Isis Pharmaceuticals Advances ISIS-SMN Rx in Infants and Children with Spinal Muscular Atrophy

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--Isis will receive $9.3 million in milestone payments --

CARLSBAD, Calif., Feb. 13, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that the first child in the 12 mg group was dosed in the ongoing Phase 2 study evaluating ISIS-SMN$_{Rx}$ in children with spinal muscular atrophy (SMA). Isis also announced today that the first child was dosed in an open–label extension study, which is being offered to those children with SMA who have completed dosing in Isis' previous studies. Isis will receive two milestone payments totaling $7.3 million for advancements in these studies. Isis also announced today that dosing in the Phase 2 study in infants with SMA is being extended. Under the extension, infants who have completed the three initially scheduled study doses will be eligible to receive an additional dose of 12 mg. Isis announced today that the first infant in the study has received a fourth dose of ISIS-SMN$_{Rx}$ approximately six months after the three initial doses were completed. For this achievement, Isis will receive a $2 million milestone payment from Biogen Idec.

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"The progress we and Biogen Idec have made on ISIS-SMN$_{Rx}$ exemplifies the value of our strategic alliance and the benefit of working closely together with combined expertise to support rapid development. We also benefit financially. Including the more than $9 million announced today, we will have received more than $45 million in upfront fees, milestone and other payments from Biogen Idec as ISIS-SMN$_{Rx}$ has advanced. This year we anticipate making significant progress in this and other programs we are working on with the Biogen Idec team," said B. Lynne Parshall, chief operating officer at Isis. "The ongoing multiple-dose studies in infants with Type I SMA and in children with Type II and Type III SMA are progressing, and we look forward to sharing the top-line data from these studies this quarter and more detailed results at the American Academy of Neurology meeting in April."

ISIS-SMN$_{Rx}$ is currently being evaluated in an open-label, multiple-dose, dose-escalation Phase 2 study in children with SMA with Type II and Type III SMA. In this study, which is designed to assess the safety, tolerability and pharmacokinetic profile of ISIS-SMN$_{Rx}$, all children have completed dosing in the initial three cohorts (doses of 3 mg, 6 mg and 9 mg) and the first child has been dosed in the 12 mg cohort. The new open-label extension study is designed to provide a single additional dose of 12 mg and is open to the more than 50 children with SMA who have completed dosing with ISIS-SMN$_{Rx}$ in other studies. Children with Type II or Type III SMA between the ages of 2 -15 may enroll in the 12 mg dose cohort of the open-label, multiple-dose Phase 2 study. The study is being conducted at centers in the United States. For further study information, please visit www.clinicaltrials.gov and search for ISIS-SMN$_{Rx}$ or by the identifier number, NCT01703988.

ISIS-SMN$_{Rx}$ is also being evaluated in an open-label, multiple-dose, dose-escalation Phase 2 study in infants with Type I SMA. In the ongoing Phase 2 study, all infants from the 6 mg dose cohort have completed the three initially scheduled doses and, under the amended protocol, are eligible to receive an additional 12 mg dose six months after their initial three scheduled doses. Isis announced late in 2013 that the study was expanded to enroll up to 20 infants and that the first infant was dosed in the 12 mg dose cohort. Infants from the 12 mg dose cohort will also be eligible to receive an additional 12 mg dose six months after they have completed the initial three scheduled doses. Infants may enroll in the Phase 2 study if they are between the ages of three weeks and seven months, live in close proximity to a study site and pass screening evaluations conducted at study sites. The study is being conducted at centers in the United States and Canada. For further study information, please visit www.clinicaltrials.gov and search for ISIS-SMN$_{Rx}$ or by the identifier number, NCT01839656.

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.

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 31 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 for the treatment of patients with HoFH. 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 potential, safety and commercialization 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, 2012, 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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