# New SPINRAZA® (nusinersen) Data Unveiled at AAN Annual Meeting Show Continued Improvement in Motor Function for Broad Age Range and Survival Benefit for Infants

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- SHINE data illustrates SPINRAZA's longer-term benefits for infantile-onset SMA, including improvements in motor function and increased event-free survival in participants followed for nearly three years
- Additional findings show that later-onset SMA patients treated with SPINRAZA walked longer distances while experiencing stable or less fatigue over time, in contrast to SMA natural history

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 23, 2018-- Biogen (Nasdaq: BIIB) today announced new findings detailing the benefits that SPINRAZA® (nusinersen) demonstrates for both infantile- and later-onset spinal muscular atrophy (SMA) populations, including improvement in motor function as well as increased survival for the most severely affected. These findings are based on interim results from the SHINE open-label extension study and an analysis of SPINRAZA's effects on mobility and fatigability in later-onset participants from the CS2/CS12 studies. The research will be presented at the American Academy of Neurology (AAN) Annual Meeting on April 21-27, 2018, in Los Angeles, California.

"These results reinforce SPINRAZA's unprecedented and compelling efficacy across a broad range of SMA populations, enabling patients to improve mobility and motor function – and, for the most severely affected, increase their chances of survival," said Alfred Sandrock, M.D., Ph.D., executive vice president and chief medical officer at Biogen. "We look forward to continuing to work with healthcare providers, institutions and SMA communities to provide access to SPINRAZA for those in need, no matter their age, disease severity or duration of the disease."

The SHINE analysis reported interim results as of June 30, 2017, from the open-label extension study for patients (n=89) with infantile-onset SMA (most likely to develop Type 1) who transitioned from the Phase 3 ENDEAR study. Participants either initiated SPINRAZA treatment in ENDEAR and continued treatment through SHINE (n=65) or transitioned from the sham-control arm in ENDEAR to active treatment with SPINRAZA in SHINE (n=24).

"This analysis demonstrates that participants improved their motor function and increased event-free survival time, whether they initiated treatment earlier, as in ENDEAR and continuing in SHINE, or later, after receiving sham-control in ENDEAR and beginning treatment in SHINE," said Diana Castro, M.D., lead study author, UT Southwestern Medical Center, Dallas, Texas. "It also confirms that those who initiated SPINRAZA treatment earlier saw greater motor milestone performance that continued to improve over time, and that no new safety concerns were identified."

The interim results showed that participants who initiated SPINRAZA in ENDEAR and continued in SHINE, as well as those who received sham in ENDEAR and initiated SPINRAZA in SHINE, experienced improvements in HINE-2 motor milestones and general motor function as measured by CHOP INTEND. The median time to death or permanent ventilation for participants who initiated SPINRAZA in ENDEAR and continued in SHINE was 73 weeks. Among participants who received sham, the median time to death or permanent ventilation was 22.6 weeks within ENDEAR. The majority of subjects who were alive and did not require permanent ventilation after they received sham in ENDEAR remained event-free after receiving SPINRAZA in SHINE for a median time of 9.2 months.

An additional analysis – which was led by researchers at Columbia University Medical Center with support from Biogen – evaluated a subset of data from CS2 and CS12, two multicenter, open-label clinical trials, to assess the change in participants' performance during the Six-Minute Walk Test (6MWT) and measures of fatigue. The analysis examined the walking ability and fatigability of ambulatory participants (n=14) ages two to 15 years with SMA Type 2 (n=1) or Type 3 (n=13) at study enrollment. Participants' baseline median distance walked was 250.5 meters and baseline median fatigue level was 14.8 percent. Following SPINRAZA treatment, their walking distance increased (a median increase of 98 meters) while simultaneously, their fatigue level remained stable or decreased (a median decrease of 3.8 percent) over nearly 3 years.

"With SPINRAZA treatment, not only were participants able to walk longer distances but they experienced a stabilization or decrease in fatigue while doing so – both of which are meaningful, real-world benefits for individuals with SMA," said Jacqueline Montes, P.T., Ed.D., N.C.S., Assistant Professor, lead study author, Columbia University Irving Medical Center, New York. "Furthermore, the analysis illustrates that SPINRAZA's benefits continue to grow over time for Type 2 and 3 SMA populations."

**About SHINE**

SHINE is an ongoing Phase 3, multicenter, open-label extension study for patients with SMA who previously participated in the nusinersen clinical trial program, including the CS3A, ENDEAR, CHERISH, CS12 and EMBRACE studies. The primary and secondary objectives of the SHINE study are to evaluate the long-term safety/tolerability and efficacy of nusinersen, respectively. Study participants will be evaluated for up to five years in SHINE.

**SPINRAZA Program Status**

SPINRAZA is the first and only approved medicine for the treatment of SMA and is currently approved in the United States, the European Union, Brazil, Japan, Switzerland, Australia, South Korea, Canada and Chile. Biogen has submitted regulatory filings in additional countries and plans to initiate additional filings in other countries. According to commercial, Early Access Program and clinical trial participant patient data as of December 31, 2017, more than 3,200 individuals with SMA are being treated with SPINRAZA worldwide.

Globally, starting 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]**

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 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. 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' 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 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 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.

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 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. 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 Alzheimer's disease and dementia, multiple sclerosis and neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry, and acute neurology. Biogen also manufactures and 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 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 Biogen's current regulatory filings, Biogen's plans for additional regulatory filings in other jurisdictions, 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. Drug development and commercialization involve a high degree of risk. 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 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 and/or 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; 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, or 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 Biogen's 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 Biogen's current beliefs and expectations and speak only as of the date of this press release. Biogen does 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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