

Bristol-Myers Squibb Selects Isis Drug Targeting Pcsk9 as Development Candidate For Prevention and Treatment of Cardiovascular Disease

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Isis To Receive \$2 Million Milestone Payment

CARLSBAD, Calif., April 8, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that Bristol-Myers Squibb Company (NYSE: BMY) has selected a compound from the companies' collaboration as a development candidate. As a result, Isis will receive a \$2 million milestone payment. The two companies have an ongoing collaboration to identify antisense drugs that target proprotein convertase subtilisin kexin 9 (PCSK9). The development candidate is an antisense inhibitor of PCSK9 that helps regulate the amount of cholesterol in the bloodstream.

The selection of this development candidate marks the achievement of the first milestone in this collaboration, which was announced on May 9, 2007. The compound was designed to selectively inhibit the production of PCSK9 and could offer a new and complementary mechanism to current lipid-lowering therapies for the prevention and treatment of cardiovascular disease.

"In less than a year, we have been able to identify and characterize a number of antisense drugs that inhibit PCSK9 in pre-clinical studies and out of those, identified an attractive development candidate. With the selection by Bristol-Myers Squibb of this development candidate, we have achieved our first milestone. The rapid progress we have made with our PCSK9 program is representative of the efficiency of our antisense technology to quickly move from target to drug," said Brett Monia, Ph.D., Vice President of Antisense Drug Discovery of Isis. "PCSK9 is a new and exciting target for the management of lipids both to prevent and treat cardiovascular disease. Furthermore, our antisense technology is uniquely suited to provide viable clinical drug candidates for PCSK9 and other targets that are not accessible using standard drug discovery approaches. This newest development candidate is the third clinical candidate to arise from our cardiovascular drug discovery program within the past four years, and we look forward to working with Bristol-Myers Squibb to advance this drug through development."

ABOUT PCSK9

PCSK9, a member of a large family of proteases, helps regulate the amount of LDL-cholesterol in the bloodstream through its interactions with the LDL-receptor. Furthermore, genetic studies in humans have demonstrated that elevation in PCSK9 concentrations can lead to severely high concentrations of LDL-cholesterol, whereas low PCSK9 concentrations are associated with low LDL-cholesterol concentrations.

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 19 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Ibis Biosciences, Inc., Isis' majority-owned subsidiary, is developing and commercializing the Ibis T5000™ Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding Isis' collaboration with Bristol-Myers Squibb, and the discovery and development of drugs for prevention and treatment of cardiovascular disease and high cholesterol including the newly selected development candidate. 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, 2007, 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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