



## Biogen's SPINRAZA® (nusinersen) Receives Positive CHMP Opinion for the Treatment of Spinal Muscular Atrophy

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*First SMA Treatment Recommended for Approval in the EU*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Biogen (NASDAQ: BIIB) today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending the granting of a marketing authorization for SPINRAZA® (nusinersen) to treat patients with spinal muscular atrophy (SMA). The CHMP reviewed SPINRAZA under an accelerated assessment program, which is a regulatory mechanism to facilitate earlier access to patients for medicines that fulfill unmet medical needs. SPINRAZA is the first treatment for SMA to be recommended by the CHMP for approval in the European Union (EU).

"The positive CHMP opinion, which was expedited under the accelerated assessment program, recognizes the compelling efficacy profile of SPINRAZA and underscores the significant unmet need for an effective SMA treatment in Europe," said Michael Ehlers, M.D., Ph.D., executive vice president, Research and Development at Biogen. "We look forward to the European Commission's decision and believe SPINRAZA has the potential to make a meaningful impact for individuals with SMA in the EU."

The CHMP positive opinion is now referred to the European Commission (EC), which grants the marketing authorization for centrally authorized medicines in the EU. The CHMP recommended an indication for the treatment of 5q SMA, which refers to the most common form of the disease and represents approximately 95% of all SMA cases.<sup>1</sup> A decision from the EC is expected in the next few months.

### Data Supporting Positive Opinion

The recommendation was primarily based on the CHMP's assessment of two pivotal controlled studies, ENDEAR (infantile-onset SMA) and CHERISH (later-onset SMA), which both demonstrated the clinically meaningful efficacy and favorable safety profile of SPINRAZA.

- In ENDEAR, a statistically significant greater percentage of individuals with infantile-onset SMA (most likely to develop Type 1) treated with SPINRAZA achieved a motor milestone response compared to untreated individuals. Motor milestones achieved in some individuals treated with SPINRAZA included the ability to kick, head control, rolling, sitting and crawling. In addition, a statistically significant reduction in the risk of death or permanent ventilation was seen in SPINRAZA-treated individuals compared to untreated individuals at the end of study analysis.
- In CHERISH, there was a statistically significant and clinically meaningful improvement in motor function in individuals treated with SPINRAZA with later-onset SMA (most likely to develop Type 2 or Type 3) compared to untreated individuals at the interim analysis. Improvements were measured by the Hammersmith Functional Motor Scale Expanded (HFMSE). The HFMSE is a reliable and validated tool specifically designed to assess motor function in children with SMA.
- Data from open-label studies in pre-symptomatic and symptomatic individuals most likely to develop Type 1, 2 or 3 were consistent with the results of the pivotal studies and were considered supportive of the recommended indication. The overall findings of these studies support the efficacy and safety of SPINRAZA in individuals with SMA.
- SPINRAZA demonstrated a favorable safety profile. SPINRAZA is to be administered by healthcare professionals experienced in doing lumbar punctures due to the risks associated with this procedure (e.g. headache, backpain, vomiting).

### SPINRAZA Program Status

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 by the United States Food and Drug Administration (FDA) in 2016.<sup>2</sup>

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

### About SMA<sup>3-7</sup>

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 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) 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.<sup>8</sup> 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 is administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,<sup>9</sup> where motor neurons degenerate in patients with SMA due to insufficient levels of SMN protein.<sup>10</sup>

There is a risk of adverse reactions occurring as part of the lumbar puncture procedure (e.g. headache, backpain, vomiting). Coagulation abnormalities and thrombocytopenia, including acute severe thrombocytopenia, have been observed after administration of some antisense oligonucleotides. Renal toxicity has been observed after administration of some antisense oligonucleotides.

#### **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](http://www.biogen.com). Follow us on social media – [Twitter](#), [LinkedIn](#), [Facebook](#), [YouTube](#).

#### **Biogen Safe Harbor**

This press release contains forward-looking statements, including statements relating to the potential benefits, safety and efficacy of SPINRAZA, the status of current regulatory filings, and plans for additional regulatory filings in other jurisdictions. These statements may be identified by words such as "believe," "except," "may," "plan," "potential," "will" and similar expressions, and are based on our current beliefs and expectations. You should not place undue reliance on these statements. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including 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, failure to obtain regulatory approvals in other jurisdictions, failure to protect intellectual property and other proprietary rights, product liability claims, third party collaboration risks, and the other risks and uncertainties that are described in the Risk Factors section of Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the U.S. Securities and Exchange Commission (SEC). Any forward-looking statements speak only as of the date of this press release and we assume no obligation to update any forward-looking statement.

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#### **Contact:**

Biogen  
MEDIA CONTACT:  
Ligia Del Bianco, +1 781-464-3260  
[public.affairs@biogen.com](mailto:public.affairs@biogen.com)  
or  
INVESTOR CONTACT:  
Ben Strain, +1 781-464-2442  
[IR@biogen.com](mailto:IR@biogen.com)