Isis Pharmaceuticals Reports Encouraging Interim Phase 1 Data On ISIS-STAT3Rx In Patients With Cancer

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Isis Initiates Phase 2 Study of ISIS-STAT3Rx in Patients with Advanced Cancer

CARLSBAD, Calif., Oct. 31, 2012 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced that preliminary data from the Phase 1 study of ISIS-STAT3$_{Rx}$ in patients with cancer were presented today at the Oligonucleotide Therapeutics Society in Boston. Interim results of the initial dose escalation study in patients with cancer 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. Based on these results, Isis has initiated a Phase 2 study in focused patient populations with advanced cancer.

"STAT3 expression has been shown to be associated with the growth, invasiveness and metastases of many types of cancer making it an attractive target. However, STAT3 has proven to be a difficult target to inhibit safely with small molecule drugs, making ISIS-STAT3$_{Rx}$ even more interesting," said David S. Hong, M.D., associate professor, department of investigational cancer therapeutics at the University of Texas MD Anderson Cancer Center. "Patients with advanced cancer have often failed multiple therapies and have no other chemotherapeutic options. For these patients there is a desperate need for new therapies that can halt their disease progression. The clinical responses observed to date suggest that inhibition of STAT3 could provide benefit to some of these patients. The early data on ISIS-STAT3$_{Rx}$ is impressive because it suggests that this drug can produce responses in patients with advanced cancer who have failed to respond to other therapies."

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. The Phase 1 study evaluated ISIS-STAT3$_{Rx}$ in patients with solid tumors and lymphoma who have relapsed or were refractory to multiple chemotherapy regimens. The Phase 2 study will evaluate the safety and efficacy of ISIS-STAT3$_{Rx}$ in focused patient populations with advanced cancers that have been linked to STAT3 who have failed all other treatment options. The endpoints for the study include measurements of anti-tumor activity, STAT3 protein levels in tumor biopsies, STAT3-related biomarkers, and safety. Efficacy will be evaluated across different types of cancer and correlated with genetic sequencing from patient tumor biopsies.

"We believe that the significant improvements in potency we have observed in our preclinical cancer studies with our Generation 2.5 chemistry should translate into an effective anti-tumor agent that is broadly applicable to many different types of cancer. The important role that STAT3 plays in tumor survival and growth made it a great target to evaluate our Generation 2.5 platform in patients," said Brett Monia, Ph.D., senior vice president, antisense drug discovery at Isis. "We are very pleased and encouraged with the safety and efficacy observed in our Phase 1 study of ISIS-STAT3$_{Rx}$. The promising data generated in our Phase 1 study has enabled us to accelerate our development plans and move into a Phase 2 study earlier than originally anticipated."

ISIS-STAT3$_{Rx}$ is designed to inhibit the production of signal transducer and activator of transcription 3 (STAT3), a protein critical for tumor cell growth and survival. Because STAT3 is overexpressed in numerous types of cancer, ISIS-STAT3$_{Rx}$ has the potential to be broadly useful for both solid and liquid tumors. ISIS-STAT3$_{Rx}$ has been shown to reduce STAT3 levels in preclinical tumor models and produce anti-tumor activity. Inhibition of STAT3 has also been shown to block the induction of tumor-associated cytokines involved in the progression of cancer, such as IL-6, IL-1, TGFb, and IL-10, which could serve as important biomarkers in clinical studies.

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 25 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™, inthe United States and Europe following regulatory approval. 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-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 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 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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