Isis Pharmaceuticals Initiates Phase 3 Study of ISIS-APOCIII Rx in Patients with FCS

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CARLSBAD, Calif., Aug. 28, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 3 study evaluating ISIS-APOCIII$_{Rx}$ in patients with familial chylomicronemia syndrome (FCS). FCS is a rare orphan disease, characterized by extremely high triglyceride levels, that affects an estimated 3,000 to 5,000 patients worldwide. The Phase 3 study of ISIS-APOCIII$_{Rx}$ is a randomized, double-blind, placebo-controlled, six month study in approximately 50 patients diagnosed with FCS. The study will evaluate the efficacy and safety of a 300 mg once weekly dose of ISIS-APOCIII$_{Rx}$. The primary endpoint of the study is percent change in fasting triglycerides from baseline after three months of dosing.

"FCS is a rare and very serious genetic disorder that is often associated with triglyceride levels higher than 2,000 mg/dL. Because of their extremely high triglyceride levels, FCS patients are at significant risk of many serious health conditions, including frequent episodes of pancreatitis, which can require hospitalization and can be life-threatening. Current treatment options do not reduce triglyceride levels enough to reduce the risk of serious illness in patients with FCS," 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 the cardiovascular franchise at Isis. "ISIS-APOCIII$_{Rx}$ provides a unique therapeutic approach in that it is designed to reduce triglyceride levels by reducing apoC-III, an important regulator of triglyceride clearance. The Phase 2 data strongly support advancing ISIS-APOCIII$_{Rx}$ into Phase 3 studies in patients with severely elevated triglycerides like FCS."

In a Phase 2 study, FCS patients treated with ISIS-APOCIII$_{Rx}$ experienced decreases in triglycerides of up to more than 1,500 mg/dL. Isis has also evaluated ISIS-APOCIII$_{Rx}$ in a broad Phase 2 program. In these studies in patients with very high to extremely high triglyceride levels, patients treated with ISIS-APOCIII$_{Rx}$ achieved substantial lowering of triglycerides (mean percent reductions of up to 71%) and apoC-III (mean percent reductions of up to 88%) and increasing of HDL-cholesterol (mean percent increases of up to 78%).

"Our focus is to bring ISIS-APOCIII$_{Rx}$ to the market for patients with severely elevated triglycerides. These patients are at significant health risk because they cannot reduce their triglycerides to safe levels with currently available medicines. We are pleased with the data from our Phase 2 program in which substantial triglyceride lowering was achieved when ISIS-APOCIII$_{Rx}$ was dosed as a single agent or in combination with fibrates in patients with a wide range of incoming triglycerides, including FCS patients," said Richard Geary, Ph.D., senior vice president of development at Isis. "Our broad experience developing drugs to treat lipid disorders, including the good working relationships we have established with the physicians and centers that treat many FCS patients should support the rapid advancement of this program. We currently plan to advance ISIS-APOCIII$_{Rx}$ without seeking a partner."

ISIS-APOCIII$_{Rx}$ is designed to target apoC-III, a protein produced in the liver that plays a central role in the regulation of serum triglycerides. ApoC-III is a genetically validated target for lowering triglycerides. Independent studies have demonstrated a link between lower apoC-III activity, which results in lower triglyceride levels, and reduced cardiovascular disease.

In addition to developing ISIS-APOCIII$_{Rx}$ for patients with FCS, Isis is also developing ISIS-APOCIII$_{Rx}$ for patients with severely elevated triglycerides, greater than 880 mg/dL, a condition that affects an estimated 50,000 patients in the United States and Europe. These patients not only have a high risk of pancreatitis but also have a high risk of type 2 diabetes and cardiovascular disease. Currently available therapies do not reduce triglycerides sufficiently in many of these patients to reduce these health risks. Isis plans to initiate the Phase 3 program in patients with severely elevated triglycerides in 2014.

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 discovery, development, and potential of drugs for cardiovascular diseases, and the development, activity, therapeutic potential and safety of ISIS-APOCIII$_{Rx}$. 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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