New Higher Dose Nusinersen Efficacy and Safety Data Presented at World Muscle Society Congress, Highlight Potential to Maximize Benefit of Nusinersen in SMA

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- Findings from Part B and Part C of the DEVOTE study support the clinical benefits of a higher dose regimen of nusinersen (50/28 mg) in both individuals previously treated and treatment-naïve to nusinersen
- Investigational regimen also shows more rapid slowing of neurodegeneration, as measured by neurofilament
- Biogen plans to submit regulatory applications around the world for approval of the nusinersen higher dose regimen

CAMBRIDGE, Mass., Oct. 08, 2024 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced detailed results from Part B and Part C of the Phase 2/3 DEVOTE study evaluating the safety and efficacy of an investigational higher dose regimen of nusinersen in spinal muscular atrophy (SMA), showing benefits in both individuals previously treated and treatment-naïve to nusinersen with infantile-onset or later-onset SMA. The investigational, higher dose regimen of nusinersen comprises a more rapid loading regimen, two 50 mg doses 14 days apart, and higher maintenance regimen, 28 mg, every 4 months, compared to the approved nusinersen regimen (SPINRAZA®). Data to be presented during the World Muscle Society (WMS) 2024 Congress (Oct. 8-12, 2024 in Prague) highlight the potential of this investigational higher dose regimen to help address remaining unmet need in SMA.

“Strikingly, the higher dose regimen lowered neurofilament more quickly, telling us that it’s more rapidly slowing neurodegeneration. We know how critical this is in people living with SMA. Over time, we see evidence of the benefit of the higher dose regimen across SMA phenotypes,” said Thomas Crawford, M.D., co-director, Muscular Dystrophy Association Clinic at Johns Hopkins Medicine. “Despite administering much more drug, the higher dose regimen appears to have a consistent safety profile with the approved 12 mg regimen.”

DEVOTE is a three-part study that enrolled 145 participants across ages and SMA types. The pivotal Part B cohort (n=75) met its primary endpoint where treatment-naïve, symptomatic infants who received the higher dose regimen saw significantly greater improvements in motor function as measured by Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) compared to a prespecified matched sham (untreated) group from the Phase 3 ENDEAR study (+15.1 vs -11.1, p<0.0001).

In addition to the primary comparisons of the higher dose regimen to the matched sham group, analyses comparing to the approved 12 mg regimen were also performed, though not adequately powered to detect significant differences between these groups. Despite the relatively small study size, secondary analyses consistently favored the higher dose group in all comparisons to sham and nearly all comparisons to the 12 mg regimen. Detailed results include:

- The higher dose regimen led to a 94% reduction in plasma neurofilament light chain (NfL), a marker of neurodegeneration, from baseline to Day 183, compared to a 30% reduction in the sham control group (p<0.0001). Additionally, more rapid NfL reductions were observed with the higher dose regimen, with greater reductions observed at Day 64 (nominal p=0.0050) as compared to the 12 mg regimen.
- At Day 302, the higher dose regimen showed a 19.6 point improvement from baseline on CHOP-INTEND compared to 21.6 point improvement with the 12 mg regimen (least-squares mean difference of -1.94; p=0.8484). At Day 302, the higher dose regimen showed a mean improvement in change in Hammersmith Infant Neurological Exam section 2 (HINE-2) compared to the 12 mg regimen (least-squares mean difference: 0.58; p=0.1734).
- The higher dose regimen reduced the risk of death or permanent ventilation by 67.8% relative to sham (HR: 0.322; nominal p=0.0006) and 29.9% relative to the 12 mg regimen (HR: 0.701; p=0.2775). A similar pattern was observed for overall survival, as well as other relevant events such as hospitalizations and serious respiratory events.
- Separately, in the Part B later-onset cohort, participants receiving the higher dose regimen (n=16) achieved numerically greater improvements on motor function assessments including the Hammersmith Functional Motor Scale – Expanded (HFMSE) and the Revised Upper Limb Module (RULM) at Day 302 over the 12 mg group (n=8) in DEVOTE, and at Day 279 as compared to pre-specified matched 12 mg (n=32) and sham control groups (n=16) from CHERISH.

Initial results were also presented from Part C (n=40) of DEVOTE, in which a diverse group of participants, age 4-65, transitioned to the higher dose regimen (one 50 mg dose followed by the 28 mg maintenance regimen) after a median of 3.9 years on the approved 12 mg regimen. Participants experienced improvements in motor function after transitioning with mean increases of 1.8 points on HFMSE and 1.2 points on RULM from baseline at Day 302.

