

Isis Pharmaceuticals Announces the Initiation of a Clinical Study of ISIS-STAT3 Rx in Patients With Liver Cancer

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CARLSBAD, Calif., May 6, 2013 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 1b/2a clinical study of ISIS-STAT3_{Rx} in patients with advanced metastatic hepatocellular carcinoma (HCC). HCC is a tumor of the liver and is one of the most common cancers worldwide with at least one million new cases diagnosed each year. ISIS-STAT3_{Rx} is an antisense drug discovered by Isis and being developed to treat patients with cancers with a strong link to STAT3, such as HCC. Isis licensed ISIS-STAT3_{Rx} to AstraZeneca as part of a strategic alliance in cancer. AstraZeneca is conducting this newly initiated study in patients with HCC.

"We are pleased to be working with AstraZeneca on the development of ISIS-STAT3_{Rx}. AstraZeneca's considerable resources, expertise and development capabilities to develop anti-cancer drugs strengthen substantially our ability to broadly evaluate ISIS-STAT3_{Rx} across a range of cancer types. Given the role of STAT3 in the growth and survival of tumors, we believe that ISIS-STAT3_{Rx} could be beneficial in the treatment of many different types of cancers. As such, together with AstraZeneca, we have designed a broad development program to explore the effects of ISIS-STAT3_{Rx} in a number of different cancers," said B. Lynne Parshall, chief operating officer at Isis. "Our early work showed that ISIS-STAT3_{Rx} treatment resulted in clear responses in patients with advanced cancer who were refractory to prior chemotherapy treatment, with an acceptable safety profile. The new study builds on this early work and expands our evaluation of ISIS-STAT3_{Rx} into liver cancer where STAT3 inhibition could also provide therapeutic benefit."

The Phase 1b/2a study will evaluate the safety and efficacy of ISIS-STAT3_{Rx} in patients with HCC who have failed first-line therapy. The endpoints for the study include measurements of anti-tumor activity, STAT3 protein levels in tumor biopsies and STAT3-related biomarkers. The study will also evaluate safety. Although HCC is common, it is considered a very difficult to treat cancer that does not respond well to chemotherapy.

"STAT3 is important for the growth, invasiveness and metastases of many types of cancer, which makes it a very attractive target. The potency we have observed in our preclinical cancer studies and the early evidence of clinical activity we observed in our Phase 1 study suggest that ISIS-STAT3_{Rx} could be an effective anti-tumor agent that is broadly applicable to many different types of cancer," said Brett Monia, Ph.D., senior vice president, antisense drug discovery at Isis.

ABOUT ISIS-STAT3_{Rx}

ISIS-STAT3_{Rx}, also referred to as AZD9150, is designed to specifically reduce the production of signal transducer and activator of transcription 3 (STAT3). STAT3 is a gene that blocks natural cell death and 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. ISIS-STAT3_{Rx} is the first drug in Isis' pipeline that incorporates Isis' Generation 2.5 chemistry, which was developed to increase potency of antisense drugs thereby creating opportunities for drugs like ISIS-STAT3_{Rx} to be effective in more difficult to treat cancers. In a Phase 1 safety study, ISIS-STAT3_{Rx} treatment produced an acceptable safety profile and resulted in sustained responses in two of three patients with advanced diffuse large B cell lymphoma who were refractory to multiple prior chemotherapy treatments. Isis and AstraZeneca are currently evaluating ISIS-STAT3_{Rx} in two Phase 1b/2a clinical studies in patients with HCC and advanced lymphomas. Because STAT3 is over expressed in numerous types of cancers, ISIS-STAT3_{Rx} has the potential to be broadly useful for both solid and hematological tumors.

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, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, in the United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. 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' strategic alliance with AstraZeneca, the development, activity, therapeutic potential and safety of ISIS-STAT3_{Rx}, 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 commercial potential 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, 2012, 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.

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