Isis Initiates Phase 1 Study of ISIS-APOA Rx to Treat Atherosclerosis

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CARLSBAD, Calif., April 3, 2013 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has initiated a Phase 1 clinical study for ISIS-APOA$_{Rx}$, an antisense drug targeting apolipoprotein(a) for the treatment of atherosclerosis. Apolipoprotein(a) contributes to the formation of plaque in arteries through its attachment to an LDL-C particle in a complex termed lipoprotein(a), or Lp(a). High levels of Lp(a) are associated with an increased risk of atherosclerosis, coronary heart disease, heart attack and stroke. ISIS-APOA$_{Rx}$ is designed to reduce Lp(a) by inhibiting the production of apolipoprotein(a). Isis plans to develop ISIS-APOA$_{Rx}$ to treat patients with high Lp(a) levels who are at high risk of experiencing cardiovascular events.

"Lp(a) is an independent risk factor for coronary heart disease. Although Lp(a) can be measured during a routine lipid blood panel, the lack of drugs that effectively lower Lp(a) have made treating patients with high Lp(a) levels difficult. Because elevated Lp(a) is an inherited genetic condition, patients are unable to adequately control their Lp(a) levels through diet or lifestyle changes. By inhibiting the production of apolipoprotein(a), ISIS-APOA$_{Rx}$ is designed to reduce the levels of Lp(a), thereby offering a unique and specific approach to treating patients who have high cardiovascular risk due to high Lp(a) levels," said Walter Singleton, M.D., vice president of development and chief medical officer at Isis. "ISIS-APOA$_{Rx}$ is part of Isis' strategy to create a cardiovascular disease franchise comprised of drugs that target all the key components of cardiovascular disease, including various atherogenic lipids, inflammation and thrombosis."

The Phase 1 study of ISIS-APOA$_{Rx}$ is a blinded, placebo-controlled, dose-escalation study in approximately 56 healthy volunteers. The study is designed to assess the safety, tolerability and pharmacokinetics of both single and multiple doses of ISIS-APOA$_{Rx}$.

ABOUT Lp(a)

Lp(a) is considered an independent risk factor for cardiovascular disease due to its association with an increased risk of coronary heart disease and atherosclerotic plaque formation. Lp(a) is a lipoprotein particle that is assembled in the liver that consists of an LDL-C-like particle and apolipoprotein(a). Lp(a) levels in blood can vary greatly between individuals due primarily to genetic variations in the gene that encodes for apolipoprotein(a). As a result, Lp(a) levels are genetically determined, reached by the age of two and remain constant throughout the life of the individual. Diet and lifestyle changes have little impact on Lp(a) levels and currently therapies are not able to adequately reduce elevated levels of Lp(a) to acceptable levels in patients who have severely elevated Lp(a). As a general guideline for ideal Lp(a) levels, the European Atherosclerosis Society recommends that Lp(a) levels be less than or equal to 50 mg/dL. ISIS-APOA$_{Rx}$ is designed to selectively reduce levels of Lp(a) by inhibiting the production of apolipoprotein(a).

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, inthe United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding the discovery, development, activity, therapeutic potential and safety of ISIS-APOA$_{Rx}$. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, 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. Isis' 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 Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2012, 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, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

SOURCE Isis Pharmaceuticals Inc.

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