



Ionis reports positive topline Phase 2 study results of its novel antisense treatment for hereditary angioedema

March 29, 2021

- IONIS-PKK-L Rx met its primary and all secondary endpoints, including a mean reduction of up to 97% in HAE attacks compared to placebo

CARLSBAD, Calif., March 29, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) announced today that data from a Phase 2 clinical study of IONIS-PKK-L_{Rx} met its primary and secondary endpoints, achieving significant reductions in the number of attacks suffered by patients with hereditary angioedema (HAE) compared to placebo. The study demonstrated a mean reduction of 90% in the number of monthly HAE attacks in weeks one to 17 of the study ($p < 0.001$) and a mean reduction of 97% in the number of monthly HAE attacks in weeks five to 17 ($p = 0.003$). In weeks five to 17, 92% of patients treated with IONIS-PKK-L_{Rx} were attack-free compared to 0% in the placebo group ($p < 0.001$).



IONIS-PKK-L_{Rx} was developed using Ionis' advanced ligand-conjugated antisense (LICA) technology. IONIS-PKK-L_{Rx} is one of Ionis' wholly owned medicines to treat rare diseases.

Hereditary angioedema is a rare autosomal dominant disease that results in recurrent, painful attacks of swelling affecting the arms, legs, face, intestinal track and airway. IONIS-PKK-L_{Rx} is an investigational antisense medicine designed to reduce the production of prekallikrein, or PKK, which plays a key role in the activation of inflammatory mediators associated with acute attacks of HAE. Without preventive treatment, HAE attacks can be frequent and severe and, in some patients, life-threatening. Physicians have long prescribed prophylactic treatment approaches, including C1-INH replacement therapies and more recently inhibitors of plasma kallikrein, to prevent and reduce the severity of HAE attacks. Despite these available therapies, patients with HAE may experience breakthrough attacks.

"These topline Phase 2 study results support a profile for IONIS-PKK-L_{Rx} as a potential best-in-class prophylactic treatment for patients with HAE, with excellent efficacy, safety and tolerability along with the convenience of once per month low volume subcutaneous injections," said Kenneth Newman, M.D., M.B.A., Ionis' vice president of clinical development and leader of the pulmonology and immunology franchise. "These results highlight the potential benefits and advantages of IONIS-PKK-L_{Rx} for the treatment of hereditary angioedema and more broadly underscore the power of Ionis' antisense technology to target the root causes of rare diseases like HAE."

In the Phase 2 clinical study, 20 adults with Type 1 or Type 2 HAE were randomized and received either IONIS-PKK-L_{Rx} 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. Ionis expects to present a full analysis of its Phase 2 study of IONIS-PKK-L_{Rx} at a medical conference later this year.

Ionis will host a series of webinars on rare diseases for which the company is developing potential treatments. The first webinar, on hereditary angioedema, is scheduled for Monday, April 5. Visit www.ionispharma.com for more information and to register for the webinar.

About Ionis Pharmaceuticals

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-PKK-L_{Rx} and Ionis' technologies and 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, which is on file with the SEC. Copies of this 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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