Biogen's SPINRAZA® (nusinersen) Data Show Earlier Treatment Initiation May Lead to Improved Motor Function Across a Broad Population of People Living with Spinal Muscular Atrophy

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- New data from Phase 3 ENDEAR study demonstrated earlier initiation of treatment with SPINRAZA may improve motor function outcomes in infants with Spinal Muscular Atrophy (SMA)
- Phase 2 EMBRACE interim analysis showed greater motor milestone achievement in infants and children treated with SPINRAZA, compared to those untreated, in patient populations not studied in the pivotal trials
- Interim analysis of EMBRACE also supported the dosing regimen of four loading doses in the first two months, followed by the administration of SPINRAZA every four months thereafter for infantile- and later-onset SMA

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 5, 2017-- Biogen (NASDAQ: BIIB) presented new data demonstrating that earlier initiation of treatment with SPINRAZA® (nusinersen) may improve motor function outcomes in infants and children with spinal muscular atrophy (SMA). Results continued to reinforce the favorable efficacy and safety profile of SPINRAZA. The data were shared at the 22nd International Annual Congress of the World Muscle Society in Saint Malo,France (October 3-7, 2017).

A new analysis from the Phase 3 ENDEAR study showed infants with SMA who initiated treatment earlier in the disease (shorter disease duration) demonstrated greater benefit and improvement in motor function outcomes.

As measured by the Hammersmith Infant Neurological Examination (HINE), significant differences in motor milestone responders were observed between infants treated with SPINRAZA compared to untreated infants with disease duration less than or equal to 12 weeks (75% vs. 0%; P<.0001) and those with disease duration greater than 12 weeks (32% vs. 0%; P=.0026). There was also a significant benefit in event-free survival in infants treated with SPINRAZA with disease duration less than or equal to 12 weeks (P=.0004).

"These studies contribute to a growing body of evidence that SPINRAZA can make a meaningful difference in the lives of people with SMA regardless of their age or stage of the disease," said Alfred Sandrock, M.D., Ph.D., executive vice president and chief medical officer at Biogen. "Across studies, we continue to see evidence that earlier initiation of treatment with SPINRAZA can lead to improved clinical and functional outcomes."

Interim analyses were also presented from the Phase 2 EMBRACE study which was designed to assess the efficacy and safety of SPINRAZA in individuals with infantile- and later-onset SMA who were ineligible for the two earlier pivotal studies.

The EMBRACE interim analysis showed a larger proportion of infants and children treated with SPINRAZA were HINE motor milestone responders compared to those who were untreated. Results from the interim analysis also supported the dosing regimen of four loading doses in the first two months, followed by the administration of SPINRAZA every four months thereafter, for individuals with infantile- and later-onset SMA.

In the ENDEAR and EMBRACE studies SPINRAZA demonstrated a favorable benefit-risk profile. Safety data involving the intrathecal administration of SPINRAZA showed the incidence and nature of the most common lumbar puncture-related adverse events in the clinical studies were similar in children with later-onset SMA with or without scoliosis.

For more information about SPINRAZA and prescribing information in the United States, please visit www.SPINRAZA.com. Prescribing information in the European Union is available at http://www.ema.europa.eu/ema/.

About ENDEAR and EMBRACE
ENDEAR is a randomized, double-blind, sham-procedure controlled 13-month study in patients with infantile-onset SMA. The end of study efficacy analysis included all patients (n=121) who had their final study visit after the interim analysis (n=78) and had the opportunity to attend the six-month study visit assessment. The Hammersmith Infant Neurological Examination (HINE) is a reliable and clinically validated tool to assess motor milestone achievement in infants with SMA.

EMBRACE is a Phase 2, multicenter, randomized, double-blind, sham-procedure controlled 14-month study of SPINRAZA in infants and children not eligible to participate in ENDEAR (symptom onset less than or equal to six months, less than or equal to seven months of age at screening; 2 SMN2 copies) or CHERISH (symptom onset age greater than six months, age 2-12 years at screening).

