Biogen Plans to Initiate Phase 4 Study Evaluating Benefit of SPINRAZA® (nusinersen) in Patients Treated with Zolgensma® (onasemnogene abeparvovec)

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- In the long-term follow-up study of Zolgensma® and real-world experience, it has been reported that some patients previously treated with gene therapy have been treated with SPINRAZA[1,2,3]
- The RESPOND study aims to evaluate the efficacy and safety of SPINRAZA in patients with a suboptimal clinical response to Zolgensma
- Biogen continues to advance research in spinal muscular atrophy to address the needs of the community and provide additional data to inform treatment decisions

CAMBRIDGE, Mass., July 21, 2020 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced it plans to initiate a global Phase 4 clinical study, RESPOND, to 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).

“As clinicians, we continue to pursue improved outcomes for infants and children with SMA, and the need for additional benefit in some patients treated with gene therapy has been observed. There is compelling clinical rationale for the potential for additional efficacy with SPINRAZA in these patients,” said Crystal Proud, M.D., Pediatric Neuromuscular Neurologist, Children’s Hospital of The King’s Daughters, Virginia and a member of the RESPOND study steering committee. “We expect that the RESPOND study will generate valuable data to help inform future treatment decisions for our youngest SMA patients.”

People 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, including breathing and swallowing. The RESPOND study will seek to understand if the proven efficacy of SPINRAZA and its continuous production of SMN protein may also benefit patients previously treated with gene therapy.

“Available data now show that some patients in the long-term study of Zolgensma have moved on to treatment with SPINRAZA. We believe that, for certain patients, motor neurons may be insufficiently treated by this gene therapy, and we plan to initiate this study to understand the extent to which SPINRAZA may potentially improve outcomes,” said Maha Radhakrishnan, M.D., Chief Medical Officer at Biogen. “The impact of SPINRAZA since its launch has been unprecedented compared to the natural history of the disease, with 100 percent of pre-symptomatic infants in the NURTURE study alive after nearly five years of treatment. More than 10,000 SMA patients have now been treated globally.”

In the long-term study of Zolgensma, it has been reported that, to date, 4 out of 10 patients have been subsequently treated with SPINRAZA.[1] Based on the planned study design, RESPOND will be a two-year, open-label study to evaluate the efficacy and safety of SPINRAZA in SMA patients previously treated with Zolgensma to further inform treatment decisions. Efficacy will be assessed by change from baseline on motor function measures, additional 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 primary study group aims to 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 and will generate data in patients with 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, which is four loading doses followed by maintenance doses every four months, over the two-year study period.[4]

The company plans to submit the study protocol to the regulatory authorities in the coming months and aims for the first eligible patients to be enrolled in the RESPOND study in Q1 2021. The study is projected to 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. Physicians will evaluate children for participation using 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.

About SPINRAZA® (nusinersen)[5--7]
SPINRAZA is the first therapy approved to treat infants, children and adults with spinal muscular atrophy (SMA) and is approved in more than 50 countries. As of March 31, 2020, more than 10,000 individuals have been treated with SPINRAZA. It is the only SMA treatment to combine unsurpassed real-world experience with a significant level of clinical evidence across a broad spectrum of patient populations.

SMA is a rare, genetic, neuromuscular disease that is characterized by a loss of motor neurons in the spinal cord and lower brain stem that can result in severe, progressive muscle atrophy and weakness. Approximately one in 10,000 live births have a diagnosis of SMA, and people of all ages are impacted by the disease. It is a leading genetic cause of infant mortality.

SPINRAZA, a foundation of care in SMA, is an antisense oligonucleotide (ASO), developed using Ionis Pharmaceuticals’ proprietary technology. It is designed to target a root cause of SMA by increasing the amount of full-length survival motor neuron (SMN) protein, which is critical to maintaining motor neurons. It is administered by intrathecal injection into the fluid surrounding the spinal cord where motor neurons reside to deliver the treatment where the disease starts.

SPINRAZA currently maintains an extensive clinical data set in SMA based on data from approximately 300 patients across a broad range of SMA populations demonstrating a favorable benefit:risk profile. SPINRAZA was evaluated in two randomized, double-blind, sham-controlled studies of infantile and later-onset SMA (ENDEAR and CHERISH, respectively) and supported by open-label studies that include pre-symptomatic infants (NURTURE), individuals with later-onset SMA (CS2/CS12) and an extension study of individuals who previously participated in the clinical development program (SHINE). The most common adverse events observed were respiratory infection, fever, constipation, headache, vomiting and back pain. Hypersensitivity, meningitis and hydrocephalus have been observed in the post-marketing setting. Renal toxicity and coagulation

abnormalities, including acute severe low platelet counts, have been observed after administration of some ASOs. Laboratory tests can monitor for these signs.

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals, Inc. (Nasdaq: IONS), the leader in antisense therapeutics. Biogen and Ionis conducted an innovative clinical development program that moved SPINRAZA from its first dose in humans in 2011 to its first regulatory approval in five years.

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
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 identification and treatment of SMA; the clinical development program for SPINRAZA, including the study protocol and enrollment of the RESPOND study and the timing thereof; the potential benefits and results from early treatment of SMA; and risks and uncertainties associated with drug development and commercialization. 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 relating to the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; failure to obtain regulatory approvals in other jurisdictions; risks of unexpected 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; 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.

References:

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