
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): **May 9, 2007**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

1896 Rutherford Road

Carlsbad, CA 92008

(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 1.01. Entry into a Material Definitive Agreement.

On May 9, 2007, Isis Pharmaceuticals, Inc. ("Isis") and Bristol-Myers Squibb Company announced a collaboration to discover, develop and commercialize novel antisense drugs targeting proprotein convertase subtilisin kexin 9 (PCSK9) for the prevention and treatment of cardiovascular disease.

Isis filed a press release describing this transaction. A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated May 9, 2007.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: May 8, 2007

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Executive Vice President,
Chief Financial Officer and Director

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99.1 Press Release dated May 9, 2007.

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For Immediate Release**BRISTOL-MYERS SQUIBB ENTERS CARDIOVASCULAR DISEASE COLLABORATION WITH ISIS PHARMACEUTICALS****Collaboration to Focus on Antisense Inhibitors of PCSK9**

Princeton, N.J. and Carlsbad, Calif., May 9, 2007 — Bristol-Myers Squibb Company (NYSE: BMY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced a collaboration to discover, develop and commercialize novel antisense drugs targeting proprotein convertase subtilisin kexin 9 (PCSK9) for the prevention and treatment of cardiovascular disease. PCSK9 helps regulate the amount of cholesterol in the bloodstream.

As part of the collaboration, Isis licensed to Bristol-Myers Squibb exclusive access to its PCSK9 research program. This program has recently produced new data shedding light on the mechanism by which PCSK9 contributes to high levels of low density lipoprotein (LDL) cholesterol. With its second-generation antisense PCSK9 compounds, Isis has shown in mice that reducing PCSK9 leads to increased levels of LDL receptor and consequently to lower LDL-cholesterol in the bloodstream. Decreasing LDL-cholesterol is thought to play a key role in reducing the risk of coronary artery disease.

While Bristol-Myers Squibb will fund all activities under the collaboration, both companies will be responsible for preclinical development. Bristol-Myers Squibb will be responsible for clinical development, regulatory, and commercialization activities. In addition, Bristol-Myers Squibb will work with Isis to leverage Isis' extensive oligonucleotide medicinal chemistry expertise for identification of follow-on PCSK9 antisense drugs with advanced antisense chemistries that may offer even greater potency and oral bioavailability.

Bristol-Myers Squibb will pay Isis a \$15 million upfront licensing fee, and will provide Isis with at least \$9 million in research funding over a period of three years. Isis will also receive up to \$168 million for the achievement of pre-specified development and regulatory milestones for the first drug in the collaboration, as well as additional milestones associated with development of follow-on compounds. Bristol-Myers Squibb will also pay Isis royalties on sales of products resulting from the collaboration.

“There is a clear need for new treatment options for many patients at high risk for cardiovascular disease due to high LDL-cholesterol levels,” said Francis Cuss, M.D., senior vice president, Discovery and Exploratory Clinical Research, Bristol-Myers Squibb. “PCSK9 is an attractive, genetically validated target in the field of cardiovascular disease, and Isis' antisense technology offers us a strong therapeutic platform for potentially bringing new cardiovascular medicines rapidly to market.”

“This collaboration is an important step in the continued validation of Isis' cardiovascular program,” said Lynne Parshall, J.D., executive vice president and chief financial officer, Isis Pharmaceuticals. “We look forward to combining our expertise in antisense technology with the strong scientific and clinical expertise of Bristol-Myers Squibb, with its cardiovascular and metabolic disease focus, to advance the PCSK9 compounds through development to patients as quickly as possible.”

About PCSK9

PCSK9 is a member of a large family of proteases that degrade specific cellular components, but the particular cellular substrate of PCSK9 is not known. PCSK9 helps regulate the amount of cholesterol in the bloodstream, and human cases of alterations in PCSK9 that have prompted interest in this target. People with too much PCSK9 have severely high LDL-cholesterol, and people with mutations that reduce the levels of PCSK9 have low LDL-cholesterol and reduced risk of coronary artery disease, with normal liver function.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global pharmaceutical and related health care products company whose mission is to extend and enhance human life. Visit Bristol-Myers Squibb on the World Wide Web at www.bms.com.

Bristol-Myers Squibb Forward-Looking Statement

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Among other risks, there can be no guarantee that any products developed from the compounds described in this release will receive regulatory approval, or that if approved, will be commercially successful. Nor is there any assurance that any or all of the development, regulatory, and sales milestones provided for in the agreement will be achieved. Bristol-Myers Squibb's collaboration with Isis for the discovery and development of drugs for cardiovascular disease and high cholesterol including PCSK9-targeted antisense drugs involves substantial risks and uncertainties. Forward-looking statements in the press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2006, its Quarterly Reports on Form 10-Q and its Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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 17 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for cancer, and inflammatory and other diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000 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. Additional information about Isis is available at www.isispharm.com.

Isis Pharmaceuticals, Inc. Forward-Looking Statement

This press release includes forward-looking statements regarding Isis' collaboration with Bristol-Myers Squibb, and discovery and development of drugs for cardiovascular disease and high cholesterol including PCSK9-targeted antisense compounds. 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, which is on file with the SEC. Copies of this and other documents are available from the Company.

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