

Isis Initiates Phase 1 Clinical Trial of ISIS-FGFR4Rx a Peripherally Acting Drug to Treat Obesity

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CARLSBAD, Calif., Dec. 20, 2011 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 1 study of ISIS-FGFR4Rx, an antisense drug designed to treat obesity. ISIS-FGFR4Rx specifically reduces the production of fibroblast growth factor receptor 4 (FGFR4) in the liver and fat tissues, which decreases the body's ability to store fat while simultaneously increasing fat burning and energy expenditure. Because ISIS-FGFR4Rx does not distribute to the brain or central nervous system (CNS), ISIS-FGFR4Rx should not produce any CNS side effects. Many anti-obesity drugs primarily work to suppress appetite by acting in the brain, commonly resulting in CNS side effects.

"Obesity is an epidemic in the United States and much of the rest of the industrialized world. Obesity is a serious condition that increases the risk of diabetes, heart disease, stroke, arthritis and some cancers. Severely obese patients make up the most rapidly growing part of the obese population. In these severely obese patients, bariatric, or weight-loss, surgery is a preferred therapeutic option; however long-term weight loss remains a challenge for these patients," said Richard Geary, Ph.D., Senior Vice President of Development at Isis. "Many of the recent therapies under development or on the market to treat obesity have unacceptable safety profiles. Clearly there is a significant need for a treatment approach that can cause weight loss without deleterious side effects."

"We are developing ISIS-FGFR4Rx for patients who are severely obese and for the treatment of obesity in patients who are at high risk for cardiovascular and metabolic diseases. In preclinical studies, inhibition of FGFR4 led to robust and sustained weight reduction in obese animals, accompanied by an improvement in insulin sensitivity," said Sanjay Bhanot, M.D., Ph.D., Vice President of Clinical Development and Translational Medicine at Isis. "In obese animals, antisense inhibition of FGFR4 enhanced weight loss when administered as a single agent or in combination with an appetite-suppressing drug, suggesting that peripheral inhibition of FGFR4 in combination with other types of anti-obesity drugs could be a novel therapeutic approach for the treatment of obesity. Because ISIS-FGFR4Rx selectively alters fat metabolism in metabolically active tissues such as liver and fat without distributing to the brain or heart, we do not expect ISIS-FGFR4Rx to produce cardiac or CNS side effects."

ISIS-FGFR4Rx is the first drug in Isis' metabolic franchise to treat obesity and utilizes technology Isis in-licensed from Verva Pharmaceuticals.

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 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic and severe and rare/neurodegenerative diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, mipomersen, following regulatory approval, which is expected in 2012. 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 discovery, development, activity, therapeutic potential and safety of ISIS-FGFR4Rx. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the planned commercialization of mipomersen, 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, 2010 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, including Regulus Therapeutics Inc., its jointly owned subsidiary.

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