Isis Reports Positive Data from KYNAMRO® (mipomersen sodium) FOCUS FH Phase 3 Study in Patients with Severe Heterozygous Familial Hypercholesterolemia

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CARLSBAD, Calif., Aug. 3, 2015 /PRNewswire/ -- Isis Pharmaceuticals Inc. (NASDAQ: ISIS), today announced that the FOCUS FH phase 3 study of KYNAMRO® (mipomersen sodium) in patients with severe heterozygous familial hypercholesterolemia (severe HeFH) met its primary efficacy endpoint, a statistically significant reduction in LDL-cholesterol after 60 weeks of treatment of once weekly injections of 200 mg of KYNAMRO compared to placebo. LDL-cholesterol reduction was similar to that observed in previous phase 3 studies. In addition, based on the data available for review, the safety profile of KYNAMRO observed in the FOCUS FH trial was similar to the safety profile reported in previous phase 3 studies. Genzyme will provide a more in depth review of the safety and efficacy data at a future medical meeting.

"We are pleased with the outcome of this fifth KYNAMRO randomized placebo controlled phase 3 trial, which shows statistically significant reductions in LDL-cholesterol in severe HeFH," said Richard Geary, Ph.D., senior vice president of development at Isis Pharmaceuticals. "It is encouraging to see sustained LDL-C reductions over 60 weeks that were similar to what we've observed in previous phase 3 studies and a safety profile consistent with previous phase 3 and long-term extension studies. We look forward to the full analysis and presentation of this investigational data at an upcoming scientific meeting."

"These investigational data provide additional information about KYNAMRO in the treatment of patients with severely elevated LDL-cholesterol and we look forward to further analysis of these data," said Genzyme's President and CEO, David Meeker, M.D.

ABOUT FOCUS FH
FOCUS FH was a multicenter, randomized, placebo-controlled, double-blind, parallel-group study that enrolled 310 patients aged 18 and older, followed by an open-label continuation. Cohort 1 included patients with severe HeFH with LDL-C ≥ 200 mg/dL plus coronary heart disease or LDL-C ≥ 300 mg/dL. Cohort 2 included patients with HeFH with LDL-C ≥ 160 mg/dL and <200 mg/dL plus coronary heart disease. Within each cohort, patients were randomized 2:1 to either 200 mg once weekly, 70 mg thrice weekly, or placebo for a 60 week study duration. Upon completion of the 60 week blinded treatment, patients had the option to enter the open label continuation period for 26 weeks and receive the full dose regimen of KYNAMRO according to the dosing schedule they were randomized to during the blinded treatment phase. The trial was conducted at 131 sites worldwide. The primary efficacy endpoint evaluated was the LDL-C percent change from baseline to week 61 for cohort 1 and each dose regimen.

ABOUT KYNAMRO® (mipomersen sodium) Injection 200 mg/mL
KYNAMRO is an oligonucleotide inhibitor of apolipoprotein B-100 synthesis indicated as an adjunct to lipid-lowering medications and diet to reduce low density lipoprotein-cholesterol (LDL-C), apolipoprotein B (apo B), total cholesterol (TC), and non-high density lipoprotein-cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). The safety and effectiveness of KYNAMRO have not been established in patients with hypercholesterolemia who do not have HoFH. The effect of KYNAMRO on cardiovascular morbidity and mortality has not been determined. The safety and effectiveness of KYNAMRO as an adjunct to LDL apheresis have not been established; therefore, the use of KYNAMRO as an adjunct to LDL apheresis is not recommended

About Homozygous Familial Hypercholesterolemia (HoFH)
HoFH is a rare genetic disease characterized by extreme cholesterol levels. People with HoFH have inherited mutations that limit the body's ability to clear cholesterol. HoFH is extremely rare. As with other rare diseases, the true prevalence of HoFH may be underestimated because of inadequate data and under-diagnosis. Today, it is estimated that HoFH affects about 44,000 people globally. Medical literature includes different criteria for marking an HoFH diagnosis. HoFH may be diagnosed by clinical or genetic parameters, and may be considered in cases of unusually high LDL-C. Because HoFH is genetic, it is important that all family

members of people with HoFH know their cholesterol levels, regardless of their age.

ABOUT ISIS PHARMACEUTICALS, INC.
Isis is exploiting its leadership position in RNA-targeted technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 38 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 has numerous drugs in Phase 3 development in severe/rare diseases and cardiovascular diseases. These include volanesorsen, a drug Isis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with familial chylomicronemia syndrome and familial partial lipodystrophy; ISIS-TTR_{Rx}, a drug Isis is developing with GSK to treat patients with the polyneuropathy and cardiomyopathy forms of TTR amyloidosis; and ISIS-SMN_{Rx}, a drug Isis is developing with Biogen to treat infants and children with spinal muscular atrophy, a severe and rare neuromuscular disease. 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 Isis' collaboration with Genzyme, a Sanofi company, and the development, activity, therapeutic benefit and safety of KYNAMRO in treating patients with high cholesterol. 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, 2014, 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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SOURCE Isis Pharmaceuticals, Inc.

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