# Ionis announces enrollment completion of Phase 3 Lp(a) HORIZON cardiovascular outcomes study of pelacarsen

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- *Pelacarsen is a potentially first-in-class treatment specifically targeting elevated lipoprotein(a) (Lp(a)), an independent, inherited and causal risk factor for cardiovascular disease*
- *There are currently no approved pharmacological therapies to effectively lower Lp(a), which cannot be effectively addressed by diet and other lifestyle changes*
- *Topline results expected 2025*

CARLSBAD, Calif., July 20, 2022 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today announced that Novartis has completed patient enrollment of the pivotal Phase 3 Lp(a) HORIZON cardiovascular outcomes study of pelacarsen, with 8,325 study participants. Lp(a) HORIZON is evaluating the safety and efficacy of pelacarsen in reducing cardiovascular events in patients with cardiovascular disease and elevated levels of Lp(a). Topline data from the study are expected in 2025. Novartis licensed pelacarsen from Ionis in 2019.

Pelacarsen, formerly IONIS-APO(a)-$L_{Rx}$, is an investigational antisense medicine designed to inhibit the production of apolipoprotein(a) in the liver to reduce elevated lipoprotein(a) or Lp(a) levels, an independent, inherited and causal risk factor for cardiovascular disease (CVD) and calcific aortic valve stenosis. High Lp(a) levels, which are associated with significant risk of coronary heart disease, cannot be reduced with lifestyle modifications or with existing lipid-lowering therapies. Pelacarsen uses Ionis' **Li**gand-**C**onjugated **A**ntisense (LICA) technology platform.

"Completing enrollment of this pivotal outcomes study brings us closer to the day when this potentially transformative treatment is available to patients," said Sotirios "Sam" Tsimikas, M.D., senior vice president, clinical development and cardiovascular franchise leader at Ionis, who specializes in Lp(a). "There are no approved pharmacological therapies to effectively lower Lp(a) for the more than eight million patients living with cardiovascular disease and elevated levels of Lp(a) worldwide. We are grateful to the patients, investigators and site staff who are participating to make the Phase 3 Lp(a) HORIZON study possible."

Data from a Phase 2 study showed pelacarsen reduced Lp(a) levels below the recommended threshold of risk for CVD events (<50 mg/dL, <125 nmol/L) in 98% of participants with the dose being used in the Lp(a) HORIZON study.

Additional information about Lp(a) HORIZON (NCT04023552) may be found at ClinicalTrials.gov.

## About Lp(a) HORIZON

Lp(a) HORIZON is a global, multicenter, double-blind, placebo-controlled pivotal Phase 3 study conducted by Novartis. The study is designed to support an indication for the reduction of cardiovascular risk in patients with established CVD and elevated Lp(a) with 80 mg of pelacarsen administered monthly via subcutaneous administration. The study has enrolled 8,325 participants. Topline results are expected in 2025.

The primary objectives of the study are to demonstrate superiority compared to placebo in reducing the risk of expanded MACE (Major Adverse Cardiac Events) such as cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and urgent coronary re-vascularization requiring hospitalization in the overall study population with established CVD and Lp(a) ≥ 70 mg/dL, and in the population with Lp(a) ≥ 90 mg/dL.

## About Lp(a)

Lp(a) is a lipoprotein particle assembled in the liver that consists of an LDL-C-like particle and apolipoprotein(a). Lp(a) levels in the blood can vary greatly between individuals primarily due to genetic variations and do not correlate with LDL-C levels. Even patients with LDL-C lowered to target levels (<70 mg/dL) remain at high-risk of cardiovascular events if they have high levels of Lp(a). Elevated Lp(a) is a genetically determined condition that is not responsive to lifestyle changes, therefore patients are unable to adequately control their Lp(a) levels through improved diet or increased physical activity. Elevated Lp(a) is recognized as an independent, genetic cause of coronary artery disease, heart attack, stroke, peripheral arterial disease and aortic stenosis. Currently, there is no effective drug therapy to specifically and robustly lower elevated levels of Lp(a).

## About Pelacarsen

Pelacarsen, licensed by Novartis for exclusive worldwide development, manufacturing and commercialization, is an investigational antisense medicine designed to reduce apolipoprotein(a) production in the liver to offer a direct approach for reducing circulating lipoprotein(a), or Lp(a), an atherogenic, pro-inflammatory and thrombogenic lipoprotein that induces additional cardiovascular risk independent of LDL-cholesterol, in patients already treated with LDL-C-lowering therapies (such as statins or PCSK9 inhibitors).

## 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 cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming a leading, fully integrated biotechnology company.

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

## Ionis' Forward-looking Statements

This press release includes forward-looking statements regarding Ionis' business and the therapeutic and commercial potential of Ionis' technologies, pelacarsen 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 Dec. 31, 2021 and the most recent Form 10-Q quarterly filing, which are on file with the Securities and Exchange Commission. 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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Ionis Pharmaceuticals Investor Contact: 760-603-2331; Ionis Pharmaceuticals Media Contact: 760-603-4679