

Isis Initiates Phase 1 Study in Patients With Cancer With the First Generation 2.5 Antisense Drug, ISIS-STAT3Rx

March 7, 2012

CARLSBAD, Calif., March 7, 2012 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 1 study of ISIS-STAT3Rx, a Generation 2.5 antisense drug designed to treat cancer. ISIS-STAT3Rx specifically reduces the production of signal transducer and activator of transcription 3 (STAT3). Because STAT3 is over expressed in numerous types of cancers, ISIS-STAT3Rx has the potential to be broadly useful for both solid and liquid tumors. The ISIS-STAT3Rx development plan is initially focused on key cancers where there is a high unmet medical need and a strong link to STAT3, such as hepatocellular carcinoma (HCC) and ovarian cancer. Advancements in Isis' technology platform have resulted in the improved potency of Generation 2.5 antisense drugs creating opportunities for drugs like ISIS-STAT3Rx to be effective in the more difficult to treat types of cancer.

"The role of STAT3 as a key factor critical for tumor cell growth and survival of cancer cells has made STAT3 widely viewed as an important target of interest," said David S. Hong, M.D., Assistant Professor, Department of Investigational Cancer Therapeutics at the University of Texas MD Anderson Cancer Center. "STAT3 is a well understood transcription factor involved in multiple survival mechanisms that intersect with the growth, metastasis and invasiveness of cancer. The ability to selectively inhibit STAT3 could allow us to effectively treat some of the most difficult to treat cancers."

"We and many others are very interested in STAT3 as a therapeutic target because of the important role STAT3 plays in the survival and growth of difficult to treat cancers. The marked improvements in potency of our Generation 2.5 antisense drugs that we have seen in cancer models cause us to believe that these drugs could have a profound impact in treating cancer," said Brett Monia, Ph.D., Senior Vice President, Drug Discovery and Corporate Development at Isis. "We are very excited about the potential of our Generation 2.5 STAT3 drug to treat human cancers with high unmet medical needs as we continue to be the leader in antisense innovation. The advancement of our first drug incorporating our new, more potent Generation 2.5 chemistry is a key milestone and should allow us to further extend the reach of our technology into new targets, new tissues, and new disease opportunities."

ISIS-STAT3Rx is the first Generation 2.5 drug in Isis' pipeline. It is designed to treat cancer by inhibiting the production of STAT3, a gene that blocks natural cell death and that is critical for tumor cell growth and survival. Inhibition of STAT3 has been shown to block the induction of tumor-associated cytokines involved in the progression of cancer, such as IL-6, IL-1, TGF β , and IL-10, which could serve as important biomarkers in clinical studies. Analyses of these cytokines in Phase 1 could serve as an early indicator of anticancer activity of ISIS-STAT3Rx in patients with cancer.

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 26 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, KYNAMRO, 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-STAT3Rx and the therapeutic benefit of antisense drugs that incorporate Isis' Generation 2.5 chemistry. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the planned commercialization of KYNAMRO, 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, 2011, which is on file with the SEC. Copies of this 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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