Ionis Presents New Data from NEURO-TTR Study and Highlights Programs from Its Neurological Disease Franchise at ANA Congress

October 15, 2017

Inotersen treatment resulted in a 20-point benefit in mNIS+7 compared to placebo
Ionis antisense programs featured in 11 platform and poster presentations at ANA

CARLSBAD, Calif., Oct. 15, 2017 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in antisense therapeutics, today announced that new data from the Phase 3 NEURO-TTR study with inotersen in patients with hereditary TTR amyloidosis (hATTR) with polyneuropathy were presented at the 142nd annual meeting of the American Neurological Association (ANA) in San Diego, California. In the study, inotersen-treated patients achieved a mean 19.73-point benefit in the mNIS+7 co-primary endpoint after 15 months of treatment, compared to placebo-treated patients (p = 0.00000004), further demonstrating the clinically meaningful benefit of inotersen treatment. A statistically significant benefit in mNIS+7 was also observed at eight months. Key safety findings of thrombocytopenia and renal events identified during the study were shown to be monitorable and manageable with routine blood and urine testing. Multiple other innovative drugs from Ionis' portfolio of drugs for patients with serious neurological and neurodegenerative diseases will be highlighted as part of the Antisense Oligonucleotide Treatment of Genetic Neurological Diseases plenary session on Tuesday, October 17.

"The pivotal inotersen data presented today represent new hope for patients suffering with hATTR. A 20-point benefit in mNIS+7 is unprecedented and could mean the difference between the ability to walk and being confined to a wheelchair for patients suffering from this debilitating and fatal disease," said Annabel Wang, associate professor of neurology at the University of California, Irvine, School of Medicine. "Based on benefit observed in neurological and quality of life endpoints, inotersen treatment has shown the potential to effectively change the relentless progression of this disease and offers a convenient, at-home administration method, providing patients further liberation from the burden of hATTR."

In addition to the inotersen program update, Ionis antisense programs will be featured in eleven platform and poster presentations throughout the meeting, including:

- Highlights from the discovery and development program for SPINRAZA® (nusinersen), the first and only drug approved for the treatment of spinal muscular atrophy.
- Development overviews for IONIS-HTT_{Rx} for the treatment of patients with Huntington's disease and IONIS-$MAPT_{Rx}$ for the treatment of patients with tauopathies, including Alzheimer's disease and frontotemporal dementia.
- Presentations featuring Ionis' antisense programs designed to treat amyotrophic lateral sclerosis, Parkinson's disease and Alexander disease.

"Ionis' leadership in neurodegeneration is well highlighted at ANA. The programs featured at this medical meeting presented by us and our collaborators validate the breadth and potential impact of our neurological disease franchise. We are rapidly expanding and advancing our neurological disease pipeline, adding more innovative drugs, each with the potential to transform the treatment of severe neurological and neurodegenerative disease," said C. Frank Bennett, PhD, senior vice president of research and leader of the neurological disease franchise at Ionis Pharmaceuticals. "We are pleased with the impact SPINRAZA has already made on the SMA community. We are now applying what we learned from SPINRAZA to our other neurological disease drugs in development."

Ionis antisense programs will be featured in the following platform and poster presentations at the 2017 ANA congress:

- 'Safety and Efficacy of Inotersen in Patients with Hereditary Transthyretin Amyloidosis with Polyneuropathy (NEURO-TTR)' oral presentation on Tuesday, October 17 by Annabel Wang, MD, University of California, Irvine
- 'Antisense Oligonucleotide Therapy in ALS, Huntington's Disease and Beyond' oral presentation on Tuesday, October 17 by Don Cleveland, PhD, Chair, Department of Cellular and Molecular Medicine, University of California, San Diego
- 'ASO Therapy for SMA: Harnessing the Power of a Backup Gene' oral presentation on Tuesday, October 17 by Adrian R. Krainer, PhD, Cold Spring Harbor Laboratory and ANA's 2017 F.E. Bennett Memorial Lecture Award Recipient
- 'Getting the Message: Antisense Oligonucleotide Therapy for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy' oral presentation on Tuesday, October 17 by Richard Finkel, MD, FANA, Nemours Children's Hospital
- 'Antisense Oligonucleotide Therapy for Huntington's Disease: A Clinical Trials Perspective' oral presentation on Tuesday, October 17 by Sarah J. Tabrizi, MBChB, FRCP, PhD, FMedSci, UCL Huntington's Disease
- 'Rationale for and Development of IONIS-$MAPT_{Rx}$, the First *Tau*-lowering Antisense Oligonucleotide, in Patients with Mild AD' poster presentation on Monday, October 16 by Laurence Mignon, Ionis Pharmaceuticals
- 'ASO Lowering of SOD1 Markedly Extends Survival and Reverses Muscle Denervation in SOD1 ALS Rodent Models' oral presentation on Monday, October 16 by Timothy Miller, MD, PhD, Washington University in St. Louis

- 'Modeling C9ORF72 Disease: A Crucial Step for Therapeutic Development in ALS and Frontotemporal Dementia' oral presentation on Sunday, October 15 by Clotilde Lagier-Tourenne, MD, PhD, Massachusetts General Hospital
- 'LRRK2 Antisense Oligonucleotides Ameliorate -Synuclein Inclusion Formation and Provide Neuroprotection in a Parkinson's Disease Mouse Model' poster presentation on Sunday, October 15 by Hien Tran Zhao, PhD, Ionis Pharmaceuticals
- 'Snca Targeted Antisense Oligonucleotides Modulate Progression of Pathological Deposition in Alpha Synuclein Rodent Transmission Models of Parkinson's Disease' poster presentation on Sunday, October 15 by Tracy Cole, PhD, Ionis Pharmaceuticals
- 'Antisense Suppression of GFAP as a Therapeutic Strategy for Alexander Disease' poster presentation on Sunday, October 15 by Berit Powers, PhD, Ionis Pharmaceuticals

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 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. 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 SPINRAZA, inotersen, IONIS-HTT_{Rx}, IONIS-$MAPT_{Rx}$ 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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SOURCE Ionis Pharmaceuticals, Inc.

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