Ionis Pharmaceuticals Announces Plans to Open Expanded Access Program to Provide Inotersen to Patients with Hereditary TTR Amyloidosis in the U.S.

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- Ionis plans to open multiple sites in the U.S.

CARLSBAD, Calif., Oct. 27, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that it plans to open an expanded access program (EAP) for eligible patients with hereditary transthyretin amyloidosis (hATTR) with polyneuropathy in the coming months. Ionis plans to open the first wave of EAP sites in the U.S.

"The announcement of this EAP for inotersen brings hope for people with hATTR, their caregivers, families, and physicians. Our community is excited about the NEURO-TTR study results they have seen and many patients are looking forward to the opportunity to participate in an EAP in hopes of experiencing benefit themselves," said Muriel Finkel, president of the Amyloidosis Support Group. "We are excited about the opportunity to have a potentially life-altering new therapy available. We are eager for the continued advancement of potential new therapies and additional research that we hope can someday cure this progressive, fatal genetic disease."

"We are pleased with the benefit we have observed in measures of quality of life and disease progression in inotersen-treated patients compared to placebo-treated patients in our Phase 3 clinical program," said Sarah Boyce, chief business officer at Ionis. "We are on track to complete the regulatory filings for market authorization in the U.S. and EU before year end. We are making good progress in our discussions with potential partners and also making substantial progress in preparing for the commercial launch of inotersen next year. We believe inotersen has the potential to transform the lives of patients with hereditary TTR amyloidosis."

ABOUT INOTERSEN

Inotersen is an antisense drug designed to reduce the production of transthyretin, or TTR, to treat patients with TTR amyloidosis (ATTR), a severe, rare and fatal disease. In patients with ATTR, both the mutant and wild type (wt) TTR builds up as fibrils in tissues, such as the peripheral nerves, heart, gastrointestinal system, eyes, kidneys, central nervous system, thyroid and bone marrow. The presence of TTR fibrils interferes with the normal functions of these tissues. As the TTR protein fibrils enlarge, more tissue damage occurs and the disease worsens, resulting in poor quality of life and eventually death.

The U.S. Food and Drug Administration has granted Orphan Drug Designation and Fast Track Status to inotersen for the treatment of patients with polyneuropathy due to hATTR. The European Medicines Agency has granted Orphan Drug Designation to inotersen for the treatment of patients with ATTR.

ABOUT INOTERSEN PHASE 3 CLINICAL STUDY

Inotersen completed a Phase 3 study, NEURO-TTR, in patients with polyneuropathy due to hereditary TTR amyloidosis (hATTR) in May 2017. Results from the study demonstrated benefit compared to placebo across both primary endpoints of the study: the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN) and the modified Neuropathy Impairment Score +7 (mNIS+7) at both 8 and 15 months of treatment. Inotersen-treated patients benefited significantly in the quality of life primary endpoint compared to placebo, with a difference in magnitude of 11.68 points in the Norfolk QoL-DN score at 15 months of treatment (mean change from baseline of 0.99 vs. 12.67, p=0.0006). Inotersen-treated patients also benefited significantly in the co-primary endpoint of disease control, mNIS+7, with a mean 19.73-point benefit observed after 15 months of treatment, compared to placebo-treated patients (p = 0.00000004). We believe these results support a favorable benefit-risk profile for inotersen in patients with hATTR.

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 global markets for the treatment of spinal muscular atrophy (SMA). Biogen is responsible for commercializing SPINRAZA. Drugs that have successfully completed Phase 3 studies include inotersen, an antisense drug Ionis is developing to treat patients with hereditary TTR amyloidosis (hATTR), 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. Volanesorsen filings for marketing approval have been submitted in the U.S., EU and Canada. Inotersen is 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' business and the therapeutic and commercial potential of inotersen and other products in development. 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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