Biogen Presents Data at 2019 AAN Annual Meeting Affirming Longer-Term Safety and Durability of Treatment with SPINRAZA® (nusinersen)

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- Treatment with SPINRAZA resulted in clinically meaningful improvements in motor-function and survival in individuals with spinal muscular atrophy
- Treating pre-symptomatic infants with SPINRAZA helped patients in the NURTURE study achieve motor milestones more consistent with normal development
- More than 7,500 individuals have been treated with SPINRAZA worldwide in over 40 countries across the expanded access program, clinical trials and post-marketing setting

CAMBRIDGE, Mass., May 06, 2019 (GLOBE NEWSWIRE) -- Biogen Inc. (Nasdaq: BIIB) today announced new data affirming the safety and durability of SPINRAZA® (nusinersen) and highlighting its clinically meaningful benefits for individuals with spinal muscular atrophy (SMA). Data from the SHINE extension study, with patients followed for up to four years, the NURTURE study of pre-symptomatic infants and an evaluation of phosphorylated neurofilament heavy chain (pNF-H) as a biomarker will be featured presentations at the 71st annual meeting of the American Academy of Neurology (AAN) in Philadelphia, PA (May 4-10, 2019).

“Each milestone in these studies marks a new chapter in what it means to live with SMA, and the insight provided is invaluable in understanding the long-term experience of this rare disease,” said Alfred Sandrock, Jr., M.D., Ph.D., executive vice president and chief medical officer at Biogen. “These results confirm previous data from our trials, which demonstrated that early treatment with SPINRAZA can make a critical difference in survival and achieving motor milestones. The data also demonstrate that improvements in motor milestones were achieved in individuals who began treatment with SPINRAZA at a later age. This is a powerful development for the SMA community.”

Watch this video with a story about the experience of a family facing infantile-onset SMA, (most likely to develop SMA Type 1) here: http://www.globenewswire.com/NewsRoom/AttachmentNg/b057996c-8146-4a1e-bdbf-06eccae12cc7

Interim results from the ENDEAR-SHINE open-label extension study of infants (n=89) followed for up to four years demonstrated that treatment with SPINRAZA resulted in additional or new motor function improvements on the Children’s Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND). The infants also exhibited improved event-free survival rates compared to the natural history of the disease. There were no new safety findings. Additional highlights from ENDEAR-SHINE include:

- As of October 15, 2018, study participants who received SPINRAZA in ENDEAR and SHINE (n=65) increased average CHOP INTEND score by 16.8 points after nearly three years of treatment.
- Those in the sham-control arm in ENDEAR and that received SPINRAZA in SHINE (n=24) increased average CHOP INTEND score by 8.2 points after over 1.5 years of treatment.
- Patients receiving SPINRAZA in ENDEAR and SHINE continued to achieve motor milestones during SHINE. Both those who began treatment younger (n=30, less than or equal to 5.42 months) and older (n=21, greater than 5.42 months) demonstrated the ability to sit without support, 60 and 38 percent respectively. At nearly three years of follow-up, infants in the younger age group demonstrated greater improvements in CHOP INTEND score (19.4 vs. 13.8 points).
- Patients treated with SPINRAZA in ENDEAR and SHINE demonstrated a longer period of survival without need for permanent ventilation (median 75.0 weeks). This compared to event-free survival among patients initiating treatment in SHINE (median 22.6 weeks). Among patients who received sham in ENDEAR and SPINRAZA in SHINE, the median time of event-free survival was reached in ENDEAR while untreated. Among infants who initiated treatment in SHINE and were alive without permanent ventilation at baseline, 58 percent remained alive without permanent ventilation at the data cutoff.

Data from CHERISH-SHINE, which evaluated individuals with later-onset SMA (n=125, most likely to develop SMA Type 2 or 3), demonstrated that earlier treatment resulted in greater improvements in motor function and continued improvement or stabilization of motor function scores. Mean change in Hammersmith Functional Motor Scale Expanded (HFSME) score was 3.7 for participants treated with SPINRAZA in SHINE and CHERISH. This compared to a positive 0.4 change from baseline among participants in the CHERISH sham-control arm and who received SPINRAZA in SHINE. During CHERISH, sham-control participants experienced a 0.4 decline in HFSME. Four participants in the youngest age group in the study (n=39, less than 3.69 years) were walking independently at Day 690 compared to no patients at baseline. There were no new safety findings. Patients were followed for up to four years, adding to the long-term safety profile of SPINRAZA.

Data from the NURTURE study showed that pre-symptomatic treatment of infantile-onset SMA (n=25, most likely to develop SMA Type 1 or 2) resulted in motor milestone achievements more consistent with normal motor development. Evaluations were conducted at a median age of 26 months. All infants were able to sit without support and 88 percent could walk with assistance and 77 percent could walk without assistance. All infants were alive and none required permanent ventilation. No new safety concerns were identified. In the natural history of SMA, individuals are unable to sit without support (SMA Type 1) or walk (SMA Type 1 or 2) and often require respiratory and nutritional interventions in order to live past the age of two (SMA Type 1). The May 2018 data was previously presented.

An evaluation of pNF-H in plasma highlighted its potential to predict disease activity and suggested that it may be a useful biomarker in SMA. Baseline

measure of pNF-H was higher in individuals with SMA (n=302) than those without SMA (n=34). Individuals from the NURTURE, ENDEAR and CHERISH studies treated with SPINRAZA experienced rapid pNF-H declines followed by stabilization at lower levels. The results are part of ongoing work to identify biomarkers that could provide insight on disease progression in SMA. {Encore presentation}.

