SPINRAZA® (Nusinersen) Approved in the European Union as First Treatment for Spinal Muscular Atrophy

June 1, 2017

Approved to Treat Broad Range of People with SMA

Robust Data From Phase 3 Studies Demonstrated Positive Impact on Motor Milestone Achievement; Increased Survival in Infants with SMA

CAMBRIDGE, Mass.--(BUSINESS WIRE)--The European Commission (EC) has granted a marketing authorization for SPINRAZA® (nusinersen) for the treatment of 5q spinal muscular atrophy (SMA), Biogen (NASDAQ:BIIB) announced today.[1] 5q SMA is the most common form of the disease and represents approximately 95% of all SMA cases.[2] SPINRAZA is the first approved treatment in the European Union (EU) for SMA, a leading genetic cause of death in infants that is marked by progressive, debilitating muscle weakness. SPINRAZA was reviewed under the European Medicines Agency's (EMA) accelerated assessment program, intended to expedite access to patients with unmet medical needs.

"Today we join individuals and families affected by SMA across Europe in celebrating the approval of SPINRAZA. Based on the robust efficacy and safety profile demonstrated in the clinical trials, we believe SPINRAZA will have a meaningful impact on infants, children and adults living with this devastating disease," said Michel Vounatsos, chief executive officer at Biogen. "As part of our mission to improve the lives of those affected by SMA, we remain steadfast in our commitment to work with healthcare professionals, advocacy groups and government agencies to ensure people who could benefit from SPINRAZA receive access to this important treatment as quickly as possible."

The approval of SPINRAZA is primarily based on results from two pivotal multicenter, controlled studies, including end of study data from ENDEAR (infantile-onset SMA) and an interim analysis of CHERISH (later-onset SMA), both of which demonstrated the clinically meaningful efficacy and favorable benefit-risk profile of SPINRAZA. The approval was also supported by open-label data in pre-symptomatic and symptomatic individuals with, or likely to develop, Types 1, 2 and 3 SMA.

In the ENDEAR end of study analysis, a statistically significant greater percentage of patients achieved the definition of motor milestone responder in the SPINRAZA group (51%) compared to the sham-control group (0%) ($p<0.0001$). Some infants in the SPINRAZA group achieved motor milestones including full head control, ability to roll, sitting, and standing. Additionally, infants treated with SPINRAZA demonstrated a statistically significant reduction (47%) in the risk of death or permanent ventilation ($p=0.0046$).

In the CHERISH pre-specified interim analysis, there was a statistically significant and clinically meaningful improvement in motor function in children with later-onset SMA (most likely to develop Type 2 or Type 3) treated with SPINRAZA compared to untreated children. Improvements were measured by the Hammersmith Functional Motor Scale Expanded (HFMSE) and demonstrated a treatment difference of 5.9 points in the mean change from baseline to Month 15 in the HFMSE score ($p=0.0000002$). The HFMSE is a reliable and validated tool specifically designed to assess motor function in children with SMA. The Phase 3 end of study data were consistent with the interim analysis and presented at the American Academy of Neurology annual meeting in Boston, Mass., April 2017.

"The overall clinical findings support the efficacy and safety of SPINRAZA in a broad range of individuals with SMA, including significant improvements in motor development and reduction in risk of death in infants," said Prof. Dr. Jan Kirschner from the Medical Center University of Freiburg, Germany. "These unprecedented improvements bring new hope to a community where there previously were no approved treatments available to address the loss of motor function over time. We are now seeing motor improvements with SPINRAZA that are never seen in the natural course of the disease."

SPINRAZA must be administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,[3] where motor neurons degenerate in individuals with SMA due to insufficient levels of survival motor neuron (SMN) protein.[4]

SPINRAZA demonstrated a favorable benefit-risk profile. Thrombocytopenia, renal toxicity and coagulation abnormalities, including acute severe thrombocytopenia, have been observed after administration of other subcutaneously or intravenously administered antisense oligonucleotides. There is a risk of adverse reactions occurring as part of the lumbar puncture procedure (e.g. headache, backpain, vomiting).

The timing of SPINRAZA availability in the EU will vary by country, per local reimbursement and access pathways. Biogen has been working with health systems and government agencies across the EU to help patients secure access to SPINRAZA.

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. The EAP has led to the initiation and ongoing treatment of more than 350 eligible individuals with infantile-onset SMA (most likely to develop Type 1) in 17 European countries.

For SPINRAZA prescribing information in the EU, please visit http://www.ema.europa.eu/ema/.

SPINRAZA Program Updates

SPINRAZA was first approved by the U.S. Food and Drug Administration (FDA) on December 23, 2016 within three months of regulatory filing. Biogen has also submitted regulatory filings in Japan, Canada, Australia, Switzerland, and Brazil and plans to initiate additional filings in other countries in 2017.

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. Based on the EC authorization of SPINRAZA, Ionis will receive a $50 million milestone payment. Ionis is also eligible to receive tiered royalties on global sales of SPINRAZA up to a percentage in the mid teens.

About SMA [5-9]

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.[10] 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.

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 "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 beliefes 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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