Isis Pharmaceuticals Reports Data From Phase 2 Study of ISIS-PTP1B Rx in Patients With Type 2 Diabetes

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CARLSBAD, Calif., Feb. 3, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today top-line results from a Phase 2 study of ISIS-PTP1B$_{Rx}$ in patients with type 2 diabetes. In the Phase 2 study patients treated with ISIS-PTP1B$_{Rx}$ achieved statistically significant reductions in body weight and hemoglobin A1c (HbA1c). In patients treated with ISIS-PTP1B$_{Rx}$, a mean reduction in HbA1c of 0.7 percentage points from baseline was achieved at 36 weeks, compared to a mean reduction of 0.2 percentage points for placebo-treated patients (p=0.03). Patients treated with ISIS-PTP1B$_{Rx}$ also experienced a mean reduction in body weight from baseline at 36 weeks (p=0.01). Isis plans to report the full data from this study at a medical meeting later this year.

"Despite currently available therapies, many patients with type 2 diabetes are still unable to control their blood glucose levels and eventually require the use of insulin therapy. The only class of insulin sensitizers currently available is limited in use due to side effects We designed ISIS-PTP1B$_{Rx}$ to act as an insulin sensitizer to enhance glycemic control by specifically targeting protein-tyrosine phosphatase 1B (PTP-1B). The results from this study and our earlier clinical experience with PTP-1B suggest that addressing this novel therapeutic target for type 2 diabetes with ISIS-PTP1B$_{Rx}$ may have the potential to offer a safer more effective approach for patients with type 2 diabetes who are progressing in their disease," said Sanjay Bhanot, M.D., Ph.D., vice president of clinical development and translational medicine at Isis Pharmaceuticals. "We are particularly encouraged that the improvements in glucose control and body weight continued to increase through the treatment period suggesting that longer-term treatment with ISIS-PTP1B$_{Rx}$ could provide even greater glucose control."

"ISIS-PTP1B$_{Rx}$ is a drug that has the potential to address several unique segments of the type 2 diabetes population and has the potential to both delay the need for insulin as well as to make insulin therapy more effective, thereby addressing a significant unmet medical need. We and our advisors believe that ISIS-PTP1B$_{Rx}$ could be developed for patients with type 2 diabetes who are failing oral antidiabetic therapies or GLP-1 agonists, thereby delaying the need to initiate insulin therapy. These data also support the development of ISIS-PTP1B$_{Rx}$ for patients who are insulin-resistant, remain uncontrolled even on high doses of insulin and in whom an insulin sensitizer could provide significant benefit. In addition, the combination of glucose control and weight loss demonstrated by ISIS-PTP1B$_{Rx}$ in this study has the potential to be a significant advance in the treatment of obese patients with type 2 diabetes. We are in the process of discussing future development plans with potential partners in the diabetes space who could provide the expertise and resources necessary to enhance the value of this drug," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals.

The Phase 2 study of ISIS-PTP-1B$_{Rx}$ was a double-blinded, randomized, placebo-controlled study in 92 patients with type 2 diabetes who had uncontrolled blood sugar despite treatment with stable metformin with or without sulfonylurea therapy. Patients received 200 mg of ISIS-PTP1B$_{Rx}$ or placebo for 26 weeks added to their stable doses of their background therapies. In this study, the average incoming HbA1c level was 8.6 percent and the average BMI was 34 kg/m^2. Patients in this study were not required to conform to any type of restrictive or weight-loss diet beyond the standard dietary restrictions they adhered to upon entry into the study. In this study, ISIS-PTP1B$_{Rx}$ was generally well tolerated. The most common adverse event was infrequent injection site reactions, which were predominantly mild and resolved rapidly. There were no flu-like symptoms, no clinically significant abnormalities in laboratory parameters and no cases of severe hypoglycemia.

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 33 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 the development, activity, therapeutic potential and safety of ISIS-PTP1B$_{Rx}$ in treating patients with type 2 diabetes. 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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