Lp(a) HORIZON achieves 50% enrollment in trial to assess the safety and efficacy of pelacarsen in reducing recurrent cardiovascular events

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- Ionis-discovered pelacarsen continues to advance as potential first new therapy for Lp(a)-driven cardiovascular disease

CARLSBAD, Calif., Aug. 2, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (NASDAQ: IONS) today announced that pelacarsen, formerly known as AKCEA-APO(a)-L_{Rx}, and licensed by Novartis (NYSE: NVS) for exclusive worldwide development and commercialization, continues to advance in the clinic as the potential first-in-class treatment for lipoprotein(a) or Lp(a)-driven cardiovascular disease. The Novartis pivotal Phase 3 cardiovascular outcomes study of pelacarsen, Lp(a) HORIZON (NCT04023552), has reached 50% enrollment with a target goal of 7,680 trial participants.

Pelacarsen is an investigational antisense medicine that uses Ionis' proprietary **Li**gand **C**onjugated **A**ntisense (LICA) technology platform. It is designed to inhibit the production of apolipoprotein(a) in the liver to target elevated Lp(a) levels, an independent genetic risk factor for cardiovascular diseases (CVD), that are determined at birth and cannot be controlled with diet or exercise. High Lp(a) levels are associated with significant risk of cardiovascular disease, including heart attacks and strokes. There are no approved pharmacological therapies to effectively lower Lp(a).

"We are pleased by Novartis progress in advancing the Lp(a) HORIZON study and enrolling nearly 4,000 study participants around the world. Pelacarsen represents a potential first-in-class treatment to address a significant unmet need with the potential to become the new standard of care for Lp(a)-driven cardiovascular disease," said Sotirios "Sam" Tsimikas, M.D., senior vice president, clinical development and cardiovascular franchise leader at Ionis, who specializes in Lp(a). "Ionis' vision is that pelacarsen emerges as an effective therapy to improve cardiovascular outcomes through normalizing Lp(a) levels, as there are an estimated eight million people globally living with elevated Lp(a) and cardiovascular disease."

Data from a Phase 2 study published in the *New England Journal of Medicine* showed pelacarsen provided potent dose-dependent reductions of Lp(a) compared to placebo, with a favorable safety and tolerability profile in patients who had elevated Lp(a) levels and established CVD. These data support the potential of antisense-mediated reduction of Lp(a) with pelacarsen.

Ionis earned a $25 million milestone payment from Novartis for achieving 50% enrollment in the pivotal Phase 3 study. In 2017, Novartis entered a collaboration agreement with Ionis for pelacarsen. In February 2019, Novartis exercised an option to license the rights to develop and commercialize pelacarsen for targeted cardiovascular therapy for $150 million. Under the terms of the agreement, Novartis is exclusively responsible for worldwide development and commercialization of pelacarsen and Ionis is eligible to receive up to $675 million in regulatory and sales milestones. Ionis is also eligible to receive tiered royalties in the mid-teens to low 20% range on net sales of pelacarsen.

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

About Lp(a) HORIZON

Lp(a) HORIZON is a pivotal, global multicenter, double-blind, placebo-controlled pivotal Phase 3 study conducted by Novartis. The trial 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 a targeted enrollment of 7,680 participants. The estimated study completion date is in 2024.

The primary objectives of the trial 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 pelacarsen

Pelacarsen, licensed by Novartis for exclusive worldwide development 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). Elevated Lp(a) is recognized as an independent, genetic cause of coronary artery disease, heart attack, stroke and peripheral arterial disease. Currently, there is no effective drug therapy to specifically and robustly lower elevated levels of Lp(a). Lp(a) levels are determined at birth and, therefore, lifestyle modification, including diet and exercise, does not impact Lp(a) 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).

Pelacarsen is being developed for patients who are at significant risk of CVD because of their elevated Lp(a).

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) is considered a key driver for cardiovascular disease due to its association with an increased risk of coronary heart disease. There is evidence that elevated Lp(a) levels may contribute directly to coronary artery disease, heart attacks, strokes and peripheral artery disease. Lp(a) levels in the blood can vary greatly between individuals primarily due to genetic variations and do not correlate with LDL-C levels. Because elevated Lp(a) is a genetically determined condition that is not responsive to lifestyle changes, patients are unable to adequately control their Lp(a) levels through improved diet or increased physical activity. Moreover, current therapies are not able to normalize Lp(a) levels in patients who have high Lp(a). Although Lp(a) can be measured by a variety of reliable and readily available simple tests, the lack of drugs to effectively lower Lp(a) has made treating patients with Lp(a)-driven cardiovascular disease difficult.

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, 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 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.

View original content to download multimedia:https://www.prnewswire.com/news-releases/lpa-horizon-achieves-50-enrollment-in-trial-to-assess-the-safety-and-efficacy-of-pelacarsen-in-reducing-recurrent-cardiovascular-events-301346042.html

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