Isis Pharmaceuticals Initiates Phase 1 Study of ISIS-DMPK Rx to Treat Myotonic Dystrophy Type 1

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Isis Earns $14 Million Milestone Payment from Biogen Idec
ISIS-DMPKRx is the Second Generation 2.5 Antisense Drug to Enter the Clinic

CARLSBAD, Calif., June 9, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has initiated a Phase 1 study for ISIS-DMPK$_{Rx}$. Isis earned a $14 million milestone payment from Biogen Idec associated with this achievement. ISIS-DMPK$_{Rx}$ is designed to reduce the production of toxic dystrophia myotonica-protein kinase (DMPK) RNA in cells, including muscle cells, for the treatment of Myotonic Dystrophy Type 1 (DM1).

"ISIS-DMPK$_{Rx}$ is an example of the broad applicability of our antisense technology to develop novel drugs to treat patients with severe and rare diseases. ISIS-DMPK$_{Rx}$ is the first drug to enter our pipeline that is designed to target a toxic RNA, the first systemically administered drug to enter development from our Biogen Idec partnerships and the second generation 2.5 drug to enter clinical development," said C. Frank Bennett, Ph.D., senior vice president of research at Isis. "Myotonic dystrophy represents an ideal opportunity for antisense as the disease-causing gene produces a toxic RNA, which is not accessible by traditional therapeutic approaches but is uniquely accessible with our antisense technology. We look forward to rapidly advancing the development of ISIS-DMPK$_{Rx}$."

"Our collaboration with Biogen Idec has been very productive. ISIS-DMPK$_{Rx}$ has rapidly advanced to the clinic, and we continue to make progress across the board in our drug discovery programs with Biogen Idec. All of these successes substantially advance our neuromuscular disease franchise and translate into the potential for significant revenue as our drugs and programs progress," said B. Lynne Parshall, chief operating officer at Isis.

DM1 is a rare genetic neuromuscular disease characterized by progressive muscle atrophy, weakness and muscle spasms. DM1, the most common form of muscular dystrophy in adults, 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 toxic RNA, which 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 more than one symptom of the disease. ISIS-DMPK$_{Rx}$ is designed to improve the underlying genetic defect that causes DM1.

"Myotonic dystrophy is a progressive and debilitating disease that affects thousands of patients for whom there are no direct therapeutic options. The innovative science behind ISIS-DMPK$_{Rx}$ is compelling and targets the underlying genetic defect that causes myotonic dystrophy," said Molly White, executive director of the Myotonic Dystrophy Foundation. "ISIS- DMPK$_{Rx}$ has a chance to fill the therapeutic void for DM1 patients and transform the hopes and future of thousands of patients and families."

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's 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 spinal muscular atrophy (SMA), ISIS-SMN$_{Rx}$, and myotonic dystrophy type 1 (DM1), ISIS-DMPK$_{Rx}$.

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 Isis' strategic relationship with Biogen Idec and the discovery, development, activity, therapeutic potential, safety and commercialization of ISIS-DMPK$_{Rx}$ for the treatment of patients with DM1. 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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