

Isis Pharmaceuticals Earns \$7.5 Million Milestone Payment From AstraZeneca

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AstraZeneca advances ISIS-STAT3 Rx in Clinical Development

CARLSBAD, Calif., Nov. 5, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has earned a \$7.5 million milestone payment, the first of two milestone payments totaling \$15 million, from AstraZeneca for the advancement of ISIS-STAT3_{Rx}, also referred to as AZD9150, in patients with advanced cancers. Isis will earn the second \$7.5 million milestone payment from AstraZeneca upon initiation of a Phase 2 study. Isis has completed a clinical study of ISIS-STAT3_{Rx} in patients with advanced cancers and plans to present results from this study at an upcoming medical meeting. AstraZeneca is currently evaluating ISIS-STAT3_{Rx} in a Phase 1/2 clinical study in patients with advanced metastatic liver cancer. AstraZeneca plans to initiate additional clinical studies to further evaluate ISIS-STAT3_{Rx}.



"AstraZeneca's expertise and resources in the area of oncology drug development are a significant benefit for the clinical development of ISIS-STAT3_{Rx}," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals. "We are pleased, not only with the substantial resources and expertise that AstraZeneca has brought to this program, but also with their commitment to advancing ISIS-STAT3_{Rx} into clinical development."

Under the amended terms of agreement, Isis has earned a \$7.5 million milestone payment today. Upon initiation of the Phase 2 study, Isis will earn a second \$7.5 million milestone payment and an additional \$10 million milestone payment. In total, Isis is eligible to receive up to \$70 million in milestone payments as ISIS-STAT3_{Rx} advances through clinical development. In addition, Isis is eligible to earn up to \$170 million in regulatory milestone payments plus royalties on the commercial sales of the drug.

About ISIS-STAT3_{Rx}

ISIS-STAT3_{Rx} is the first drug in Isis' pipeline that incorporates Isis' Generation 2.5 chemistry, which Isis 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. 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. In addition, STAT3 is an important mediator of signaling in the JAK2/STAT3 pathway, which has been previously shown to be an important target for drug development. Because STAT3 is activated in numerous types of cancer, ISIS-STAT3_{Rx} has the potential to be broadly useful for both solid and hematologic 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, TGF, 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 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 and rare and cardiovascular disease. These include a novel triglyceride lowering drug, ISIS-APOCIII_{Rx}, for patients with familial chylomicronemia syndrome; ISIS-TTR_{Rx}, which Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN_{Rx}, which 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 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 Pharmaceuticals' 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 Pharmaceuticals' 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 Pharmaceuticals' 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 Pharmaceuticals' programs are described in additional detail in Isis Pharmaceuticals' 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.

Isis Pharmaceuticals[®] is a registered trademark of Isis Pharmaceuticals, Inc. KYNAMRO[®] is a registered trademark of Genzyme Corporation.

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