Isis Pharmaceuticals Initiates Phase 1/2 Study of ISIS-DMPK Rx in Patients With Myotonic Dystrophy Type 1

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ISIS-DMPK Rx Extends the Targeting of Antisense Drugs to Include Muscle Tissue

CARLSBAD, Calif., Dec. 16, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has initiated a study for ISIS-DMPK$_{Rx}$ in patients with Myotonic Dystrophy Type 1 (DM1). DM1 is a rare genetic neuromuscular disease caused by the production of toxic dystrophia myotonica-protein kinase (DMPK) RNA in cells. ISIS-DMPK$_{Rx}$ is specifically designed to reduce toxic DMPK RNA.

"The Myotonic Dystrophy Foundation is pleased that Isis is advancing to the next phase of clinical trials for ISIS-DMPK$_{Rx}$," said Molly White, executive director of the Myotonic Dystrophy Foundation. "Myotonic Dystrophy, the most common form of muscular dystrophy, is a devastating disease with no therapeutic option. Myotonic dystrophy research has accelerated significantly in the last 10 years, helping bring about the innovative science behind ISIS-DMPK$_{Rx}$, a drug that specifically targets the genetic defect that causes myotonic dystrophy type 1. We applaud Isis for investing in and leading drug development efforts for myotonic dystrophy type 1, and we appreciate the commitment Isis Pharmaceuticals has made to improve the lives of patients in our community."

"We have an innovative and productive partnership with Biogen Idec in developing drugs to treat severe and rare diseases, like DM1. In just under two and a half years, we have been able to discover and complete early development on ISIS-DMPK$_{Rx}$, which includes completing a Phase 1 single ascending-dose study in healthy volunteers. Today we advance this program into patients," said B. Lynne Parshall, chief operating officer at Isis. "The speed at which we have advanced ISIS-DMPK$_{Rx}$ highlights the productive and collaborative nature of our partnership."

DM1 is a rare genetic neuromuscular disease primarily characterized by progressive muscle atrophy, weakness and myotonia. DM1 is the most common form of muscular dystrophy in adults and affects approximately 150,000 patients in the United States, Europe and Japan. Patients with DM1 have a genetic defect in their DMPK gene in which a sequence of three nucleotides repeats extensively, creating an abnormally long RNA, which becomes toxic as it accumulates in the nucleus of cells and prevents the production of proteins needed for normal cellular function. The number of triplet repeats increases from one generation to the next, resulting in the possibility of more severe disease in each subsequent generation. There are currently no disease-modifying therapies that address the disease.

"Myotonic dystrophy represents an ideal opportunity for antisense as the disease-causing gene produces a toxic RNA, which accumulates within cells, including muscle, and is not accessible by traditional therapeutic approaches. ISIS-DMPK$_{Rx}$ has the potential to address the underlying genetic defect that causes DM1. This study is important as it is the first study in which we will be observing the effects of our drug in patients with myotonic dystrophy, and it is the first study in which we are targeting a toxic RNA," said C. Frank Bennett, Ph.D, senior vice president of research at Isis. "ISIS-DMPK$_{Rx}$ is our third generation 2.5 drug to enter clinical development. In this study we plan to evaluate and determine the approximate therapeutic dose of an antisense drug needed to affect the concentration of a target in muscle tissue."

The Phase 1/2 study is a randomized, placebo-controlled, dose-escalation study evaluating the safety and tolerability of ISIS-DMPK$_{Rx}$. The six-week study will evaluate multiple ascending doses of ISIS-DMPK$_{Rx}$ in approximately 36 patients with DM1. More information and a complete list of study related criteria can be found here: www.clinicaltrials.gov (NCT02312011).

ABOUT ISIS and BIOGEN IDEC

Biogen Idec and Isis have established four collaborations focused on leveraging antisense technology to advance the treatment of neurological and neuromuscular disorders. This alliance combines Isis expertise in antisense technology to evaluate potential neurological targets and discover antisense drugs with Biogen Idec's capability to develop therapies for neurological disorders. Isis is primarily responsible for drug discovery and early development of antisense therapies. Biogen Idec has the option to license each antisense program at a particular stage in development. Current development-stage programs include antisense drugs to treat patients with spinal muscular atrophy (SMA), ISIS-SMN$_{Rx}$, myotonic dystrophy type 1 (DM1), ISIS-DMPK$_{Rx}$, and an undisclosed neurodegenerative disease, ISIS-BIIB3$_{Rx}$.

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 34 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 and rare and cardiovascular diseases. These include a novel triglyceride lowering drug, ISIS-APOCIII$_{Rx}$, for patients with familial chylomicronemia syndrome; ISIS-TTR$_{Rx}$, which Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN$_{Rx}$, which Isis is developing with Biogen Idec 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 relationship with Biogen Idec and the discovery, development, activity, therapeutic potential, safety and commercialization of ISIS-DMPK$_{Rx}$. 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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