Ionis initiates Phase 3 clinical program of donidalorsen in patients with hereditary angioedema

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- OASIS-HAE is the registrational study in Ionis' donidalorsen Phase 3 clinical program and further expands Ionis' late-stage pipeline

- Donidalorsen is one of Ionis' wholly owned medicines the company plans to commercialize

CARLSBAD, Calif., Nov. 18, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in RNA-targeted therapies, announced today initiation of OASIS-HAE, the registrational study in the donidalorsen (formerly IONIS-PKK-L_{Rx}) Phase 3 clinical program. 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 hereditary angioedema (HAE). Donidalorsen uses Ionis' **LI**gand-**C**onjugated **A**ntisense, or LICA, technology.

"Initiating the Phase 3 program for donidalorsen moves us one step closer to bringing a potential best-in-class prophylactic treatment to market for people with HAE globally experiencing recurrent painful and severe HAE attacks," said Kenneth Newman, M.D., M.B.A., Ionis' vice president of clinical development and leader of the immunology and pulmonology franchise. "Advancing this program underscores our commitment to the HAE patient community to deliver transformative treatments."

OASIS-HAE is a double-blind, randomized, placebo-controlled registrational study in up to 84 patients with hereditary angioedema, Types 1 and 2. Patients will be randomized to receive monthly or bi-monthly subcutaneous donidalorsen for 25 weeks. Following the placebo-controlled portion of the study, patients may enter the 52-week open-label extension study.

New Phase 2 data recently presented at ACAAI highlighted an overall reduction in moderate to severe attacks, and a reduction in these attacks starting with the second dose. For the final month of the study, all donidalorsen treated patients were attack-free. In this study, donidalorsen was safe and well tolerated.

For more information on the OASIS-HAE clinical study please visit www.clinicaltrials.gov.

About Donidalorsen Phase 2 study

In the Phase 2 clinical study, 20 adults with Type 1 or Type 2 HAE were randomized and received either donidalorsen 80mg (n=14) or placebo (n=6) subcutaneously once monthly for 17 weeks. The primary endpoint was the reduction of monthly HAE attacks compared to placebo. Secondary endpoints included the reduction of monthly attacks in weeks five to 17, reduction in the number of moderate or severe attacks in weeks one to 17, the number of moderate or severe attacks in weeks five to 17 and the number of attacks requiring acute therapy in weeks five to 17. The majority of adverse events during the study were mild with a frequency that was similar between groups. The most common treatment-emergent adverse events (TEAEs) were headache and nausea, which were seen more frequently in the placebo arm compared to the active treatment arm.

About Hereditary Angioedema

HAE is a rare and potentially fatal 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 U.S. 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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