Isis Pharmaceuticals Announces Initiation of an Investigator-Sponsored Phase 2 Study of ISIS-TTR Rx in Patients with TTR Cardiomyopathy Amyloidosis

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CARLSBAD, Calif., Dec. 17, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the initiation of an investigator-sponsored, open-label Phase 2 study evaluating ISIS-TTR_{Rx} in patients with wild-type transthyretin amyloidosis (wt-TTR amyloidosis, previously referred to as senile systemic amyloidosis, or SSA). The Phase 2 study will be conducted by Dr. Rodney Falk, the director of the Cardiac Amyloidosis Program and a cardiovascular medicine specialist at the Brigham and Women's Hospital in Boston.

"Together with GSK, we are conducting a robust development plan designed to establish ISIS-TTR_{Rx} as a best-in-class treatment for all patients with TTR amyloidosis. Already, we have demonstrated that ISIS-TTR_{Rx}, given as one, once a week, self-administered, at home injection, can robustly reduce TTR levels in patients with both the polyneuropathy and cardiomyopathy forms of the disease, and we have preliminary evidence of disease stabilization in patients with TTR-related cardiomyopathy," said Brett Monia, Ph.D., senior vice president of drug discovery and franchise leader for oncology and rare diseases at Isis Pharmaceuticals. "Dr. Falk is a leading expert in TTR amyloidosis and has extensive knowledge of wt-TTR cardiomyopathy. As such, Dr. Falk is an ideal physician to evaluate the effects of ISIS-TTR_{Rx} in these patients, who have the same type of disease as those who are represented in his large natural history database."

The Phase 2, investigator-initiated study will evaluate treatment with ISIS-TTR_{Rx} in approximately 50 patients with wt-TTR amyloidosis. Patients must have evidence of cardiac disease as indicated by an interventricular septum thickness (IVS) of ≥1.3cm with a positive cardiac biopsy. The effects of ISIS-TTR_{Rx} on cardiac disease stabilization will be measured by cardiac imaging at 6, 12 and 18 months. Data from this study will provide additional information on ISIS-TTR_{Rx} and can also be included in the robust data package Isis and GSK are generating to support regulatory filings for ISIS-TTR_{Rx} in all patients with TTR amyloidosis. For further study information, please visit www.clinicaltrials.gov and search for ISIS-TTR_{Rx}.

In addition to the Phase 2 study initiated today, ISIS-TTR_{Rx} is being evaluated in the following studies:

- Isis is evaluating ISIS-TTR_{Rx} in a Phase 3 randomized, double-blind, placebo-controlled, international study (NEURO-TTR) 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.
- Isis is evaluating ISIS-TTR_{Rx} in an open-label extension study that is eligible to patients with FAP who have completed the NEURO-TTR Phase 3 study. To date, all eligible patients have enrolled in the open-label extension study.
- GSK plans to initiate a small Phase 3 study evaluating ISIS-TTR_{Rx} in patients with FAP in Japan.
- GSK plans to initiate a Phase 3 randomized, double-blind, placebo-controlled, multicenter, international study (CARDIO-TTR) in patients with familial amyloid cardiomyopathy (FAC) and wt-TTR amyloidosis who also have a history of heart failure. The study will measure the effects of ISIS-TTR_{Rx} on a clinical composite outcome that includes mortality, cardiac transplant and cardiovascular hospitalization.
- Dr. Merrill D. Benson, professor of pathology and lab medicine and molecular genetics at Indiana University School of Medicine, is evaluating ISIS-TTR_{Rx} in an open-label, investigator-sponsored, Phase 2 study in patients with TTR amyloid cardiomyopathy, which includes patients with FAC and patients with wt-TTR amyloidosis.

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 one 300 mg, once weekly, at home self-administered low-volume subcutaneous injection and is designed to inhibit the production of all forms of TTR protein, including both familial and wild-type, offering a singular approach to treat all types of TTR amyloidosis. ISIS-TTR_{Rx} has already demonstrated sustained and robust TTR reductions in multiple clinical studies in multiple indications of TTR-related amyloidosis.

ABOUT TTR AMYLOIDOSIS

TTR amyloidosis is a severe, progressive and fatal disease with multiple overlapping clinical manifestations. There are three forms of TTR amyloidosis, FAP, FAC and wt-TTR amyloidosis, and all are caused by the inappropriate formation and aggregation of TTR amyloid deposits in various tissues and organs, including peripheral nerves, heart, intestinal tract, eyes, kidneys, central nervous system, thyroid and bone. The progressive accumulation of TTR amyloid deposits in these tissues and organs leads to organ failure and eventually death. Although TTR amyloidosis is fatal, therapeutic options for the treatment of patients with TTR amyloidosis are very limited and there are currently no disease-modifying drugs available.

FAP is characterized by the accumulation of misfolded mutated TTR protein primarily in the peripheral nerves. Patients with FAP experience ongoing debilitating nerve damage throughout their body resulting in the progressive loss of motor functions, such as walking. These patients also accumulate TTR in other major organs, which progressively compromises their function and eventually leads to death within five to fifteen years of disease onset.

There are an estimated 10,000 FAP patients worldwide.

TTR-related cardiomyopathy is characterized by the accumulation of misfolded TTR protein primarily in the cardiac muscle. Patients experience ongoing debilitating heart damage resulting in progressive heart failure, which results in death within 5 to 7 years from disease onset. TTR-related cardiomyopathy includes both the genetic form of the disease, FAC, and the wild-type form of the disease, wt-TTR amyloidosis. There are an estimated 40,000 FAC patients worldwide. Patients with FAC begin to experience symptom onset between 50 and 60 years of age, whereas patients with wt-TTR amyloidosis usually begin to experience symptom onset ten or more years later, generally over 70 years of age. There are an estimated 200,000 wt-TTR amyloidosis patients worldwide.

Often patients with the polyneuropathy form of TTR amyloidosis will also have TTR build up in the heart and also experience cardiomyopathy symptoms. Similarly, patients with the cardiomyopathy form of TTR amyloidosis may often have TTR build up in their peripheral nerves and can experience nerve damage and progressive difficulty with motor functions.

ABOUT ISIS PHARMACEUTICALS, INC.
Isis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Isis has created a large pipeline of first-in-class or best-in-class drugs, with over a dozen drugs in mid- to late-stage development. Drugs currently in Phase 3 development 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 all forms of TTR amyloidosis; and nusinersen, a drug Isis is developing with Biogen to treat infants and children with spinal muscular atrophy. 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 Pharmaceuticals' strategic alliance with GSK, and the development, activity, therapeutic and commercial potential and safety of ISIS-TTR_{Rx} to treat all forms of TTR amyloidosis. 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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To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/isis-pharmaceuticals-announces-initiation-of-an-investigator-sponsored-phase-2-study-of-isis-ttr-rx-in-patients-with-ttr-cardiomyopathy-amyloidosis-300194029.html

SOURCE Isis Pharmaceuticals, Inc.

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