Phase 2 study results of Ionis' novel antisense treatment for hereditary angioedema to be presented at ACAAI annual meeting

November 7, 2021

- Positive Phase 2 study results demonstrate significant efficacy of donidalorsen (formerly IONIS-PKK-LRx) in the reduction of hereditary angioedema attacks

- Based on the results of the Phase 2 study, Ionis plans to initiate a Phase 3 program of donidalorsen in people with HAE

CARLSBAD, Calif., Nov. 7, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in RNA-targeted therapies, announced today that positive results from the Phase 2 study of its investigational antisense medicine, donidalorsen (formerly IONIS-PKK-L_{Rx}), will be presented at the American College of Asthma, Allergy & Immunology (ACAAI) Annual Scientific Meeting in New Orleans and via livestream, November 4-8. The Phase 2 study results support the clinical profile of donidalorsen as a potential, best-in-class prophylactic treatment for patients with hereditary angioedema (HAE), and underscore Ionis' commitment to advancing antisense technology to target the root cause of diseases.

HAE is a rare and potentially fatal autosomal dominant disease that results in recurrent, painful attacks of swelling affecting the hands, feet, limbs, face, abdomen, larynx and trachea. Donidalorsen is an investigational antisense medicine designed to reduce the production of prekallikrein, which plays a key role in the activation of inflammatory mediators associated with acute attacks of HAE. Donidalorsen was developed using Ionis' advanced **LI**gand-**C**onjugated **A**ntisense (LICA) technology.

Topline results of the Phase 2 study, reported earlier this year, showed that donidalorsen met its primary and all secondary endpoints, achieving significant reductions in the number of attacks suffered by patients with hereditary angioedema (HAE) compared to placebo. These data support advancing donidalorsen into Phase 3 development, which Ionis plans to initiate this year.

"A Phase 2 Study Evaluating an Antisense Oligonucleotide to Prekallikrein in Patients with Hereditary Angioedema" will be presented on Sunday, Nov. 7 at 3:03 p.m. CT (recorded presentation) by Danny Cohn, M.D., Ph.D., Department of Vascular Medicine, Amsterdam Universities Medical Center, Amsterdam, The Netherlands. Dr. Cohn, a primary investigator in the study, will present results of the Phase 2 study during *Oral Abstracts Session 2B (Angioedema/urticaria, food allergy, allergy diagnostics and immunotherapy)*. Additional details can be found on the ACAAI website.

About Hereditary Angioedema
HAE is a rare genetic disease that is characterized by rapid and painful attacks of inflammation in the hands, feet, limbs, face, abdomen, larynx and trachea. HAE affects approximately 20,000 patients in the United States and Europe and can be fatal if swelling occurs in the larynx. In patients with frequent or severe attacks, doctors may use prophylactic treatment approaches to prevent and reduce the severity of HAE attacks.

About Ionis Pharmaceuticals, Inc.
For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry-leading neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

To learn more about Ionis, visit www.ionispharma.com and follow us on twitter @ionispharma.

Ionis' Forward-looking Statement
This press release includes forward-looking statements regarding Ionis' business, and the therapeutic and commercial potential of Ionis' technologies, donidalorsen 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, including those related to the impact COVID-19 could have on our business, and including but not limited to those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. 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, 2020, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available from the Company.

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