Isis Initiates Phase 2/3 Study of ISIS-TTR Rx and Earns $7.5 Million Milestone Payment From GlaxoSmithKline

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CARLSBAD, Calif., Feb. 19, 2013 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has earned a $7.5 million milestone payment from GlaxoSmithKline (GSK) related to the initiation of a Phase 2/3 clinical study for ISIS-TTR$_{Rx}$. ISIS-TTR$_{Rx}$ is an antisense drug in development with GlaxoSmithKline (GSK) for the treatment of transthyretin (TTR) amyloidosis, a severe and rare genetic disease characterized by progressive dysfunction of peripheral nerve and/or heart tissues. Isis and GSK recently amended the clinical development plan and financial terms relating to ISIS-TTR$_{Rx}$ to support this registration-directed Phase 2/3 clinical study on ISIS-TTR$_{Rx}$.

"TTR amyloidosis is a severe and rare genetic disease that leads to death. TTR amyloidosis affects approximately 50,000 patients worldwide and current treatments are limited. Patients with familial amyloid polyneuropathy, or FAP, experience TTR build up in their peripheral nerves and experience the loss of motor functions, such as walking," said Merrill D. Benson, M.D., Professor of Medical Genetics at Indiana University. "By inhibiting the production of TTR protein, ISIS-TTR$_{Rx}$ could offer an alternative approach to treating patients with FAP. Furthermore, a drug that can reduce TTR levels could potentially slow or arrest progression of this terrible disease."

The Phase 2/3 study of ISIS-TTR$_{Rx}$ is a randomized, double-blinded, placebo-controlled, international study designed to support an application for marketing approval of ISIS-TTR$_{Rx}$ in patients with FAP. The fifteen month study will enroll approximately 200 patients randomized 2:1 to receive 300 mg/week of ISIS-TTR$_{Rx}$ or placebo and will measure the effects of ISIS-TTR$_{Rx}$ on neurological dysfunction and on quality-of-life. The United States Food and Drug administration granted ISIS-TTR$_{Rx}$ fast track designation and orphan drug status for the treatment of FAP.

"The rapid development of ISIS-TTR$_{Rx}$ from a research-stage program to a drug in late-stage clinical development in just over two years represents the strong commitment of both teams to bring this novel drug to patients who are in need of new therapeutic options," said B. Lynne Parshall, chief operating officer at Isis. "The encouraging data from our Phase 1 study, in which our drug was well tolerated and produced significant reductions in TTR protein, supported the advancement of ISIS-TTR$_{Rx}$ directly into this registration-directed Phase 2/3 study. While we will continue to manage the clinical development of ISIS-TTR$_{Rx}$, we will benefit from GSK's late-stage clinical development, regulatory and commercial expertise."

ISIS-TTR$_{Rx}$ is part of the Isis-GSK strategic alliance to develop RNA therapeutics for rare and infectious diseases. For the initiation of the Phase 2/3 study, Isis will receive a $7.5 million milestone payment and is eligible to earn an additional $50 million in pre-licensing milestone payments to support the Phase 2/3 study of ISIS-TTR$_{Rx}$. In addition, Isis is eligible to receive regulatory and sales milestone payments and double-digit royalties on sales of ISIS-TTR$_{Rx}$.

ABOUT ISIS-TTR$_{Rx}$

Transthyretin amyloidosis is a genetic disease in which the patient inherits a mutant gene that produces a misfolded form of TTR, which progressively accumulates in tissues, impairing their function. In patients with transthyretin amyloidosis, both the mutant and normal forms of TTR can build up as fibrils in tissues, including heart, peripheral nerves, and the gastrointestinal tract. The presence of TTR aggregates interferes with the normal functions of these tissues, and as the TTR protein aggregates enlarge more tissue damage occurs and the disease worsens. There are two common types of transthyretin amyloidosis, familial amyloid cardiomyopathy, or FAC, which affects more than 40,000 patients worldwide, and FAP, which affects more than 10,000 patients worldwide. Patients with FAC have TTR build up in the heart muscle and succumb to heart failure five to six years after symptom onset. Patients with FAP have TTR build up in peripheral nerve tissue leading to the loss of nerve function and wasting. ISIS-TTR$_{Rx}$ is an investigational drug that is designed to inhibit the production of all forms of TTR, and could offer an alternative approach to treat all types of transthyretin-related amyloidosis.

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 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, inthe United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets, including Europe. 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 GlaxoSmithKline, the discovery, development and potential of drugs for severe and rare diseases, and the development, activity, therapeutic potential and safety of ISIS-TTR$_{Rx}$. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, 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, 2011 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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