The New England Journal of Medicine Publishes Final Results from Phase 1/2 Study of Tofersen for a Genetic Form of ALS

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- *Tofersen is an investigational molecule for superoxide dismutase 1 (SOD1) amyotrophic lateral sclerosis (ALS), the second most common genetic form of ALS, a progressive neurodegenerative disease*
- *Final Phase 1/2 study results demonstrated proof-of-concept and proof-of-biology of tofersen, which is currently being investigated in the ongoing Phase 3 VALOR study*
- *Biogen is committed to developing therapies that target the genetic cause of ALS and other difficult-to-treat conditions*

CAMBRIDGE, Mass., July 08, 2020 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced that positive results from a Phase 1/2 study of tofersen (BIIB067) for the potential treatment of superoxide dismutase 1 (SOD1) amyotrophic lateral sclerosis (ALS) were published in *The New England Journal of Medicine*. A mutation in the SOD1 gene is believed to be a genetic driver of disease in approximately two percent of all ALS cases.

“By evaluating genetically validated targets such as SOD1 in defined populations, we believe we can more quickly identify how to treat this devastating disease,” said Toby Ferguson, M.D., Ph.D., Vice President and Head of the Neuromuscular Development Unit at Biogen. “Biogen is committed to furthering ALS research in an effort to potentially bring a therapy to people living with this rapidly progressing neurological condition.”

Biogen continues to invest in ALS clinical development despite discontinuing the dexpramipexole program in 2013 due to disappointing results from the Phase 3 EMPOWER study. The company has applied important learnings from the EMPOWER study to its broad 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.

The Phase 1/2 Study Results
The Phase 1/2 study of tofersen was a randomized, placebo-controlled, single- and multiple-ascending dose study that evaluated the safety, pharmacokinetics, pharmacodynamics and exploratory efficacy endpoints in individuals living with SOD1-ALS. In the multiple ascending dose (MAD) portion of the study, participants with SOD1-ALS were randomized to receive tofersen (20 mg, 40 mg, 60 mg or 100 mg) or placebo for 12 weeks.

The primary objective of the MAD portion of the study was to evaluate the safety, tolerability and pharmacokinetics of tofersen. The most commonly reported adverse events in people who received one or more doses of tofersen (n=38) were headache, procedural pain, post-lumbar puncture syndrome and falls. Five tofersen- and two placebo-treated people experienced serious adverse events. One death occurred in the placebo group during the trial due to respiratory failure secondary to ALS and 2 deaths occurred in the tofersen group during a follow up period due to pulmonary embolism and respiratory failure (20 mg and 60 mg group, respectively).

“The data published in *The New England Journal of Medicine* are an important step in understanding the potential of tofersen and genetic disease drivers as targets for ALS,” said Timothy Miller, M.D., Ph.D., co-principal investigator and ALS Center Director at Washington University School of Medicine, St. Louis. “We are encouraged by these study results and will continue to evaluate the efficacy and safety of tofersen as a potential treatment for SOD1-ALS.”

The secondary outcome was the change from baseline in cerebrospinal fluid (CSF) SOD1 protein concentration. Treatment with tofersen 100 mg (n=10) over a 3-month period resulted in a 36 percent reduction of SOD1 concentration compared to 3 percent in the placebo group (n=12).

Exploratory measures demonstrated numerical trends towards slowing of clinical decline as measured by the ALS Functional Rating Scale Revised (ALSFRS-R) as well as slow vital capacity and muscle strength measured by handheld dynamometer (HHD) compared to placebo. The mean change in ALSFRS-R score from baseline to day 85 was -1.19 in the tofersen 100 mg group compared to -5.63 in the placebo group on a 48-point scale. Across exploratory clinical measures, separation from the placebo group was primarily driven by the fast-progressing subgroup.

“SOD1-ALS is a neurological disease with no treatment options that reliably slow or halt its rapid progression,” said Merit Cudkowicz, M.D., co-principal investigator and the director of the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital. “We are dedicated to this research with the goal of bringing a new treatment option to this community with great unmet need.”

A Phase 3 study, VALOR, is currently ongoing and will assess the efficacy and safety of tofersen versus placebo in adults with SOD1-ALS.

About Tofersen
Tofersen is an antisense oligonucleotide (ASO) being evaluated for the potential treatment of SOD1-ALS. Tofersen binds to SOD1 mRNA, allowing for its degradation by RNase-H in an effort to reduce synthesis of SOD1 protein production. Tofersen demonstrated proof-of-biology and proof-of-concept in a Phase 1/2 study. Biogen licensed tofersen from Ionis Pharmaceuticals, Inc. under a collaborative development and license agreement.

About Amyotrophic Lateral Sclerosis
Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that results in the loss of motor neurons in the brain and the spinal cord that is responsible for controlling voluntary muscle movement. People with ALS may experience a gradual weakening of muscles, causing them to lose their strength and ability to speak, move and eventually breathe. There is a growing body of evidence that mutations within multiple genes are believed to cause the disease. SOD1-ALS, which accounts for two percent of all ALS cases, is a subset of ALS. Genetic testing may help determine if a person’s ALS is due to a SOD1 gene mutation, even in individuals without a family history of the disease.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases as well as related therapeutic adjacencies. One of the world’s first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray and Nobel Prize winners Walter Gilbert and Phillip Sharp. Today Biogen has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first approved treatment for

spinal muscular atrophy, commercializes biosimilars of advanced biologics and is focused on advancing research programs in multiple sclerosis and neuroimmunology, Alzheimer's disease and dementia, neuromuscular disorders, movement disorders, ophthalmology, immunology, neurocognitive disorders, acute neurology and pain.

We routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor Statement
This news release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including statements about results from the Phase 1/2 study of tofersen; the potential clinical effects of tofersen; the potential benefits, safety and efficacy of tofersen; the clinical development program for tofersen; 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 tofersen; 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 these statements or the scientific data presented.

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; and the direct and indirect impacts of the ongoing COVID-19 pandemic on our business, 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 are based on our current beliefs and expectations and speak only as of the date of this news release.

We do not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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*This release was updated on July 9, 2020 to correctly indicate the mean change in ALSFRS-R score from baseline to day 85 was -5.63 in the placebo group.