



## **Biogen's SPINRAZA™ (nusinersen) Receives Notice of Compliance from Health Canada for the Treatment of 5q Spinal Muscular Atrophy (SMA)**

### ***First SMA Treatment Approval in Canada***

**Mississauga, ON. July 4, 2017** – Biogen Canada Inc. today announced that Health Canada has approved SPINRAZA™ (nusinersen) for the treatment of patients with 5q spinal muscular atrophy (SMA). SPINRAZA is the first treatment to be approved in Canada for SMA, a leading genetic cause of death in infants and toddlers that is marked by progressive, debilitating muscle weakness.<sup>1</sup>

SPINRAZA is indicated for the treatment of 5q SMA, which is the most common form of the disease and represents approximately 95% of all SMA cases.<sup>2</sup>

"Today, Biogen is very proud to share the news that Health Canada has approved SPINRAZA for the treatment of 5q SMA. Based on the robust efficacy and safety profile demonstrated in the clinical trials, we believe SPINRAZA will have a meaningful impact on individuals living with this devastating disease," said Wildon Farwell, Senior Director, Clinical Development at Biogen. "Biogen is committed and willing to continue 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."

### **Data Supporting Health Canada Approval**

The Health Canada approval of SPINRAZA was based on positive results from multiple clinical studies in more than 170 patients. The data package included the interim analysis of ENDEAR, a Phase 3 controlled study evaluating SPINRAZA in infantile-onset, as well as open-label data in pre-symptomatic and symptomatic patients with, or likely to develop, infantile and later-onset SMA.

In ENDEAR, infantile-onset SMA patients treated with SPINRAZA achieved and sustained clinically meaningful improvement in motor function compared to untreated study participants. In addition, a greater percentage of patients on SPINRAZA survived compared to untreated patients. In open-label studies, some patients achieved milestones such as ability to sit unassisted, stand or walk when they would otherwise be unexpected to do so and maintained milestones at ages when they would be expected to be lost. The overall findings of these studies support the effectiveness of SPINRAZA across the range of SMA patients, and appear to support the early initiation of treatment.

SPINRAZA demonstrated a favourable benefit-risk profile.<sup>3</sup> The most common side effects found in participants in the clinical trials for SPINRAZA were upper respiratory infection, lower respiratory infection and constipation. SPINRAZA is to be administered by healthcare professionals experienced in doing lumbar punctures due to the risks associated with this procedure.

### **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) on December 23, 2016.<sup>4</sup>

On June 21, 2017, the European Commission (EC) granted a marketing authorization for SPINRAZA for the treatment of 5q spinal muscular atrophy (SMA) in the European Union. Biogen has also submitted regulatory filings in Japan, Australia, Brazil and Switzerland and plans to initiate additional filings in other countries in 2017.<sup>5</sup>

### **About SMA<sup>6-10</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 severe 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 infantile-onset 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 later onset SMA produce greater amounts of SMN protein and have less severe, but still life-altering forms of SMA.

### **About SPINRAZA<sup>TM</sup> (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>11</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>12</sup> where motor neurons degenerate in patients with SMA due to insufficient levels of SMN protein.<sup>13</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.<sup>2</sup>

## 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.ca](http://www.biogen.ca).

## 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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