Isis Pharmaceuticals Initiates Phase 1b/2a Study Of ISIS-SMNRx In Patients With Spinal Muscular Atrophy

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Ongoing Phase 1 Study Shows ISIS-SMNRx Well-Tolerated in Children with SMA

CARLSBAD, Calif., Nov. 1, 2012 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 1b/2a study evaluating ISIS-SMNRx in children with spinal muscular atrophy (SMA). SMA is a severe and rare genetic neuromuscular disease characterized by muscle atrophy and weakness and is the most common genetic cause of infant mortality.

"SMA is a devastating disease that leads to the premature loss of nerve cells in the spinal cord necessary for normal muscle function. Children with SMA generally appear normal at birth, with muscle wasting and atrophy developing as early as a few months after birth. In the most severe form of the disease, children never sit or walk and have a significantly shortened lifespan. Although the genetic cause of SMA is well understood, the identification of an effective drug that will halt or improve the disease process has not occurred," said Richard Finkel, M.D., chief, division of neurology, Nemours Children's Hospital, Orlando, Florida. "ISIS-SMNRx is specifically designed to intervene in the nerve cell's RNA machinery by improving splicing efficiency. This results in an increase in the production of a normal protein, SMN, which is deficient in children with SMA. This promising new approach could for the first time have a profound effect in children with SMA."

The Phase 1b/2a study of ISIS-SMNRx is a multiple-dose, dose-escalation study designed to assess the safety, tolerability and pharmacokinetic profile of the drug in children with SMA between the ages of 2-15 who are medically stable. In the ongoing Phase 1 study in children with SMA, all patients have completed dosing and ISIS-SMNRx was well tolerated as a single dose administered directly into the cerebral spinal fluid. In the Phase 1b/2a study, children with SMA will receive either two or three doses of ISIS-SMNRx during the course of the study. Data from this study will also provide information to aid in identifying the dose for the Phase 2/3 registration-directed program in patients with SMA.

"SMA represents a serious unmet medical need with no currently available treatments. Based on its mechanism of action, ISIS-SMNRx could be an effective treatment for these very sick children. The rapid advancement of this drug into a multiple-dose Phase 1b/2a study reflects the support from the SMA community and the success of the collaboration between Isis and Biogen Idec. Isis and Biogen Idec are committed to advancing the program for children with SMA," said C. Frank Bennett, Ph.D., senior vice president of research at Isis. "ISIS-SMNRx is our first drug to intervene in the splicing of RNA to increase the production of a normal protein, SMN. We believe that antisense drugs could offer novel new therapeutics for a number of neurodegenerative diseases where there are limited therapeutic options available. The encouraging safety data from this program and our preclinical and clinical experience in other neurodegenerative diseases support the broadening of our efforts to develop antisense drugs to treat a number of severe neurodegenerative diseases."

About ISIS-SMNRx

ISIS-SMNRx is designed to treat all types of childhood SMA by altering the splicing of a closely related gene (SMN2) to increase production of fully functional SMN protein. The United States Food and Drug Administration granted orphan drug status and fast track designation to ISIS-SMNRx for the treatment of patients with SMA. Isis is currently in collaboration with Biogen Idec (NASDAQ:BIIB) to develop and potentially commercialize the investigational compound ISIS-SMNRx to treat all types of SMA. Under the terms of the January 2012 agreement, Isis is responsible for global development and Biogen Idec has the option to license the compound until completion of the first successful Phase 2/3 trial.

About SMA

SMA is a severe genetic disease that affects approximately 30,000-35,000 patients in the United States, Europe and Japan. One in 50 people, the equivalent of about 6 million people in the United States, are carriers of the SMA gene. Carriers experience no symptoms and do not develop the disease. However, when both parents are carriers, there is a one in four chance that their child will have SMA. SMA is caused by a loss of, or defect in, the survival motor neuron 1 (SMN1) gene leading to a decrease in the survival motor neuron (SMN) protein. SMN is critical to the health and survival of nerve cells in the spinal cord responsible for neuromuscular growth and function. The severity of SMA correlates with the amount of SMN protein. Infants with Type 1 SMA, the most severe form of the disease, produce very little SMN protein and have a life expectancy of less than two years. Children with Type II have greater amounts of SMN protein but still have a shortened lifespan and are never able to stand independently. Children with Type III have a normal lifespan but accumulate life-long physical disabilities as they grow.

Isis acknowledges support from the following organizations for ISIS-SMNRx: Muscular Dystrophy Association, SMA Foundation, Families of SMA and intellectual property licensed from Cold Spring Harbor Laboratory and the University of Massachusetts Medical School.

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 25 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, KYNAMRO™, inthe United States and Europe following regulatory approval. 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 Biogen Idec, and the discovery, development, activity, therapeutic and commercial potential and safety of ISIS-SMNRx. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the planned commercialization 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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