Biogen Announces First Patient Treated in RESPOND Study Evaluating Benefit of SPINRAZA® (nusinersen) in Patients Treated With Zolgensma® (onasemnogene abeparvovec)

January 8, 2021

- The global Phase 4 RESPOND study will evaluate the efficacy and safety of SPINRAZA in patients with a suboptimal clinical response to Zolgensma
- Clinical and real-world experience have reported that some patients previously treated with Zolgensma have also been treated with SPINRAZA[1,2,3,4]
- Biogen remains committed to exploring the potential of SPINRAZA to optimize outcomes for patients with SMA

CAMBRIDGE, Mass., Jan. 08, 2021 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced that the first patient has been treated in the global clinical study, RESPOND. The Phase 4 study will examine the clinical benefit and assess the safety of SPINRAZA® (nusinersen) in infants and children with spinal muscular atrophy (SMA) who still have unmet clinical needs following treatment with gene therapy Zolgensma® (onasemnogene abeparvovec). RESPOND will be conducted at approximately 20 sites worldwide and aims to enroll up to 60 children with SMA.

“SMA treatments have changed what is possible for children born with the disease but they have also raised new questions,” said Dr. Nicole Gusset, President of SMA Europe and mother of a child with SMA. “We appreciate that the RESPOND study will collect data to help provide answers so individuals living with SMA can make informed treatment decisions.”

Children with SMA do not produce enough survival motor neuron (SMN) protein, which is critical for the maintenance of motor neurons that support sitting, walking and basic functions of life like breathing and swallowing. The RESPOND study will seek to understand if the proven efficacy of SPINRAZA and its mechanism of action, which leads to continuous production of SMN protein, may also benefit patients who have been insufficiently treated with gene therapy.

“In clinical practice, there is a sense of urgency to address motor neuron loss in SMA from the earliest sign or even prior to symptoms, to prevent additional disease progression,” said Julie Parsons, M.D., professor of Clinical Pediatrics and Neurology and Haberfeld Family Endowed Chair in Pediatric Neuromuscular Disorders at Children’s Hospital Colorado and the University of Colorado School of Medicine, and primary investigator of the RESPOND study. “In some patients treated with gene therapy, we have recognized that further motor neuron protection may be needed. Our hope is that results from RESPOND will demonstrate if SPINRAZA can optimize treatment for some of our youngest patients.”

RESPOND is a two-year, open-label study to evaluate the efficacy and safety of SPINRAZA in SMA patients previously treated with Zolgensma to further optimize treatment decisions. The primary endpoint is the total score on the Hammersmith Infant Neurological Examination Section 2. Secondary endpoints include safety, change from baseline on additional motor function measures, other clinical outcomes (e.g., swallowing) and caregiver burden. Neurofilament levels, an exploratory endpoint, will also be evaluated as a marker of biological disease activity.

The study will enroll 60 children up to 3 years old who are determined by the investigator to have the potential for additional clinical improvement after receiving Zolgensma. It has been reported that, to date, 40 percent of children in the long-term study of Zolgensma have been subsequently treated with SPINRAZA.[1] Physicians will use criteria that may include one or more of the following: suboptimal motor function (e.g., a score lower than 50 on the Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders [CHOP INTEND]); the need for respiratory support; abnormal swallowing or feeding ability; or other factors deemed relevant by the investigator.

The primary study group will include 40 infants aged 9 months or younger (at the time of first SPINRAZA dose) who have 2 copies of *SMN2* (likely to develop SMA Type 1) and received Zolgensma at 6 months old or younger. A second study group will include 20 children within a broader age range (up to 3 years old at the time of first SPINRAZA dose). After a screening period, participants will receive the approved 12 mg dose of SPINRAZA: four loading doses, followed by maintenance doses every four months,[5] over the two-year study period.

More information on the study (NCT04488133) is available at clinicaltrials.gov.

About SPINRAZA® (nusinersen)
SPINRAZA is approved to treat infants, children and adults with spinal muscular atrophy (SMA) and is available in more than 50 countries. As a foundation of care in SMA, more than 11,000 individuals have been treated with SPINRAZA worldwide.[6]

SPINRAZA is an antisense oligonucleotide (ASO) that targets the root cause of SMA by continuously increasing the amount of full-length survival motor neuron (SMN) protein produced in the body.[5] It is administered directly into the central nervous system, where motor neurons reside, to deliver treatment where the disease starts.[5]

SPINRAZA has demonstrated sustained efficacy across ages and SMA types with a well-established safety profile based on data in patients treated up to 7 years, combined with unsurpassed real-world experience.[7] The SPINRAZA clinical development program encompasses 10 clinical studies, which have included more than 300 individuals across a broad spectrum of patient populations,[7] including two randomized controlled studies (ENDEAR and CHERISH). The ongoing SHINE and NURTURE open-label extension studies are 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), the leader in antisense therapeutics. 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 Spinal Muscular Atrophy (SMA)
SMA is a rare, genetic, neuromuscular disease that affects individuals of all ages. It is characterized by a loss of motor neurons in the spinal cord and lower brain stem, resulting in progressive muscle atrophy and weakness.[8] SMA is caused by a deficiency in the production of survival motor neuron (SMN) protein due to a damaged or missing *SMN1* gene, with a spectrum of disease severity.[8] Some individuals with SMA may never sit; some sit but never walk; and some walk but may lose that ability over time.[9] In the absence of treatment, children with the most severe form of SMA would not be expected to reach their second birthday.[8]

SMA impacts approximately one in 11,000 live births,[10] is a leading cause of genetic death among infants[10] and causes a range of disability in teenagers and adults.[9]

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. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor
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, about the potential benefits, safety and efficacy of SPINRAZA; the results of certain real-world data; the identification and treatment of SMA; our research and development program for the treatment of SMA; the potential benefits and results from early treatment of SMA; the enrollment of the RESPOND study; risks and uncertainties associated with drug development and commercialization; and the potential of our commercial business, including SPINRAZA. These statements may be identified by words such as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "possible," "potential," "will," "would" and other words and terms of similar meaning. 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 risks that we may not fully enroll the RESPOND study or it will take longer than expected; unexpected concerns that may arise from additional data, analysis or results obtained during the RESPOND study; the occurrence of adverse safety events; risks of unexpected costs or delays; the risks of other unexpected hurdles; failure to protect and enforce our data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; regulatory authorities may require additional information or further studies; product liability claims; third party collaboration risks; 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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