SPINRAZA Program Status
SPINRAZA is the first approved medicine for the treatment of SMA and is currently approved in the United States, the European Union, Brazil, Japan and Canada. Biogen has submitted regulatory filings in additional countries and plans to initiate additional filings in other countries.

Globally, in 2016, in response to the urgent need for treatment for the most severely affected individuals living with SMA, Biogen sponsored one of the largest, pre-approval Expanded Access Programs (EAP) in rare disease, free of charge.

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals (NASDAQ: IONS), a 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 SMA[1-5]
Spinal muscular atrophy (SMA) is characterized by loss of motor neurons in the spinal cord and lower brain stem, resulting in severe and progressive muscular atrophy and weakness. Ultimately, individuals with the most severe type of SMA can become paralyzed and have difficulty performing the basic functions of life, like breathing and swallowing.

Due to a loss of, or defect in, the SMN1 gene, people with SMA do not produce enough SMN protein, which is critical for the maintenance of motor neurons. The severity of SMA correlates with the amount of SMN protein. 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 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 SPINRAZA® (nusinersen)
SPINRAZA is being developed globally for the treatment of SMA.

SPINRAZA is an antisense oligonucleotide (ASO), using Ionis Pharmaceuticals' proprietary antisense technology, that is designed to treat SMA caused by mutations or deletions in the SMN1 gene located in chromosome 5q that leads to SMN protein deficiency. SPINRAZA alters the splicing of SMN2 pre-mRNA in order to increase production of full-length SMN protein.[6] 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 the potential to increase the amount of full-length SMN protein in individuals with SMA.

SPINRAZA must be administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,[7] where motor neurons degenerate in individuals with SMA due to insufficient levels of survival motor neuron (SMN) protein.[8]

SPINRAZA demonstrated a favorable benefit-risk profile. The most common adverse reactions reported for SPINRAZA were upper respiratory infection, lower 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 antisense oligonucleotides. Individuals may be at increased risk of bleeding complications. Renal toxicity has been observed after administration of some antisense oligonucleotides. SPINRAZA is present in and excreted by the kidney.

About Biogen
Through cutting-edge science and medicine, Biogen discovers, develops and delivers innovative therapies worldwide for people living with serious neurological and neurodegenerative diseases. Founded in 1978, Biogen is a pioneer in biotechnology and today the Company has the leading portfolio of medicines to treat multiple sclerosis, has introduced the first and only approved treatment for spinal muscular atrophy and is at the forefront of neurology research for conditions including Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. Biogen also manufactures and commercializes biosimilars of advanced biologics. For more information, please visit www.biogen.com. Follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor
This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 relating to the potential benefits, safety and efficacy of SPINRAZA, the results of certain real-world data, the status of current regulatory filings, plans for additional regulatory filings in other jurisdictions, planning and timing for commercial launch, and availability of patient access and reimbursement pathways, which may vary on a country-by-country basis. These forward-looking statements may be accompanied by words such as "aim," "anticipate," "believe," "could," "estimate," "except," "forecast," "intend," "may," "plan," "potential," "possible," "will" and other words and terms of similar meaning. You should not place undue reliance on these statements or the scientific data presented. Drug development and commercialization involve a high degree of risk. 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 commercialization of SPINRAZA, which may be impacted by, among other things, the level of preparedness of healthcare providers to treat patients, difficulties in obtaining or changes in the availability of reimbursement for SPINRAZA, the effectiveness of sales and marketing efforts, problems with the manufacturing process for SPINRAZA, the occurrence of adverse safety events, unexpected concerns that may arise from additional data or analysis; regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of Biogen's drug candidates or expansion of product labeling; or Biogen may encounter other unexpected hurdles which may be impacted by, among other things, the occurrence of adverse safety events, failure to obtain regulatory approvals in certain jurisdictions, failure to obtain regulatory approvals in other jurisdictions, failure to protect intellectual property and other proprietary rights; product liability claims; or 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 Biogen's most recent annual or quarterly report and in other reports Biogen has 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 press 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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