

## Isis Earns \$6 Million Milestone Payment From Bristol-Myers Squibb for BMS-PCSK9Rx

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CARLSBAD, Calif., March 8, 2010 /PRNewswire via COMTEX/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has earned a \$6 million milestone payment from Bristol-Myers Squibb Company (NYSE: BMY) related to the acceptance of initial regulatory filings to begin Phase 1 clinical studies for BMS-PCSK9Rx. BMS-PCSK9Rx is an antisense drug that arose out of the ongoing collaboration between Bristol-Myers Squibb and Isis to identify antisense drugs targeting PCSK9 to lower low-density lipoprotein (LDL) cholesterol.

"We are pleased with the success of our partnership with Bristol-Myers Squibb, and our ability to deliver a drug candidate within the first year of the collaboration. We are looking forward to Bristol-Myers Squibb initiating a Phase 1 clinical trial shortly. The speed of development of BMS-PCSK9Rx exemplifies the efficiency of our technology and our ability to quickly advance from the discovery of a gene to a drug in the clinic," said Stanley T. Crooke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis. "Targeting PCSK9 offers a unique approach to lowering LDL cholesterol, which is a key component in preventing and managing cardiovascular disease. We continue to advance and mature the breadth and depth of our pipeline and the therapeutic opportunities that we can take advantage of with our technology."

BMS-PCSK9Rx is an antisense drug that targets proprotein convertase subtilisin kexin 9, or 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 concentrations of LDL-cholesterol. Isis designed BMS-PCSK9Rx to selectively inhibit the production of PCSK9 and to offer a new and complementary mechanism to current lipid-lowering therapies to prevent and treat cardiovascular disease.

### **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 22 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alynham Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,600 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

This press release includes forward-looking statements regarding Isis' collaboration with Bristol-Myers Squibb Company, the discovery and development of drugs for cardiovascular disease and high cholesterol, and the development, activity, therapeutic potential and safety of BMS-PCSK9Rx in the prevention and treatment of cardiovascular disease. 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 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, 2009, which is 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, including Regulus Therapeutics Inc.

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