
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K/A

(Amendment No.1)

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

Date of report (Date of earliest event reported): **September 13, 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 September 13, 2007 Isis Pharmaceuticals, Inc. ("Isis") announced a broad collaboration with Ortho-McNeil, Inc., a Johnson & Johnson company, to discover, develop and commercialize antisense drugs to treat metabolic diseases, including Type 2 diabetes. At that time, the agreement was subject to clearance under the Hart-Scott-Rodino Antitrust Improvements Act.

On October 2, 2007, Isis announced that it received clearance under the Hart-Scott-Rodino Antitrust Improvements Act for the agreement.

Isis filed press releases describing this transaction. Copies of this press release are attached as Exhibits 99.1 and 99.2 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1	Press Release dated September 13, 2007*
99.2	Press Release dated October 2, 2007

*Previously filed

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: October 1, 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 September 13, 2007*
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*Previously filed

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**Isis Pharmaceuticals' Contacts:**

Kristina Lemonidis
 Associate Director, Investor Relations
 760-603-2490

Amy Blackley, Ph.D.
 Manager, Corporate Communications
 760-603-2772

ISIS ANNOUNCES HSR APPROVAL AND CLOSURE OF ITS COLLABORATION WITH ORTHO-MCNEIL, INC.

CARLSBAD, Calif., October 2, 2007 - - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced that it has received clearance under the Hart-Scott-Rodino Antitrust Improvements Act for its collaboration with Ortho-McNeil, Inc., a Johnson & Johnson company, which was announced on September 13, 2007.

As part of the collaboration, Isis is granting to Ortho-McNeil worldwide development and commercialization rights to two of its diabetes drugs, ISIS 325568 and ISIS 377131, which selectively inhibit the production of glucagon receptor (GCGR) and glucocorticoid receptor (GCCR), respectively. Additionally, Ortho-McNeil will provide funding to Isis to support the joint discovery of novel drugs to treat metabolic diseases, including diabetes and obesity.

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 a wide variety of 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.

This press release includes forward-looking statements regarding Isis' collaboration with Ortho-McNeil, Inc., and its financial and business development activities. 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.

Isis Pharmaceuticals, Ibis Biosciences and Ibis T5000 are registered trademarks or trademarks of Isis Pharmaceuticals, Inc.

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