Isis Pharmaceuticals Initiates Phase 3 Study of ISIS-SMN Rx in Infants with Spinal Muscular Atrophy

August 1, 2014

-- ENDEAR Trial To Enroll 110 SMA Infants at Sites Globally
-- Dosage of First Infant Will Trigger $18 Million Milestone Payment

CARLSBAD, Calif., Aug. 1, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the initiation of a pivotal Phase 3 study evaluating ISIS-SMN$_{Rx}$ in infants with spinal muscular atrophy (SMA), the most common genetic cause of infant mortality. Isis plans to dose the first infant in this study within the next few weeks, at which time Isis will earn an $18 million milestone payment from its development partner, Biogen Idec. The Phase 3 study, ENDEAR, is the first of several planned studies in a broad and comprehensive late-stage clinical development program for ISIS-SMN$_{Rx}$. Isis plans to initiate a second pivotal study in children with SMA later this year.

"The successful advancement of ISIS-SMN$_{Rx}$ from a preclinical drug candidate to late-stage studies within just a few years reflects the effectiveness of our strategic alliance with Biogen Idec and the benefit of working closely together with combined expertise, and the support from the SMA community. As we continue development of ISIS-SMN$_{Rx}$ and initiate the two pivotal studies in infants and children with SMA, we are in the planning stages for clinical studies in additional patient populations," said B. Lynne Parshall, chief operating officer at Isis. "The clinical and preclinical data we have generated to date, including data in multiple open-label clinical studies, across multiple measures with ISIS-SMN$_{Rx}$, support the initiation of these studies, which fully assess the safety and efficacy benefits of this experimental treatment."

"Families of SMA is pleased that Isis is advancing to the next phase of clinical trials for ISIS-SMN$_{Rx}$. Controlled trials are the gold standard in proving the safety and efficacy of any drug," said Kenneth Hobby, president of Families of SMA. "SMA is a devastating disease with no current therapeutic options. Families of SMA applauds Isis for progressing its development program in an expedient manner, and looks forward to additional trials in patients with SMA beginning later in 2014."

ENDEAR, a Phase 3 study of ISIS-SMN$_{Rx}$, is a randomized, double-blind, sham-procedure controlled thirteen month study in approximately 110 infants diagnosed with SMA. The study will evaluate the efficacy and safety of a 12 mg dose of ISIS-SMN$_{Rx}$ with a primary endpoint of survival or permanent ventilation. Additional efficacy endpoints are also included in the study. For further study information, please visit www.clinicaltrials.gov and search for ISIS-SMN$_{Rx}$ or the identifier number NCT02193074 or visit the ISIS-SMN$_{Rx}$ study site at www.smastudy.com.

ABOUT ISIS-SMN$_{Rx}$

ISIS-SMN$_{Rx}$ is designed to alter 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-SMN$_{Rx}$ for the treatment of patients with SMA. Isis is currently in collaboration with Biogen Idec to develop and potentially commercialize the investigational compound, ISIS-SMN$_{Rx}$, 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 study or the completion of two Phase 2/3 studies.

Isis acknowledges support from the following organizations for ISIS-SMN$_{Rx}$: 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 SMA

SMA is a severe genetic disease that affects approximately 30,000-35,000 patients in the United States, Europe and Japan. 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. One in 50 people, the equivalent of about 6 million people in the United States, are carriers of a defective SMN1 gene, which is unable to produce fully functional SMN protein. 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. The severity of SMA correlates with the amount of SMN protein. Infants with Type I 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.

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 SMA, ISIS-SMN_{Rx}, and myotonic dystrophy type 1, 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' alliance with Biogen Idec, the discovery, development, activity, therapeutic and commercial potential and safety of ISIS-SMN_{Rx} and the discovery, development and therapeutic potential of an antisense drug for the treatment of spinal muscular atrophy. 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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