# Ionis antisense medicine being evaluated in an investigator-initiated clinical study of COVID-19 patients in Brazil

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**- Study will evaluate the effectiveness of IONIS-PKK-LRx in reducing the severity of respiratory complications in COVID-19 patients**

CARLSBAD, Calif., Oct. 15, 2020 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in antisense therapeutics, announced today that IONIS-PKK-$L_{Rx}$ is being evaluated in an investigator-initiated Phase 2 clinical study to determine its effectiveness in reducing the severity of respiratory complications in patients with COVID-19. The trial coordinators are Fernando G. Zampieri, M.D., Ph.D., and Alexandre Biasi Cavalcanti, M.D., Hospital do Coracao (HCor Research Institute), Sao Paulo, Brazil. The study will enroll up to 110 patients at 25 hospitals in Brazil. Ionis has provided IONIS-PKK-$L_{Rx}$ and funding to the Brazilian Research for Intensive Care Network (BRICNet) to support the study.

IONIS-PKK-$L_{Rx}$ is designed to inhibit bradykinin signaling by halting synthesis of prekallikrein (PKK), a precursor of the enzyme kallikrein, which is involved in the formation of bradykinin, a protein that promotes inflammation and dilates blood vessels. There is growing evidence that the pulmonary edema (fluid in the lungs) and associated morbidities in severe COVID-19, such as the respiratory distress syndrome, are, in part, caused by a dysregulation in bradykinin signaling, referred to as a "bradykinin storm". A therapy that prevents or reduces this bradykinin storm could potentially decrease the number of severe cases of COVID-19 in Brazil.

"Bradykinin elevations in the body can cause blood vessels to become leaky, causing inflammation in the surrounding tissue. In the lungs, this is often associated with severe COVID-19 cases. We are hopeful that IONIS-PKK-$L_{Rx}$ can alleviate some of the worst symptoms caused by the infection and we look forward to seeing data from the study," said Kenneth Newman, M.D., M.B.A., Ionis' vice president of clinical development and leader of the pulmonology and immunology franchise.

In the study, a single dose of IONIS-PKK-$L_{Rx}$ or placebo will be administered subcutaneously to hospital patients who present with symptoms consistent with COVID-19. The primary endpoint is the number of days alive and free of oxygen support up to 15 days.

Learn more about the Phase 2 study here: Antisense Therapy to Block the Kallikrein-kinin Pathway in COVID-19 (ASKCOV).

IONIS-PKK-$L_{Rx}$ is also undergoing a Phase 2 clinical study in patients with hereditary angioedema (HAE). In September, the New England Journal of Medicine published encouraging data showing safety and efficacy in two patients with uncontrolled, severe HAE. These data support the continued development of IONIS-PKK-$L_{Rx}$ as a potential treatment in patients with severe HAE for whom current therapies offer limited therapeutic benefit.

IONIS-PKK-$L_{Rx}$ is one of 20 potentially transformative antisense programs in the growing Ionis-owned pipeline that the company is prioritizing and preparing for commercialization.

**About IONIS-PKK-$L_{Rx}$**

IONIS-PKK-$L_{Rx}$ is an investigational antisense medicine designed to reduce the production of prekallikrein, or PKK, in patients with hereditary angioedema, or HAE, a rare, genetic, potentially fatal disease characterized by rapid and painful attacks of inflammation in the hands, feet, limbs, face, abdomen, larynx and trachea. IONIS-PKK-$L_{Rx}$ was developed using Ionis' advanced **LI**gand **C**onjugated **A**ntisense (LICA) technology platform. PKK plays an important role in the activation of inflammatory mediators associated with acute attacks of HAE. Current prophylactic treatment approaches are limited and have major tolerability issues, leaving patients with few therapeutic options. IONIS-PKK-$L_{Rx}$ is also undergoing an investigator-initiated Phase 2 clinical study in Brazil to evaluate its effectiveness in reducing the severity of respiratory complications in patients with COVID-19.

**Ionis' Forward-looking Statement**

This press release includes forward-looking statements regarding Ionis' business and the therapeutic potential of IONIS-PKK-$L_{Rx}$. 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, 2019, 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.

In this press release, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals and its subsidiaries.



**About Ionis Pharmaceuticals**

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable drug discovery platform called antisense technology that can treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs. We created the first and only approved treatment for all patients, children and adults with spinal muscular atrophy as well as the world's first RNA-targeted therapeutic approved for the treatment of

polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to potentially treat a broad range of disease, including neurological, cardio-renal, metabolic, infectious, and pulmonary diseases.

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

View original content to download multimedia:http://www.prnewswire.com/news-releases/ionis-antisense-medicine-being-evaluated-in-an-investigator-initiated-clinical-study-of-covid-19-patients-in-brazil-301152861.html

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