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- Data from the first clinical study of IONIS-ENAC-2.5 Rx to be presented at North American Cystic Fibrosis Conference

CARLSBAD, Calif., Oct. 13, 2020 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in antisense therapeutics, announced today that data from a clinical trial of IONIS-ENAC-2.5$_{Rx}$ demonstrated a significant decrease in the expression of epithelial sodium channel (ENaC) in healthy subjects. The study showed a mean 55.6 percent decrease ($p<0.05$) in ENaC mRNA expression at the 75 mg dose in the multidose segment of the trial. The study represents the first time an antisense medicine delivered directly to the lung via a nebulizer has shown a significant reduction in ENaC messenger RNA levels. In preclinical studies, ENaC mRNA reductions of 40 percent or more resulted in significant improvement in mouse models of CF lung disease.

IONIS-ENAC-2.5$_{Rx}$ is an investigational antisense medicine designed to reduce the expression of ENaC in the lung. ENaC is believed to be hyperactive in cystic fibrosis, which is caused by mutations in the cystic fibrosis transmembrane regulator gene. Data from the Phase 1 study will be presented via e-poster at the 2020 North American Cystic Fibrosis Conference, which will hold virtual sessions and discussions Oct. 21-23.

Cystic fibrosis is a life-threatening disease affecting approximately 30,000 people in the U.S. and about 70,000 worldwide. Although CF is a multisystem disease, the main cause of morbidity and mortality is lung disease, characterized by small airway obstruction due to mucus accumulation, decreased mucus clearing and subsequent inflammation, infections and lung function decline.

"We are very encouraged by these data, which demonstrate attractive tolerability and safety for IONIS-ENAC-2.5$_{Rx}$ with substantial target reduction and the convenience of once weekly administration. The data also confirm our expectations for aerosol delivery of antisense medicines for lung diseases based on a wealth of preclinical data," said Brett P. Monia, Ph.D., Ionis' chief executive officer. "These results point to the exciting potential for aerosol delivery of other Ionis medicines that we plan to advance to the clinic, including treatments for chronic obstructive pulmonary disease, or COPD, and severe asthma."

The company also plans to initiate a clinical study to evaluate IONIS-ENAC-2.5$_{Rx}$ in patients with COPD associated with chronic bronchitis starting later this year. IONIS-ENAC-2.5$_{Rx}$ is one of more than 20 potentially transformative antisense medicines in the growing Ionis-owned pipeline that the company is prioritizing and preparing for commercialization.

The primary endpoint of the study was evaluation of safety and pharmacokinetics of IONIS-ENAC-2.5$_{Rx}$ delivered via a Pari eFlow mesh nebulizer. In the single escalating dose study, 32 subjects in four cohorts received a single dose of 3, 10, 37.5, or 100 mg and were followed for 30 days. In the multiple ascending dose study, 24 subjects in three cohorts received four doses of 10, 37.5, or 75 mg once weekly, with an additional dose administered during the first week. An additional cohort of eight subjects received a 37.5 mg dose given thrice weekly for 10 doses. Subjects were followed for 13 weeks after dosing. Fiberoptic bronchoscopy including bronchial brushings and bronchoalveolar lavage was performed during screening and after completion of dosing in the MAD cohorts. Quantitative RT-PCR was performed from the bronchial cell brushings to evaluate ENaC mRNA levels.

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.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of IONIS-ENAC-2.5$_{Rx}$ 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, 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.

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