The pNF-H and NURTURE presentations were selected by AAN from more than 3,000 other presentations as abstracts of distinction for their scientific merit.

About SPINRAZA® (nusinersen)[1-4]
SPINRAZA is the first and only approved medicine for the treatment of spinal muscular atrophy (SMA) and is currently available in more than 40 countries. As of March 31, 2019, more than 7,500 individuals with SMA are being treated with SPINRAZA worldwide, based on patients across the post-marketing setting, Expanded Access Program (EAP) and clinical trial participants.

SPINRAZA is an antisense oligonucleotide (ASO) developed using Ionis' proprietary antisense technology that is designed to treat the root cause of SMA. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein. ASOs are short synthetic strings of nucleotides designed to selectively bind to target RNA and regulate gene expression. Through use of this technology, SPINRAZA has been shown to increase the amount of full-length SMN protein in individuals with SMA. SPINRAZA is administered via intrathecal injection, which delivers therapies directly into the cerebrospinal fluid (CSF) around the spinal cord, where motor neurons degenerate in individuals with SMA due to insufficient levels of SMN protein.

In the clinical trial program, SPINRAZA demonstrated a favorable benefit-risk profile. The most common adverse reactions that occurred in the SPINRAZA group were respiratory infection and constipation. Serious adverse reactions of atelectasis were more frequent in SPINRAZA-treated patients. Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some ASOs. Individuals may be at increased risk of bleeding complications. Renal toxicity has been observed after administration of some ASOs. SPINRAZA is present in and excreted by the kidney.

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

About the SPINRAZA Clinical Program
NURTURE is an ongoing, open-label study of infants up to six weeks of age at time of first dose, who were genetically diagnosed with SMA and had not experienced any symptoms by the time of first dose. Data presented at the World Muscle Society in October 2018 demonstrated unprecedented efficacy in treating patients pre-symptomatically. In that analysis, all NURTURE study participants were alive and did not require permanent ventilation, in contrast to natural history of SMA. Study participants achieved motor milestones with 100 percent sitting independently and 88 percent able to walk. All NURTURE study participants were 14 months or older at the time of the analysis.
Participants included infants with two copies of the SMN2 gene (n=15) who are most likely to develop a fatal, early-onset form of SMA known as Type 1, and infants with three copies of the SMN2 gene (n=10) who are most likely to develop SMA Type 2 or 3. People living with SMA Types 2 and 3 may never be able to walk or will lose that ability over time. No new safety concerns were identified.

The ENDEAR study was a thirteen-month, international, phase 3, multicenter, double-blind, sham-controlled study of 121 patients with infantile-onset SMA (most likely to develop Type 1). Results from the pivotal study, which were published in the New England Journal of Medicine, evaluated the efficacy and safety in patients that onset of signs and symptoms of SMA before six months of age. Patients treated with SPINRAZA in the ENDEAR study achieved clinically meaningful improvement in achievement of motor milestones compared to untreated study participants with 51 percent vs. 0 percent demonstrating Hammersmith Infant Neurological Examination section 2 (HINE-2) motor milestone response, an assessment which evaluates eight motor-milestone categories, based on the defined criteria.

CHERISH was a fifteen-month, phase 3, randomized, double-blind, sham-controlled study investigating SPINRAZA in 126 non-ambulatory patients with later-onset SMA (most likely to develop SMA Type 2 or 3). Patients included had onset of signs and symptoms at greater than 6 months of age, and an age of 2 to 12 years at screening. The final analysis of CHERISH data found that children receiving SPINRAZA experienced a highly statistically significant and clinically meaningful improvement in motor function compared to those who did not receive treatment with a treatment difference of 4.9 points on the Hammersmith Functional Motor Scale Expanded. SPINRAZA demonstrated a favorable benefit-risk profile in the study.

About SMA[2,5]
SMA is a rare, genetic, neuromuscular disease that is characterized by loss of motor neurons in the spinal cord and lower brain stem, resulting in severe and progressive muscle atrophy and weakness. About 1 in 10,000 live births have a diagnosis of SMA. Ultimately, individuals with SMA can lose the ability to walk and have difficulty performing the basic functions of life, such as breathing and swallowing, which results in significant healthcare intervention and caregiver assistance. Left untreated, the majority of infants with the most severe form of the disease (Type 1) do not live beyond their second birthday without respiratory intervention. People with childhood or adult onset SMA (Type 2 or 3) produce greater amounts of SMN protein resulting in less severe, but still life-altering forms of the disease.

Due to a deletion of, or mutation in, the SMN1 gene, people with SMA do not produce enough survival motor neuron (SMN) protein, which is critical for the maintenance of motor neurons. The severity of SMA correlates with the amount of SMN protein an individual has. People with Type 1 SMA, the form that requires the most intensive and supportive care, produce very little SMN protein and do not achieve the ability to sit without support or typically live beyond two years without respiratory support. People with Type 2 and Type 3 SMA produce greater amounts of SMN protein and have less severe, but still life-altering forms of SMA.

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, and today has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first and only approved treatment for spinal muscular atrophy, and is focused on advancing neuroscience research programs in MS and neuroimmunology, Alzheimer's disease and dementia, movement disorders, neuromuscular disorders, acute neurology, neurocognitive disorders, pain, and ophthalmology. Biogen also commercializes biosimilars of advanced biologics.

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; and the

identification and treatment of SMA. 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. 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 the occurrence of adverse safety events and/or unexpected concerns that may arise from additional data or analysis; 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; product liability claims; and third party collaboration risks. 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 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.

Reference:

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