Advances in Ionis' Novel Antisense Technology to be Presented at 2018 Society for Neuroscience Meeting

October 31, 2018

12 presentations highlighting latest data from Ionis' Neurodegenerative Program including first-in-class therapies for untreatable diseases such as Alzheimer's, ALS, Alexander, and spinocerebellar ataxia type 3

CARLSBAD, Calif., Oct. 31, 2018 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in antisense therapeutics, today announced that Ionis and its collaborators will present data from its neurological disease programs at the Society for Neuroscience (SfN) Annual Meeting in San Diego, California from November 3-7, 2018. Data and topics covered in a platform presentation and 11 posters will include:

- The therapeutic potential of antisense therapies targeting glial cells in rare and fatal demyelinating disorders, including Alexander disease, multiple sclerosis, traumatic injuries and stroke.
- The demonstration of sustained reductions in ataxin-3 (ATXN3) protein and complete rescue of motor and behavioral impairments using ATXN3-targeted antisense oligonucleotides in spinocerebellar ataxia type 3 (SCA3) mouse models, supporting continued development.
- The observed reductions and reversal of disease markers in animal models of Alzheimer's disease pathogenesis in Down syndrome treated with β amyloid antisense therapy.
- The *in vivo* screening platform for amyotrophic lateral sclerosis (ALS) targets used to validate the preclinical efficacy of IONIS-SOD1$_{Rx}$ (also known as BIIB067).
- Investigations into mechanisms to enhance antisense oligonucleotides crossing the blood brain barrier.

Following is a schedule of Ionis and collaborator data presentations (All times listed are in Pacific Time):

Oral Presentation:

- Monday, November 5, 8:00 a.m.-8:15 a.m. 'A novel murine knock-in model for progranulin-deficient frontotemporal dementia with nonsense-mediated mRNA decay'.

Poster Presentations:

- Saturday, November 3, 1:00 p.m.-2:00 p.m. 'Specific reprogramming of the memory-formation blocking gene Hdac2 with an antisense-oligonucleotide'.
- Saturday, November 3, 4:00 p.m.-5:00 p.m. 'APP-directed antisense oligonucleotides reduced APP gene expression in mouse models of Down Syndrome'.
- Sunday, November 4, 1:00 p.m.-2:00 p.m. 'Pharmacodynamics of antisense oligonucleotides in the CNS of rodents and primates following central administration'.
- Sunday, November 4, 1:00 p.m.-2:00 p.m. 'An *in vivo* screening platform for ALS targets using ALS rodent models'.
- Sunday, November 4, 2:00 p.m.-3:00 p.m. 'Evaluating HDAC6 as therapeutic target for Amyotrophic Lateral Sclerosis by antisense-mediated inhibition in the adult mouse CNS'.
- Sunday, November 4, 2:00 p.m.-3:00 p.m. 'Targeting Keap1 as a therapeutic approach for neurodegenerative disease'.
- Monday, November 5, 8:00 a.m.-12:00 p.m. 'Prediction of rTMS treatment outcome in depression: A machine learning approach'.
- Monday, November 5, 1:00 p.m.-2:00 p.m. 'Blood to brain delivery mechanisms of cholesterol conjugated antisense oligonucleotides'.
- Monday, November 5, 4:00 p.m.-5:00 p.m. 'Imaging the pharmacokinetics and pharmacodynamics of intrathecally administered antisense oligonucleotides in the rat'.
- Tuesday, November 6, 11:00 a.m.-12:00 p.m. 'Antisense oligonucleotides ameliorate disease in spinocerebellar ataxia type 3 mice'.
- Wednesday, November 7, 11:00 a.m.-12:00 p.m. 'Antisense oligonucleotides (ASOs) efficiently target glial cells and provide a novel therapeutic platform for demyelinating disorders'.

Complete abstracts for the presentations can be accessed on the SfN website. The above listed dates are subject to change. Details on presentation

times or changes to presentation dates can be found on the SfN website. Please check www.sfn.org for the latest information.

About Antisense Technology
The instructions for making a protein are transcribed from a gene, or DNA, into a different genetic molecule called messenger RNA (mRNA). This process starts with the partial uncoiling of the two complementary strands of the DNA. One strand acts as a template and information stored in the DNA template strand is copied into a complementary RNA. Messenger RNA, or mRNA, are mature, fully processed RNA that code for proteins. Ribosomes, the cell's factories for manufacturing proteins, translate mRNA into proteins.

The mRNA sequence that carries the information for protein production is called the 'sense' strand. The complementary nucleotide chain that binds specifically to the mRNA sense strand is referred to as the "antisense" strand. Information contained in mRNA can be used to design chemical structures called antisense oligonucleotides (ASOs) or antisense drugs, which resemble DNA and RNA and are the complement of RNA.

Antisense drugs bind with high selectivity to the mRNA they are designed to target and interrupt the cell's protein production process by preventing the mRNA instructions from reaching the ribosome, thus inhibiting the production of the protein. Antisense drugs can also be designed to increase protein production for diseases caused by the lack of a particular protein or can modify the processing, or splicing, of the mRNA, which can alter the composition of the protein.

About Ionis Pharmaceuticals, Inc.
As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, proprietary antisense technology platform with the potential to treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs – such as children and adults with spinal muscular atrophy (SMA). We created SPINRAZA® (nusinersen)* and are proud to have brought new hope to the SMA community by developing the first and only approved treatment for this disease.

Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 drugs with the potential to treat patients with cardiovascular disease, rare diseases, neurological diseases, infectious diseases and cancer. We created TEGSEDI™ (inotersen) the world's first RNA-targeted therapeutic approved for the treatment of polyneuropathy of hereditary transthyretin (TTR) amyloidosis (ATTR) in adult patients that our affiliate Akcea Therapeutics is commercializing. Together with Akcea, we are also bringing new medicines to patients with cardiometabolic lipid disorders.

To learn more about Ionis follow us on twitter @ionispharma or visit http://ir.ionispharma.com/.

*Spinraza is marketed by Biogen.

Ionis' Forward-looking Statement
This press release includes forward-looking statements regarding the therapeutic and commercial potential of Ionis' technologies and products in development, including SPINRAZA® and TEGSEDI™ (inotersen). 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, 2017, and most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of this 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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