for our existing products, sales, pricing, growth, reimbursement and launch of our marketed and pipeline products; the potential impact of increased product competition in the biopharmaceutical and healthcare industry, as well as any other markets in which we compete, including increased competition from new originator therapies, generics, prodrugs and biosimilars of existing products and products approved under abbreviated regulatory pathways; our ability to effectively implement our corporate strategy; difficulties in obtaining and maintaining adequate coverage, pricing, and reimbursement for our products; the drivers for growing our business, including our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks related to commercialization of biosimilars, which is subject to such risks related to our reliance on third-parties, intellectual property, competitive and market challenges and regulatory compliance; the risk that positive results in a clinical trial may not be replicated in subsequent or confirmatory trials or success in early stage clinical trials may not be predictive of results in later stage or large scale clinical trials or trials in other potential indications; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; and the occurrence of adverse safety events, restrictions on use with our products, or product liability claims; and any other risks and uncertainties that are described in other reports we have filed with the U.S. Securities and Exchange Commission, which are available on the SEC's website at www.sec.gov.

These statements speak only as of the date of this press release and are based on information and estimates available to us at this time. Should known or unknown risks or uncertainties materialize or should underlying assumptions prove inaccurate, actual results could vary materially from past results and those anticipated, estimated or projected. Investors are cautioned not to put undue reliance on forward-looking statements. A further list and description of risks, uncertainties and other matters can be found in our Annual Report on Form 10-K for the fiscal year ended December 31, 2024 and in our subsequent reports on Form 10-Q. Except as required by law, we do not undertake any obligation to publicly update any forward-looking statements whether as a result of any new information, future events, changed circumstances or otherwise.

Digital Media Disclosure
From time to time, we have used, or expect in the future to use, our investor relations website (investors.biogen.com), the Biogen LinkedIn account (linkedin.com/company/biogen-) and the Biogen X account (https://x.com/biogen) as a means of disclosing information to the public in a broad, non-exclusionary manner, including for purposes of the SEC's Regulation Fair Disclosure (Reg FD). Accordingly, investors should monitor our investor relations website and these social media channels in addition to our press releases, SEC filings, public conference calls and websites, as the information posted on them could be material to investors.

References:

1. QALSODY Prescribing Information, Cambridge, MA: Biogen.
2. 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 Accessed: December 2025.
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: December 2025.
4. 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.
5. Scotter EL, Chen HJ, Shaw CE. TDP-43 Proteinopathy and ALS: Insights into Disease Mechanisms and Therapeutic Targets. Neurotherapeutics. 2015;12(2):352-363. doi:10.1007/s13311-015-0338-x.

MEDIA CONTACT:
Biogen
Madeleine Shin
+ 1 781 464 3260
public.affairs@biogen.com

INVESTOR CONTACT:
Biogen
Tim Power
+1 781 464 2442
IR@biogen.com