Isis Pharmaceuticals Reports Interim Results from ISIS-SMN Rx Phase 2 Study in Infants with Spinal Muscular Atrophy

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On track to initiate Phase 3 study in infants with SMA in the middle of this year
Conference Call Scheduled for Monday, February 24, 2014 at 8:30 am Eastern Time

CARLSBAD, Calif., Feb. 21, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) today provided an update on its ongoing open label, multiple dose Phase 2 study of ISIS-SMN$_{Rx}$ in infants with spinal muscular atrophy (SMA). To date, all four infants in the 6 mg cohort have been in the study for over six months and are now approximately nine and a half to 16 months in age with an average age of approximately 12 and a half months. All four infants are alive and none have required permanent respiratory assistance.

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"We are pleased with the tolerability we have observed with ISIS-SMN$_{Rx}$ to date. This is the first study to investigate ISIS-SMN$_{Rx}$ in infants with SMA. Even though these are interim results from a small number of infants, we are encouraged by the observation that all four infants in the 6 mg cohort are still alive and not on permanent ventilation. These interim results, while early, provide support for advancing ISIS-SMN$_{Rx}$ into a Phase 3 study in infants," said C. Frank Bennett, Ph.D., senior vice president of research. "We look forward to the longer-term results from this ongoing study and plan to report more detailed data at the upcoming American Academy of Neurology meeting in April."

In the ongoing Phase 2 study, doses of either 6 mg or 12 mg are administered intrathecally on Days 1, 15 and 85. All infants from the 6 mg dose cohort have completed the three initially scheduled doses and are now eligible to receive a maintenance dose of 12 mg six months after their initial three scheduled doses. In the 12 mg cohort, 10 infants have received at least one dose of ISIS-SMN$_{Rx}$ to date. Of these 10 infants, nine still remain in the study. One infant in the 12 mg cohort succumbed to pneumonia early in the treatment portion of study. In both cohorts, ISIS-SMN$_{Rx}$ has been well tolerated.

"Infants with type 1 SMA have the most severe form of this disease. It is tragic that, because of the severity of their disease, about half of these patients won't make it to their first birthday and most won't make it to their second birthday," said Dr. Tom Crawford, professor of neurology and pediatrics at Johns Hopkins Children's Center. "A recent study on the natural history of infants with Type I SMA showed that half of infants with Type I SMA had died or been put on permanent ventilation by about 10 months of age. In that study, this number increases to 80 percent by 18 months of age. These data are relevant for the study reported today as the characteristics of the infants evaluated in the natural history study are similar to the infants in this study."

Isis plans to present additional detail from this study at the upcoming American Academy of Neurology conference on April 29, 2014.

Conference Call
At 8:30 a.m. Eastern Time Monday, February 24, 2014, Isis will conduct a live conference call to discuss the top-line results from this study. Interested parties may listen to the call by dialing 866-652-5200, or access the audio webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

Isis announced late in 2013 that the Phase 2 infant 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.

ISIS-SMN$_{Rx}$ is also currently being evaluated in an open-label, multiple-dose, dose-escalation Phase 1b/2a 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$_{Rx}$, doses of 3 mg, 6 mg, 9 mg and 12 mg were administered intrathecally. The 3 mg, 6 mg and 12 mg doses are administered on Days 1, 29 and 85. The 9 mg dose is administered on Days 1 and 85. All children have completed dosing in the initial three dose cohorts and the first child has been dosed in the 12 mg cohort. The new open-label extension study is designed to provide an 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. For further study information, please visit www.clinicaltrials.gov and search for ISIS-SMN$_{Rx}$ or by the identifier number, NCT01703988.

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 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.

SOURCE Isis Pharmaceuticals, Inc.

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