Drugs from Isis' Lipid Franchise Highlighted at European Society of Cardiology Congress 2014

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KYNAMRO®, ISIS-APOCIIIRX AND ISIS-APO(A)RX DATA PRESENTED

CARLSBAD, Calif., Sept. 2, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that data from three drugs in its lipid franchise were highlighted in four presentations at the 2014 European Society of Cardiology (ESC) Congress in Barcelona Spain. Isis has created a lipid franchise of antisense drugs designed to provide effective and safe therapeutic options to treat patients with lipid disorders. This franchise is composed of one commercialized drug and several other drugs in clinical development designed to treat cardiovascular conditions by reducing specific lipid parameters that are risk factors for cardiovascular disease. Data presented include:

- A retrospective analysis of data from a long-term extension study of KYNAMRO® (mipomersen sodium) injection. In this analysis patients with heterozygous familial hypercholesterolemia (HeFH) and homozygous familial hypercholesterolemia (HoFH) treated for one year with KYNAMRO experienced a reduction in Major Adverse Cardiovascular Events (MACE) from 25.72/1000 months (in the two years prior to KYNAMRO® treatments) to 4.85/1000 months.
- An overall summary of the Phase 2 program for ISIS-APOCIII$_{Rx}$ in which treatment with ISIS-APOCIII$_{Rx}$ produced consistent, robust and statistically significant reductions in triglycerides, apoC-III and non-HDL and increases in HDL-cholesterol in all patient populations evaluated.
- Data from the Phase 1 study of ISIS-APO(a)$_{Rx}$ in which treatment with ISIS-APO(a)$_{Rx}$ produced dose-dependent and significant reductions in Lp(a) levels in healthy volunteers.

In two invited presentations, Dr. John Kastelein, M.D., Ph.D., professor of medicine, chairman of the department of vascular medicine, Academic Medical Center, University of Amsterdam, presented data from a retrospective analysis of 104 patients who enrolled in the long-term extension study of KYNAMRO after having completed one of the KYNAMRO Phase 3 studies in patients with FH. All patients who completed at least one year of treatment with KYNAMRO were included in the analysis. In this retrospective analysis, the rate of MACE in patients treated with KYNAMRO for one year were adjudicated by an independent committee and compared to the rate of MACE in the same patients based on their medical history prior to treatment with KYNAMRO. During the one year of treatment with KYNAMRO, the patients had a rate of MACE of 4.85/1000 months compared to a rate of MACE of 25.72/1000 months for the same patients in the two years prior to treatment ($p < 0.0001$). The rate of MACE was defined in this analysis as myocardial infarction, stroke, unstable angina and revascularization procedures.

"The statistical significant decrease in rate of MACE in patients treated with KYNAMRO represents an important finding and complements the therapeutic profile of KYNAMRO," said Dr. Kastelein. "These results are encouraging and support the potential for therapeutic benefit in patients with homozygous FH, the most aggressive form of familial hypercholesterolemia."

In one of the invited presentations, Dr. Kastelein also provided an overview of the results from the Phase 2 program for ISIS-APOCIII$_{Rx}$, a novel triglyceride-lowering drug. Isis is currently evaluating ISIS-APOCIII$_{Rx}$ in a Phase 3 study in patients with familial chylomicronemia syndrome (FCS) and plans to initiate additional Phase 3 studies in patients with severely elevated triglycerides, including patients with triglyceride levels greater than 880 mg/dL. In the Phase 2 program, in all patient groups studied, irrespective of their incoming triglyceride levels, treatment with ISIS-APOCIII$_{Rx}$ consistently reduced apoC-III by up to 88 percent, triglycerides by up to 71 percent, and increased HDL-cholesterol by up to 78 percent, with a positive effect on non-HDL. In all of the clinical studies, ISIS-APOCIII$_{Rx}$ had a tolerability profile supportive of continued development. In addition, the final data analysis from the Phase 2 study evaluating ISIS-APOCIII$_{Rx}$ as a single agent in patients with very high to severely high triglycerides was presented by Dr. Vickie Alexander, Ph.D., director of clinical development at Isis, in a poster as part of the lipoproteins in cardiovascular prevention session on Sunday, August 31 at the ESC Congress.

In a separate presentation, Dr. 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 the cardiovascular franchise at Isis, presented data from the Phase 1 study of ISIS-APO(a)$_{Rx}$ in healthy volunteers with baseline elevated Lp(a) levels. In this study, treatment with ISIS-APO(a)$_{Rx}$ produced dose-dependent reductions of up to 89 percent in lipoprotein(a) or Lp(a), an independent risk factor for coronary artery disease. In addition to Lp(a) activity, subjects treated with 300 mg/week of ISIS-APO(a)$_{Rx}$ also experienced an up to 90 percent reduction in oxidized phospholipids, lipids that play an important role in proinflammatory and proatherogenic processes believed to be associated with Lp(a). The tolerability profile for ISIS-APO(a)$_{Rx}$ in this study supported further development and Isis is currently evaluating ISIS-APO(a)$_{Rx}$ in a Phase 2 study in patients with elevated 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 benefit, safety and commercial potential of KYNAMRO in treating patients with homozygous FH and the discovery, development, activity, therapeutic potential and safety of ISIS-APOCIII$_{Rx}$ and 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