Across parts of DEVOTE, the higher dose regimen was generally well tolerated and showed a safety profile similar to that of the approved 12 mg regimen. In the 12 mg regimen the most common adverse events (AEs) were respiratory infection, fever, constipation, headache, vomiting and back pain. The frequency of AEs in DEVOTE was similar across the nusinersen treatment arms. The number of AEs leading to study withdrawal and death only occurred in the Part B treatment-naive cohort and were 20% (10), 24% (6) and 55% (11), in the 50/28 mg, 12 mg and matched sham arms, respectively.

“While we’ve seen great progress over the past decade in improving the lives of those with SMA, gaps remain and we can do more to address the full range of unmet needs and goals within our community,” said Kenneth Hobby, President of Cure SMA. “The DEVOTE study’s findings are promising

and show the potential for additional meaningful advancements that could further enhance motor function which impacts daily living activities for all people living with SMA."

Biogen plans to file applications for the 50/28 mg higher dose nusinersen regimen with global regulatory agencies. Nusinersen is currently commercialized under the brand name SPINRAZA in over 71 countries at the label-approved dose of 12 mg.

About the DEVOTE Study
DEVOTE was a Phase 2/3 randomized, controlled, dose-escalating study designed to evaluate the safety, tolerability, pharmacokinetics and potential for even greater efficacy of nusinersen when administered at a higher dose (50/28 mg) than the currently approved regimen (12 mg) for the treatment of spinal muscular atrophy (SMA). The study enrolled 145 participants across ages and SMA types at approximately 42 sites around the world. DEVOTE includes an open-label safety evaluation cohort (Part A), a double-blind, active control randomized treatment cohort (Part B), followed by an open-label treatment cohort (Part C) to assess the safety and tolerability of transitioning participants from the currently approved dose of SPINRAZA to the higher dose being tested in the study.

Part B is comprised of an infantile-onset cohort (n=75), which is considered pivotal, and a later-onset cohort. The primary endpoint of Part B measured the change from baseline on CHOP-INTEND at six months comparing the higher dose regimen of nusinersen to a matched, untreated sham control group from the Phase 3 ENDEAR study. ENDEAR is one of the two pivotal studies that formed the basis of regulatory approval for SPINRAZA® 12 mg.

Part C is an open-label evaluation of the higher dose regimen in children and adults who transitioned from SPINRAZA 12 mg to the 50/28 mg regimen (n=40).

More information about the DEVOTE study (NCT04089566) is available at clinicaltrials.gov.

About SPINRAZA
SPINRAZA is approved in more than 71 countries to treat infants, children and adults with spinal muscular atrophy (SMA). As a foundation of care in SMA, more than 14,000 individuals have been treated with SPINRAZA worldwide.[1]

SPINRAZA is an antisense oligonucleotide (ASO) that targets the underlying cause of motor neuron loss by continuously increasing the amount of full-length survival motor neuron (SMN) protein produced in the body.[2] It is administered directly into the central nervous system, where motor neurons reside, to deliver treatment where the disease starts.[2]

SPINRAZA has shown sustained efficacy across ages and SMA types with a well-established safety profile based on data in patients treated up to 10 years,[3,4] combined with unsurpassed real-world experience. The nusinersen clinical development program encompasses more than 10 clinical studies, which have included more than 460 individuals across a broad spectrum of patient populations, including two randomized controlled studies (ENDEAR and CHERISH). The NURTURE open-label extension study is evaluating the long-term impact of SPINRAZA. The most common adverse events observed in clinical studies were respiratory infection, fever, constipation, headache, vomiting and back pain. Laboratory tests can monitor for renal toxicity and coagulation abnormalities, including acute severe low platelet counts, which have been observed after administration of some ASOs.

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals, Inc. (Nasdaq: IONS). Please click here for Important Safety Information and full Prescribing Information for SPINRAZA in the U.S., or visit your respective country's product website.

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, including related to the potential clinical effects of SPINRAZA; the potential benefits, safety and efficacy of SPINRAZA; the clinical development program for SPINRAZA; the identification and treatment of SMA; our research and development program for the treatment of SMA; the potential of our commercial business and pipeline programs, including SPINRAZA; 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 SPINRAZA; 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 SPINRAZA; 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. Based on commercial patients, early access patients, and clinical trial participants through December 31, 2022.
2. SPINRAZA U.S. Prescribing Information. Available at:

https://www.spinraza.com/content/dam/commercial/specialty/spinraza/caregiver/en_us/pdf/spinraza-prescribing-information.pdf. Accessed: September 2024.

3. Core Data sheet, Version 13, October 2021. SPINRAZA. Biogen Inc, Cambridge, MA.

4. Finkle et al. Cure SMA 2024. “Final Safety and Efficacy Data From the SHINE Study in Participants With Infantile-Onset and Later-Onset SMA.”

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

INVESTOR CONTACT:
Biogen
Stephen Amato
+1 781-464-2442
IR@biogen.com