



## U.S. FDA Approves Biogen's SPINRAZA™ (nusinersen), The First Treatment for Spinal Muscular Atrophy

December 23, 2016

*Approved for Use in Broad Range of SMA Patients*

*SPINRAZA Improved Motor Function in SMA Patients; Greater Percentage of Infantile-Onset Patients on SPINRAZA Survived*

*FDA Approval Received Within Three Months of Regulatory Filing*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--The U.S. Food and Drug Administration (FDA) approved Biogen's (NASDAQ: BIIB) SPINRAZA™ (nusinersen) under Priority Review for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. SPINRAZA is the first and only treatment approved in the U.S. for SMA, a leading genetic cause of death in infants and toddlers that is marked by progressive, debilitating muscle weakness.

In ENDEAR, a pivotal controlled clinical study, 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 offers new hope for the SMA community and exemplifies our mission of applying cutting-edge science to make a meaningful difference in the lives of patients with devastating, life-altering diseases," said George A. Scangos, Ph.D., chief executive officer at Biogen. "We are humbled and grateful for the commitment of the patients and families who participated in the SPINRAZA clinical trial program, the tireless efforts of our investigators, and the urgency demonstrated by the FDA in rapidly reviewing and approving this treatment. We also want to acknowledge the important work of our colleagues at Ionis, who initiated this program."

The FDA 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, Types 1, 2 and 3 SMA.

"With the approval today of SPINRAZA, the future for those affected with SMA has changed. We are especially pleased that this sophisticated and rigorous clinical development plan has resulted in a broad label that may offer access to many patients," said Kenneth Hobby, president at Cure SMA. "This has been a story of all groups – families, researchers, companies and the FDA – working together as one community."

SPINRAZA will be made available for shipment in the U.S. to healthcare providers in approximately one week. Biogen anticipates there may be variation in time to treatment as institutions and treatment centers learn about SPINRAZA.

### **The SPINRAZA Phase 3 Registrational Study, ENDEAR**

ENDEAR was a randomized, double-blind, sham-controlled study in patients with infantile-onset (most likely to develop Type 1) SMA. At a planned interim analysis of ENDEAR, a greater percentage of infants treated with SPINRAZA achieved a motor milestone response compared to those who did not receive treatment (40% versus 0%;  $p < 0.0001$ ) as measured by the Hammersmith Infant Neurological Examination (HINE). Additionally, a smaller percentage of patients on SPINRAZA died (23%) compared to untreated patients (43%). Data from the other efficacy endpoints analyzed were consistently in favor of infants who received treatment.

Detailed interim results from ENDEAR will be presented at the British Paediatric Neurology Association (BPNA) Annual Conference in January 2017.

### **SPINRAZA Program Updates**

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 FDA approval of SPINRAZA, Ionis will receive a \$60 million milestone payment. Ionis is also eligible to receive tiered royalties on any potential sales of SPINRAZA up to a percentage in the mid-teens.

In October, the European Medicines Agency (EMA) validated Biogen's Marketing Authorization Application (MAA) for SPINRAZA as a treatment for SMA, and the EMA's Committee for Medicinal Products for Human Use (CHMP) granted Accelerated Assessment status. In addition, Biogen has submitted regulatory filings in Japan, Canada and Australia and will initiate additional filings in other countries in 2017.

The FDA issued Biogen a rare pediatric disease priority review voucher with the approval of SPINRAZA, which confers priority review to a subsequent drug application that would not otherwise qualify for priority review. The rare pediatric disease review voucher program is designed to encourage development of new drugs and biologics for the prevention or treatment of rare pediatric diseases.

For more information about SPINRAZA and U.S. prescribing information, visit [www.SPINRAZA.com](http://www.SPINRAZA.com).

### **About Patient Support**

As part of Biogen's commitment to patients and families living with SMA, the company has launched SMA360°™, which provides certain services that address nonmedical barriers to access in the United States. These include logistical assistance, product education, insurance benefits investigations and financial assistance. A list of the SMA360° offerings will be available in the coming days at [www.SPINRAZA.com](http://www.SPINRAZA.com).

SMA360° services from Biogen are available only to those who have been prescribed SPINRAZA. To learn more about the program and receive additional information about these services, please contact an SMA Support Coordinator at 1-844-4SPINRAZA (1-844-477-4672) Monday - Friday 8:30 a.m.-8:00 p.m. EST.

## About SMA<sup>1-5</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 most severe life-threatening form, 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.

To support awareness and education about SMA, Biogen has launched Together in SMA in the United States. Together in SMA is a program created to provide informational materials and resources to the SMA community. Learn more at [www.TogetherinSMA.com](http://www.TogetherinSMA.com).

## 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 in the 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>6</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 patients with SMA.

SPINRAZA is administered via intrathecal injection, which delivers therapies directly to the cerebrospinal fluid (CSF) around the spinal cord,<sup>7</sup> where motor neurons degenerate in patients with SMA due to insufficient levels of SMN protein.<sup>8</sup>

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. Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides.

For complete SPINRAZA prescribing information please visit [www.SPINRAZA.com](http://www.SPINRAZA.com).

## About Biogen

Through cutting-edge science and medicine, Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological, autoimmune and rare diseases. Founded in 1978, Biogen is one of the world's oldest independent biotechnology companies and patients worldwide benefit from its leading multiple sclerosis and innovative hemophilia therapies. For more information, please visit [www.biogen.com](http://www.biogen.com). Follow us on [Twitter](#).

## Biogen Safe Harbor

This press release contains forward-looking statements, including statements relating to the potential safety and efficacy of SPINRAZA, regulatory filings and approvals in other jurisdictions, and planning and timing for commercial launch. 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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SPINRAZA™ (nusinersen) was approved by the U.S. FDA in December 2016 for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. (Photo: Biogen)

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Image of the SPINRAZA™ (nusinersen) U.S. carton. SPINRAZA was approved by the U.S. FDA in December 2016 for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. (Photo: Biogen)

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Image of the SPINRAZA™ (nusinersen) carton and 12 mg/5 mL vial. SPINRAZA was approved by the U.S. FDA in December 2016 for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients. (Photo: Biogen)

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Video of the Farrell family who live in the U.S. Children Braeden and Kernen both have spinal muscular atrophy (SMA).

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