Isis Pharmaceuticals Announces Initiation of Phase 1/2 Clinical Study of ISIS-SOD1 Rx in Patients With ALS

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CARLSBAD, Calif., Dec. 11, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) today announced that its partner, Biogen, has initiated a Phase 1/2 clinical study of ISIS-SOD1$_{Rx}$ (BIIB067) in patients with amyotrophic lateral sclerosis (ALS). ISIS-SOD1$_{Rx}$ is part of Isis' strategic collaboration with Biogen to discover and develop antisense drugs to treat neurological diseases. ISIS-SOD1$_{Rx}$, previously referred to as ISIS-BIIB3$_{Rx}$, is a Gen. 2.0+ antisense drug designed to reduce the production of superoxide dismutase 1 (SOD1). A mutation in the SOD-1 gene results in an inherited form of ALS, referred to as SOD1-ALS. SOD1-ALS is the second most common familial form of ALS, accounting for up to 20 percent of familial ALS. Familial ALS represents approximately 10 percent of all cases of ALS. Currently, treatment options for patients with ALS are extremely limited with no drugs that significantly slow disease progression.

"There is substantial evidence that mutations in the SOD1 gene are responsible for a toxic gain of function that can lead to progressive loss of motor neurons in patients with SOD1-ALS. As a result, patients with SOD1-ALS experience muscle weakness, loss of movement, difficulty in breathing and swallowing and eventually succumb to their disease. Our antisense technology provides us with the unique ability to act at the genetic level to reduce the production of the SOD1 protein, including the mutant SOD1 protein that is believed to be the cause of the disease," said C. Frank Bennett, Ph.D., senior vice president of research at Isis Pharmaceuticals. "We have previously demonstrated that we can safely administer an antisense drug in patients with familial ALS by intrathecal injection. In the study initiated today, we are evaluating a more potent antisense drug designed to directly reduce the production of the SOD1 protein. This approach has the potential to provide therapeutic benefit to patients with SOD1-ALS by slowing or even halting progression of this fatal disease."

"Together with Biogen, we have made significant progress developing antisense drugs to treat neurological and neuromuscular disorders. The advancement of ISIS-SOD1$_{Rx}$ into clinical development is an important milestone for this collaboration and reflects Biogen's and our commitment to developing drugs for patients with ALS. The advancement of this program is also another example of the broad applicability of our technology to address diseases that are unapproachable by other therapeutic modalities," said B. Lynne Parshall, chief operating officer of Isis Pharmaceuticals.

ALS is a rare, fatal neurodegenerative disorder. Patients with ALS suffer progressive degeneration of the motor neurons, which results in a declining quality of life and ultimately death. ISIS-SOD1$_{Rx}$, which targets the best understood genetic cause of familial ALS, is the first antisense drug to treat ALS to enter clinical development under the strategic collaboration between Isis and Biogen. As the study progresses, Isis has the opportunity to earn a $2.5 million milestone payment from Biogen.

Biogen is conducting the randomized, placebo-controlled, dose escalation Phase 1/2 clinical study that will evaluate the safety and activity of ISIS-SOD1$_{Rx}$ in patients with ALS, including patients with SOD1-ALS. In this study, ISIS-SOD1$_{Rx}$ will be administered intrathecally as an injection directly into the cerebral spinal fluid. Intrathecal administration of other antisense drugs has been shown to be well tolerated in multiple clinical studies. For further study information, please visit www.clinicaltrials.gov and search for ISIS-SOD1$_{Rx}$.

ABOUT ISIS AND BIOGEN

Isis and Biogen have a broad strategic alliance 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's capability to develop therapies for neurological disorders. Isis is primarily responsible for drug discovery and early development of antisense therapies. Biogen 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), nusinersen; myotonic dystrophy type 1 (DM1), ISIS-DMPK-2.5$_{Rx}$; amyotrophic lateral sclerosis (ALS), ISIS-SOD1$_{Rx}$, and an undisclosed neurodegenerative disease, ISIS-BIIB4$_{Rx}$. In addition to these four drugs, Isis and Biogen have numerous opportunities to evaluate additional targets for the development of drugs to treat neurological disorders.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is the leading company in RNA-targeted drug discovery and development focused on developing drugs for patients who have the highest unmet medical needs, such as those patients with severe and rare diseases. Using its proprietary antisense technology, Isis has created a large pipeline of first-in-class or best-in-class drugs, with over a dozen drugs in mid- to late-stage development. Drugs currently in Phase 3 development include volanesorsen, a drug Isis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with familial chylomicronemia syndrome and familial partial lipodystrophy; ISIS-TTR$_{Rx}$, a drug Isis is developing with GSK to treat patients with all forms of TTR amyloidosis; and nusinersen, a drug Isis is developing with Biogen to treat infants and children with spinal muscular atrophy. 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, the discovery, development, activity, therapeutic and commercial potential and safety of ISIS-SOD1$_{Rx}$ for the treatment of amyotrophic lateral sclerosis. 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, 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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