Ionis to Independently Advance Inotersen and IONIS-FB-L Rx

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Inotersen on Track for Marketing Authorization Filings This Year
Conference Call Webcast Friday, August 11, 8:30 a.m. ET at www.ionispharma.com

CARLSBAD, Calif., Aug. 11, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today reported that the Company has retained all rights to inotersen and IONIS-FB-L_{Rx}. As part of a reprioritization of its pipeline and strategic review of its Rare Diseases business, GSK declined its options on both drugs. Ionis plans to file for marketing authorization for inotersen this year to support a commercial launch of inotersen in 2018. Inotersen is a drug designed to treat patients with TTR amyloidosis (ATTR). The first indication Ionis is pursuing for inotersen is to treat patients with polyneuropathy due to hereditary TTR amyloidosis (hATTR-PN).

"We are pleased to move forward these two important drugs ourselves. We are prepared to independently advance inotersen and remain on track to file for marketing approval of inotersen in the U.S. and EU this year," said B. Lynne Parshall, chief operating officer of Ionis Pharmaceuticals. "We want to thank our collaboration team at GSK for their support and commitment to patients with TTR amyloidosis, and their efforts to work closely with us to ensure a smooth transition so that this important medicine can be available to patients as planned."

Ionis completed the Phase 3 NEURO-TTR study of inotersen in which the drug demonstrated significant benefit on both primary clinical endpoints of neurological disease progression and quality of life in patients with hATTR-PN.

"Our goals for inotersen are to maximize its commercial success and optimize our commercial participation. To achieve these goals, we are actively considering forming a commercial subsidiary to commercialize or co-commercialize inotersen in North America, as well as other options. Our recent experience building a commercial subsidiary has prepared us for this opportunity. We have substantial interest from potential partners and are in discussions with several parties. We believe that, together with the right commercial partner, we can maximize the commercial success of the drug worldwide," said Sarah Boyce, chief business officer of Ionis Pharmaceuticals.

"We are also accelerating the expansion of our TTR program for patients with cardiomyopathy due to TTR amyloidosis and the development of our LICA follow-on drug. Our experience in the completed Phase 3 NEURO-TTR study provides important information to aid in design of a study in patients with cardiomyopathy due to TTR amyloidosis. We have already identified a more potent and convenient LICA follow-on and we expect development of the LICA drug to also proceed rapidly," said Stanley T. Crooke, chairman and chief executive officer of Ionis Pharmaceuticals. "We are deeply committed to the TTR amyloidosis patient community. Patients with TTR amyloidosis, their families and healthcare providers are desperately seeking improved therapeutic options for this devastating, progressive, fatal disease."

IONIS-FB-L_{Rx} is a ligand conjugated antisense (LICA) drug in development for the treatment of complement-mediated diseases. In a Phase 1 study completed earlier this year, IONIS-FB-L_{Rx} achieved dose-dependent reductions in plasma factor B (FB) and demonstrated a safety and tolerability profile that supports further clinical development. Ionis plans to initiate the first Phase 2 study with IONIS-FB-L_{Rx} in patients with dry age-related macular degeneration (AMD) later this year, and studies in other indications in 2018.

"IONIS-FB-L_{Rx} represents a unique opportunity to develop a treatment for underserved rare and broad patient populations affected by a variety of complement-mediated diseases," said Brett P. Monia, senior vice president of drug discovery and franchise leader for oncology and rare diseases at Ionis Pharmaceuticals. "IONIS-FB-L_{Rx} takes advantage of our LICA technology, which can potentially provide greater patient convenience by allowing for significantly lower doses and less frequent administration."

GSK, consistent with its focus on treatments for infectious diseases, continues to advance two drugs targeting hepatitis B virus (HBV) under its collaboration with Ionis: IONIS-HBV_{Rx} and IONIS-HBV-L_{Rx}. GSK is currently conducting Phase 2 studies for both drugs.

Conference Call
At 8:30 a.m. Eastern Time today, August 11, 2017, Ionis will conduct a live webcast conference call to discuss this announcement. Interested parties may listen to the call by dialing 877-443-5662 or access the webcast at www.ionispharma.com. A webcast replay will be available for a limited time at the same address.

ABOUT INOTERSEN
Inotersen (IONIS-TTR_{Rx}) is a generation 2.0+ antisense drug Ionis is developing for the treatment of patients with TTR amyloidosis (ATTR). Inotersen is administered once weekly as a single 300 mg subcutaneous injection. Ionis designed inotersen to inhibit the production of all forms of TTR protein, including both the hereditary and wild-type forms, offering a unique approach to treat all types of ATTR. Inotersen has demonstrated sustained and robust TTR reductions in clinical studies in different populations of patients with ATTR.

Ionis has successfully completed the Phase 3 NEURO-TTR study with inotersen in patients with polyneuropathy due to hereditary TTR amyloidosis (hATTR-PN). Ionis plans to file for marketing approval of inotersen in the U.S. and EU in the second half of 2017. The Company also plans to present results from the NEURO-TTR study at an upcoming medical meeting and to submit results from the study for publication in a peer-reviewed medical journal.

The U.S. Food and Drug Administration has granted Orphan Drug Designation and Fast Track Status to inotersen for the treatment of patients with familial amyloid polyneuropathy. The European Medicines Agency has granted Orphan Drug Designation to inotersen for the treatment of patients with TTR amyloidosis.

ABOUT TTR AMYLOIDOSIS

Transthyretin amyloidosis (ATTR) is a progressive, debilitating and fatal genetic disease in which patients experience TTR build up in major organs, including peripheral nerves, heart, intestinal tract, kidney and bladder.

One key manifestation of ATTR results when TTR amyloid fibrils deposit in peripheral nerves, which causes nerve damage throughout the patient's body resulting in the progressive loss of motor functions, such as walking. When this occurs, patients are diagnosed with polyneuropathy due to hereditary TTR amyloidosis (hATTR-PN). Another major manifestation of ATTR occurs when TTR amyloid fibrils build up in heart tissue, which results in cardiomyopathy due to TTR amyloidosis (ATTR-CM). In all manifestations of ATTR, TTR accumulates in major organs, progressively impacts organ function and eventually leads to death. Therapeutic options for the treatment of ATTR are very limited and there are currently no drugs approved for the treatment of ATTR in the United States.

ABOUT IONIS-FB-L_{Rx}

IONIS-FB-L_{Rx} is a generation 2.0+ ligand conjugated antisense (LICA) drug designed to reduce the production of complement factor B (FB). Complement factor B is produced predominately in the liver and circulates at high levels throughout the vascular system where it plays a pivotal role in an innate immunogenic cascade. Genetic association studies have shown that overactivation of this cascade has been associated with the development of several complement-mediated diseases, including dry age-related macular degeneration (AMD).

Ionis has completed a Phase 1 study evaluating IONIS-FB-L_{Rx} in healthy volunteers. In the Phase 1 study, IONIS-FB-L_{Rx} achieved dose-dependent reductions in FB and demonstrated a safety and tolerability profile that supports further clinical development. Ionis plans to initiate the first Phase 2 study with IONIS-FB-L_{Rx} in patients with dry AMD later this year, and studies in other indications in 2018.

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 and Canada 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' alliance with GSK and the therapeutic and commercial potential of inotersen, IONIS-FB-L_{Rx}, IONIS-HBV_{Rx} and IONIS-HBV-L_{Rx}. 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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