First-in-class therapies using advanced antisense chemistries highlighted at 2018 American Society of Hematology Annual Meeting

November 27, 2018

Wholly-owned LICA drug for beta-thalassemia, IONIS-TMPRSS6-L Rx, demonstrates therapeutic potential with positive modulation of important disease-related biomarkers and increase of serum hepcidin in initial clinical study

Ionis oncology research to be recognized with American Society of Hematology Abstract Achievement Award

CARLSBAD, Calif., Nov. 27, 2018 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in antisense therapeutics, today announced that data from the IONIS-TMPRSS6-L_{Rx} Phase 1 study, TEGSEDI™ (inotersen) and other Ionis research and development programs will be presented at the 60th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego, California, December 1-4, 2018.

The results to be reported at ASH demonstrate the potential for antisense therapeutics to address a broad range of diseases by potentially bringing transformational medicines to patients with severe diseases who have limited treatment options. IONIS-TMPRSS6-L_{Rx}, an antisense therapy in development for people suffering with beta-thalassemia and other potential indications, is one of several of Ionis' advanced **LI**gand **C**onjugated **A**ntisense, or LICA, drugs to demonstrate potent target reduction and a favorable safety and tolerability profile in humans.

Additional data and topics covered in the platform presentations and posters will include:

- The therapeutic potential of IONIS-TMPRSS6-L_{Rx}, as demonstrated by modulation of important biomarkers including observed reductions in plasma iron levels in a Phase 1 study.
- The therapeutic potential of IONIS-TMPRSS6-L_{Rx} in combination with erythropoietic stimulating agents and iron restriction to correct anemia, while improving splenomegaly and iron overload in an animal model of non-transfusion dependent beta-thalassemia.
- The use of antisense oligonucleotides to specifically modulate platelet levels as a potentially novel therapeutic approach for cancer and potentially other disorders.
- The long-term analyses of the NEURO-TTR open-label extension study and TEGSEDI's impact on the lives of patients living with polyneuropathy caused by hereditary transthyretin amyloidosis (hATTR).

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

Oral Presentations:

- Saturday, December 1, 2:15 p.m.-2:30 p.m. 'Correcting Non-Transfusion Dependent β-Thalassemia by Utilizing a Combined Therapy that Modulates EPO Activity by Limiting Erythroid Cellular Iron Intake'.
- Sunday, December 2, 5:45 p.m.-6:00 p.m. 'Long-Term Update from the Open-Label Extension of the NEURO-TTR Study in Patients with Hereditary Transthyretin Amyloidosis'.
- Monday, December 3, 7:15 p.m.-7:30 p.m. 'Antisense Oligonucleotide Targeting of Thrombopoietin Synthesis Reduces Platelet Count within the Hemostatic Range and Slows Progression of De Novo Mammary Carcinogenesis in the Mmtv-Pymt Mouse'.

Poster Presentations:

- Sunday, December 2, 6:00 p.m.-8:00 p.m. 'Inhibiting the Immunophilin FKBP12: A Potential Therapeutic Approach to Iron Overload/Low Hepcidin Disorders'.
- Monday, December 3, 6:00 p.m.-8:00 p.m. 'Transmembrane Protease, Serine 6 (TMPRSS6) Antisense Oligonucleotide (IONIS-TMPRSS6-L_{Rx}) Reduces Plasma Iron Levels of Healthy Volunteers in a Phase 1 Clinical Study'.
- Monday, December 3, 6:00 p.m.-8:00 p.m. 'Investigating Potential Mechanism(s) By Which ASO-Based Drugs Cause Thrombocytopenia'.
- Monday, December 3, 6:00 p.m.-8:00 p.m. 'Impact of Inotersen on Functioning and Activities of Daily Living for Patients with Hereditary TTR Amyloidosis: Results from a Double-Blind Placebo-Controlled Trial'.

Complete abstracts, details on presentation times and changes to presentation dates can be found on the ASH website. The above listed dates are subject to change. Please check www.hematology.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.

LICA, or **Li**gand **C**onjugated **A**ntisense, is a chemical technology we developed at Ionis that involves the attachment of a molecule called a ligand that binds with receptors on the surfaces of cells in a highly specific manner. Because these receptors are often found only on certain cell types, LICA allows us to effectively deliver our antisense drugs with specificity to certain cell types that express these receptors. Although we designed our first LICA drugs to inhibit targets in the liver, we are also developing LICA conjugation technology that we can use to target other tissues and initial results are promising.

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.

View original content to download multimedia:http://www.prnewswire.com/news-releases/first-in-class-therapies-using-advanced-antisense-chemistries-highlighted-at-2018-american-society-of-hematology-annual-meeting-300755272.html

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