Isis Pharmaceuticals Initiates Phase 1 Study of ISIS-GSK3 Rx and Earns \$3 Million Milestone Payment From GSK

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CARLSBAD, Calif., Nov. 26, 2013 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has initiated a Phase 1 study for ISIS-GSK3_{Rx} and earned a \$3 million milestone payment from GlaxoSmithKline (GSK). ISIS-GSK3_{Rx} is designed to inhibit the production of an undisclosed target to treat a common viral infection. Isis will develop ISIS-GSK3_{Rx} to Phase 2 proof-of-concept, after which GSK has an exclusive option to in-license the program and further develop and commercialize the asset.

(Logo: http://photos.prnewswire.com/prnh/20130807/LA60006LOGO)

"We are very pleased to advance ISIS-GSK3 $_{RX}$ into a clinical study in a therapeutic area where there is a significant need for better therapies" said B. Lynne Parshall, chief operating officer of Isis. "The versatility and broad applicability of our technology enables us to discover and develop antisense drugs to a diverse range of targets. We look forward to evaluating this important new drug in this underserved disease space."

As a part of its alliance with GSK, Isis is eligible to earn additional pre-licensing milestone payments from GSK as ISIS-GSK3 $_{Rx}$ advances. Isis is also eligible to receive double-digit royalties on sales of ISIS-GSK3 $_{Rx}$. The alliance applies Isis' antisense drug discovery platform to discover and develop new therapeutics against targets for rare and serious diseases, including infectious diseases and some conditions causing blindness.

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 31 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, KYNAMROTM, irthe United States for the treatment of patients with HoFH. 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' collaboration with GlaxoSmithKline, the discovery, development and potential of drugs for rare and infectious diseases, and the development, activity, therapeutic potential and safety of ISIS-GSK3_{Rx}. Any statement describing Isis' 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' 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, 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.

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc. Regulus Therapeutics™ is a trademark of Regulus Therapeutics Inc. KYNAMRO™ is a trademark of Genzyme Corporation.

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