Ionis Earns $40 Million SPINRAZA Regulatory Milestone Payment from Biogen

August 30, 2017

CARLSBAD, Calif., Aug. 30, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that it has earned a $40 million milestone payment from Biogen associated with the pricing approval of SPINRAZA® (nusinersen) in Japan. SPINRAZA was approved for individuals with infantile-onset spinal muscular atrophy (SMA) by the Pharmaceuticals and Medical Devices Agency in Japan in June 2017. To date, Ionis has earned more than $435 million from Biogen related to SPINRAZA.

"We are grateful to the Japanese SMA community, including the patients who participated in the clinical studies, along with their families and the investigators, for their dedication, perseverance and support. Each of them played a pivotal role in bringing SPINRAZA to the Japanese market and we are pleased that SPINRAZA is now available to Japanese infantile-onset individuals with SMA," said Stanley T. Crooke, chairman and chief executive officer of Ionis Pharmaceuticals. "SPINRAZA is now approved in the U.S., EU, Japan, Canada and Brazil, which brings us closer to achieving our shared goal with Biogen that all patients with SMA will have access to this life-changing medicine."

"We expect to see continued strong patient demand for SPINRAZA as the launch continues in the U.S. and with the commercial rollouts in Europe, Japan and around the globe," said B. Lynne Parshall, chief operating officer at Ionis Pharmaceuticals. "Biogen is working to expand access to SPINRAZA, with marketing authorization applications currently under review in Switzerland, Israel, South Korea and Australia, and additional filings planned. We believe the speed and breadth at which SPINRAZA has achieved marketing approval across geographies so far is a recognition of the immense value SPINRAZA may bring to patients."

Biogen licensed the global rights to develop, manufacture and commercialize SPINRAZA from Ionis Pharmaceuticals in August 2016 and is now responsible for all development, regulatory and commercialization activities and costs for SPINRAZA. SPINRAZA was first approved by the U.S. Food and Drug Administration (FDA) on December 23, 2016, within three months of regulatory filing.

ABOUT SMA
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 type 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 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. It was discovered and co-developed by Ionis Pharmaceuticals, a leader in antisense therapeutics, and Biogen. 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, where motor neurons degenerate in patients with SMA due to insufficient levels of SMN protein.

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 successfully led to the initiation and ongoing treatment of almost 600 eligible individuals with infantile-onset SMA (most likely to develop Type 1) across 24 countries.

For complete SPINRAZA U.S. prescribing information please visit www.SPINRAZA.com.

ABOUT IONIS PHARMACEUTICALS, INC.
Ionis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Ionis has created a large pipeline of first-in-class or best-in-class drugs, with over three dozen drugs in development. SPINRAZA® (nusinersen) has been approved in the U.S., Europe, Japan, Canada and Brazil for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen (IONIS-TTR_{Rx}), an antisense drug Ionis is developing to treat patients with TTR amyloidosis, and volanesorsen, an antisense drug discovered by Ionis and co-developed by Ionis and Akcea Therapeutics to treat patients with either familial chylomicronemia syndrome or familial partial lipodystrophy. Akcea, an affiliate of Ionis, is a biopharmaceutical company focused on developing

and commercializing drugs to treat patients with serious cardiometabolic diseases caused by lipid disorders. If approved, volanesorsen will be commercialized through Ionis' affiliate, Akcea. Both inotersen and volanesorsen are progressing toward regulatory filings for marketing authorization. Ionis' patents provide strong and extensive protection for its drugs and technology. Additional information about Ionis is available at www.ionispharma.com.

IONIS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Ionis' strategic relationship with Biogen and the development, activity, therapeutic potential, safety and commercialization of SPINRAZA. Any statement describing Ionis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on Form 10-K for the year ended December 31, 2016, and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.

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