Isis Pharmaceuticals Reports Data From ISIS-TTR Rx in Patients With Transthyretin Amyloid-Related Cardiomyopathy

July 27, 2015

Up to 88 percent reduction in transthyretin protein in patients with TTR-related cardiomyopathy observed

CARLSBAD, Calif., July 27, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today encouraging preliminary results from an investigator-sponsored study in patients with transthyretin amyloid-related cardiomyopathy that was presented yesterday by Dr. Merrill Benson at the 20th World Congress on Heart Disease (WCHD) in Vancouver, Canada.

"I am encouraged by the safety, tolerability, TTR lowering and apparent stabilization of cardiac disease progression we have observed in the study to date," said Merrill Benson, M.D., professor of pathology and medical genetics at Indiana University. "In this open-label study, measures of TTR amyloid cardiac disease, including echocardiographic and strain imaging evaluation, indicated little to no cardiac disease progression after six months of dosing with ISIS-TTR$_{Rx}$. These data compare favorably to our previously published work[1], which showed that patients with TTR-related cardiomyopathy exhibit disease progression at six months using similar echocardiographic measurements."

"These new data on cardiac measures in patients with TTR-cardiomyopathy give us additional confidence that the TTR-lowering we have observed in this and other clinical studies has the potential to provide therapeutic benefit to patients with TTR amyloidosis," said Brett Monia, Ph.D., senior vice president of drug discovery at Isis Pharmaceuticals.

In a presentation titled, "Transthyretin Amyloid Cardiomyopathy Treatment with an Antisense Oligonucleotide Inhibitor of TTR (ISIS-TTR$_{Rx}$)", Dr. Benson reported on preliminary results from his investigator-sponsored open-label study in patients with TTR-related cardiomyopathy. In patients who completed nine months of weekly dosing (n=3) with 300 mg of ISIS-TTR$_{Rx}$, reductions in TTR protein of up to 88% were observed with a mean reduction of 78%. In addition, patients who completed six months of dosing (n=5) were evaluated by echocardiography and showed no increase in left ventricular wall thickness. In this study, patients receive 300 mg of ISIS-TTR$_{Rx}$ once weekly for a total of 24 months with a three month follow up period.

ABOUT ISIS-TTR$_{Rx}$

ISIS-TTR$_{Rx}$ is a gen 2.0+ antisense drug Isis is developing with GSK for the treatment of TTR amyloidosis. ISIS-TTR$_{Rx}$ is administered as a once weekly subcutaneous injection and is designed to inhibit the production of all forms of TTR protein, including both mutant and wild type, offering a unique approach to treat all types of TTR amyloidosis.

ISIS-TTR$_{Rx}$ is currently being evaluated in a Phase 3 randomized, double-blind, placebo-controlled, international study in patients with familial amyloid polyneuropathy (FAP). The study is designed to support an application for marketing approval of ISIS-TTR$_{Rx}$ in patients with FAP. The fifteen month study will measure the effects of ISIS-TTR$_{Rx}$ on neurological dysfunction and on quality-of-life. For further study information, please visit www.clinicaltrials.gov and search for the identifier number NCT01737398.

ABOUT TTR AMYLOIDOSIS

TTR amyloidosis is a severe and fatal disease in which patients with TTR amyloidosis experience TTR build up in major organs, including peripheral nerves, heart, intestinal tract, kidney and bladder. Patients with TTR-related cardiomyopathy experience ongoing debilitating heart damage resulting in progressive heart failure. Therapeutic options for the treatment of TTR-related cardiomyopathy are very limited and there are currently no drugs approved for the treatment of TTR-related cardiomyopathy.

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 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' strategic alliance with GSK, and the development, activity, therapeutic and commercial potential and safety of ISIS-TTR$_{Rx}$. 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, 2014, and its most recent quarterly report on Form 10-Q, which are 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.

[1]Benson MD et al. Am J Cardiol. 2011 Jul 15;108(2):285-9.

Logo - http://photos.prnewswire.com/prnh/20130807/LA60006LOGO

SOURCE Isis Pharmaceuticals, Inc.

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