

Isis Pharmaceuticals Earns \$9M for Advancing ISIS-SMN Rx in Infants With Spinal Muscular Atrophy

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CARLSBAD, Calif., March 6, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has earned a \$9 million milestone payment from Biogen Idec related to advancing the ongoing pivotal Phase 3 study evaluating ISIS-SMN_{Rx} in infants with spinal muscular atrophy (SMA).



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 time to 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 FDA 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. Isis is conducting two Phase 3 studies with agreement from the FDA for special protocol assessments, or SPAs. A SPA is a written agreement between the FDA and a drug sponsor intended to confirm that the clinical trial protocol is adequate to meet current scientific and regulatory requirements for a potential new drug application.

Isis acknowledges support from the following organizations for ISIS-SMN_{Rx}: Muscular Dystrophy Association, SMA Foundation, Cure 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' 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 two undisclosed neurodegenerative diseases, ISIS-BIIB3_{Rx} and ISIS-BIIB4_{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 38 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/rare diseases and cardiovascular diseases. These include ISIS-APOCIII_{Rx}, a drug Isis is developing through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with severely high triglycerides, such as patients with familial chylomicronemia syndrome; ISIS-TTR_{Rx}, a drug Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN_{Rx}, a drug 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' 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, 2014, which is on file with the SEC. Copies of this 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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