Isis Pharmaceuticals Initiates Phase 2 Study of ISIS-APO(a) Rx in Patients with High Lp(a)

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CARLSBAD, Calif., July 17, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 2 study evaluating ISIS-APO(a)$_{Rx}$ in patients with high lipoprotein(a), or Lp(a), an independent risk factor for cardiovascular disease. Patients with high levels of Lp(a) have an increased risk of atherosclerosis, coronary heart disease, aortic stenosis, heart attack and stroke. ISIS-APO(a)$_{Rx}$ is designed to reduce Lp(a) by inhibiting the production of apolipoprotein(a). Isis plans to develop ISIS-APO(a)$_{Rx}$ to treat patients with high Lp(a) levels who are at high risk of experiencing life-threatening cardiovascular events.

"Until recently, the importance of evaluating Lp(a) as an independent risk factor for cardiovascular disease was largely underappreciated. Fortunately, there is a growing awareness within the cardiology community about Lp(a) and its role in cardiovascular disease. In fact, there are many patients who, despite having normal levels of LDL-cholesterol, have cardiovascular disease that is primarily caused by high Lp(a) 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. Although Lp(a) can be measured by a routine lipid blood panel, the lack of drugs to effectively lower Lp(a) has made treating patients with Lp(a)-driven cardiovascular disease difficult," said Sotirios Tsimikas, M.D., Professor of Medicine and Director of Vascular Medicine at the University of California San Diego and Vice President of Clinical Development and Leader of Cardiovascular Franchise at Isis. "By inhibiting the production of apolipoprotein(a), ISIS-APO(a)$_{Rx}$ is designed to directly reduce a patient's Lp(a) level, thereby offering a unique and specific approach to treating patients who have high cardiovascular risk due to high Lp(a) levels."

The Phase 2 study is a randomized, placebo-controlled, dose-titration study evaluating the safety and efficacy of ISIS-APO(a)$_{Rx}$. The 12 week study will evaluate 100 mg, 200 mg and 300 mg doses of ISIS-APO(a)$_{Rx}$ in approximately 60 patients with Lp(a) levels of 50 mg/dL or greater. According to the National Institutes of Health, an average normal Lp(a) level is less than 30 mg/dL and the European Atherosclerosis Society recommends that Lp(a) levels be less than or equal to 50 mg/dL.

"We believe that ISIS-APO(a)$_{Rx}$ is the first drug specifically designed to treat patients with Lp(a)-caused cardiovascular disease. Because we do not expect ISIS-APO(a)$_{Rx}$ to have any drug-drug interactions with standard-of-care drugs, we believe that ISIS-APO(a)$_{Rx}$ could be added to the many other medications taken by patients with cardiovascular disease. In our Phase 1 study in healthy volunteers, we observed robust, dose-dependent reductions in Lp(a)," said Walter Singleton, M.D., vice president of development and chief medical officer at Isis. "We look forward to evaluating ISIS-APO(a)$_{Rx}$ in patients with cardiovascular disease and high Lp(a) levels."

ISIS-APO(a)$_{Rx}$ is an antisense drug targeting apolipoprotein(a) for the treatment of atherosclerosis. Based on its substantial experience and expertise in developing drugs to treat a variety of lipid disorders, Isis is currently developing ISIS-APO(a)$_{Rx}$ on its own. Apolipoprotein(a) contributes to the formation of plaque in arteries through its attachment to an LDL-C particle in a complex called Lp(a). Currently there are no drugs on the market that can effectively lower elevated Lp(a) to recommended Lp(a) levels. Isis plans to develop ISIS-APO(a)$_{Rx}$ to treat patients with high Lp(a) levels who have either coronary heart disease or aortic stenosis. Both of these groups of patients are at high risk of cardiovascular events. ISIS-APO(a)$_{Rx}$ is part of Isis' cardiovascular disease franchise comprised of drugs that target many of the key components of cardiovascular disease, including various atherogenic lipids, inflammation and thrombosis.

ABOUT Lp(a)
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). Lp(a) levels are genetically determined and remain constant throughout the life of the individual. As a result, diet and lifestyle changes have little impact on Lp(a) levels and current therapies are not able to adequately reduce elevated levels of Lp(a) to recommended levels in patients who have high Lp(a) levels.

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 32 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, including neurological disorders, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO®, in the United States and other countries for the treatment of patients with homozygous FH. 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 development, activity, therapeutic potential and safety of ISIS-APO(a)$_{Rx}$. Any statement describing Isis' 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. 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, 2013, and its most recent quarterly report on Form 10-Q, 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, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

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D. Wade Walke, Ph.D., Vice President, Corporate Communications and Investor Relations, 760-603-2741; Amy Blackley, Ph.D., Associate Director, Corporate Communications, 760-603-2772