



Isis Adds New Drug to Its Development Pipeline: ISIS 388626 Targeting SGLT2 for the Treatment of Type 2 Diabetes

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CARLSBAD, Calif., Oct 18, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced that it has added a new diabetes drug targeting the sodium dependent glucose transporter type 2 (SGLT2) to its development pipeline. ISIS 388626, a generation 2.2 antisense drug that acts in the kidney to increase glucose excretion, complements Isis' existing pipeline of drugs in development for the treatment of diabetes, each of which act upon targets in the liver through distinct mechanisms to improve insulin sensitivity, reduce glucose production, or affect other metabolic aspects of this complex disease.

The productivity of antisense technology has allowed Isis to rapidly evaluate many potential targets for treatment of complex metabolic diseases such as diabetes and obesity in well established animal models. To date, Isis has analyzed the effects of inhibiting over 120 distinct gene targets in animals, and the efficiency of the drug discovery process should continue to provide a rich source of promising drugs with which to populate Isis' future pipeline. ISIS 388626 is the fourth development candidate to come out of Isis' extensive metabolic disease drug discovery program.

"We think ISIS 388626 is an exciting addition to our portfolio that offers a kidney-based mechanism, which will complement our other diabetes drugs in development," said Sanjay Bhanot, M.D., Ph.D., Vice President of Metabolic Diseases Research & Development, Isis Pharmaceuticals. "This is the first kidney target that we have approached with our second-generation drugs, and we are quite encouraged by what we have seen in the animal models. We know that antisense drugs distribute most readily to the liver, kidney, fat cells, bone marrow and spleen, so selecting targets in these tissues is part of our strategy for developing effective drugs. We plan to move ISIS 388626 forward toward human proof-of-concept as rapidly as possible, and we look forward to continuing to populate our metabolic disease pipeline with drugs arising from our prolific research program."

ABOUT SGLT2 AND ISIS 388626

The sodium dependent glucose transporter type 2 (SGLT2) is substantially responsible for glucose re-absorption in the kidney. Decreasing SGLT2 function promotes glucose excretion to help reduce blood sugar levels, making it an attractive target for the treatment of diabetes. In preclinical studies, Isis has demonstrated in several animal species that ISIS 388626 and other antisense inhibitors of SGLT2 effectively reduce target mRNA levels, increase urinary glucose excretion and consequently lower blood glucose levels and HbA1c without causing dangerously low levels of blood sugar known as hypoglycemia. This is consistent with expectations based on human subjects who have mutations in the SGLT2 gene and have increased urine glucose levels but are otherwise asymptomatic. ISIS 388626 effectively and specifically inhibits the production of SGLT2 in the kidney tissue, without having any effect on a related gene product, SGLT1. In addition to being Isis' first second-generation antisense drug for a kidney target, ISIS 388626 is also unique due to its 12 nucleotide length rather than the more typical 18 - 21 nucleotide sequences that comprise Isis' other drugs. This attribute simplifies manufacturing and has the potential to substantially reduce related expenses. The short sequence may also contribute to ISIS 388626's unusually high potency; it is among the most potent antisense drugs Isis has yet evaluated in preclinical models.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 18 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for a wide variety of diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000(TM) Biosensor System, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide, and Isis is a joint owner of Regulus Therapeutics, LLC, a company focused on the discovery, development and commercialization of microRNA therapeutics. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding Isis' business, its drug discovery and development pipeline, and the therapeutic and commercial potential for ISIS 388626 for the treatment of diabetes. 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, including those statements that are described as Isis' goals. 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 products. 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, 2006, and its quarterly report on Form 10-Q for the quarter ended June 30, 2007, 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" means Isis Pharmaceuticals and its subsidiaries.

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