

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): **July 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))

Item 8.01. Other Events.

On July 9, 2007, Isis Pharmaceuticals, Inc. ("Isis") announced it will receive \$26.5 million dollars from Alnylam Pharmaceuticals, Inc. as its portion of the upfront fees and equity premium in the recently announced transaction between Roche Holding AG and Alnylam.

In 2004, Isis and Alnylam entered into a strategic relationship in which Alnylam obtained an exclusive license to Isis' intellectual property for double-stranded oligonucleotide therapeutics that mediate RNAi. In return, Isis received upfront payment and financial participation in future transactions supported by Isis' patents.

According to Alnylam:

- its alliance with Roche will initially cover four therapeutic areas: oncology, respiratory diseases, metabolic diseases and certain liver diseases;
- Roche will pay Alnylam 331 million US dollars in upfront cash payments and equity investment, including 1.975 million shares of Alnylam common stock the Roche Venture Fund agreed to purchase at 21.50 US dollars per share; and
- Roche may pay Alnylam field expansion payments to increase the number of therapeutic areas.

Under the terms of Isis' strategic relationship with Alnylam, Isis has the potential to receive milestone and royalty payments and a percentage of future field expansion payments from Roche to Alnylam.

A copy of the Press Releases related to this announcement is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

This report includes forward-looking statements regarding Isis Pharmaceuticals' business, its intellectual property portfolio, and the therapeutic and commercial potential of the Company's technologies. 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'

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated July 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: July 9, 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 July 9, 2007.

Isis to Receive \$26.5 Million from Alnylam

CARLSBAD, Calif., July 9, 2007 /PRNewswire-FirstCall via COMTEX News Network/ — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it will receive \$26.5 million dollars from Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) as its portion of the upfront fees and equity premium in the recently announced transaction between Roche Holding AG and Alnylam. In addition, Isis has the potential to receive milestone and royalty payments. This transaction underscores the value of Isis' innovation and the leadership role Isis has played in the field of nucleic acid based therapeutics. The close of the agreement is subject to certain regulatory approvals and is expected to occur within approximately 30 days.

In 2004, Isis and Alnylam entered into a strategic relationship in which Alnylam obtained an exclusive license to Isis' intellectual property for double-stranded oligonucleotide therapeutics that mediate RNAi. In return, Isis received an upfront payment and financial participation in future transactions supported by Isis' patents.

"Isis' technology and intellectual property have proven to be critical in creating siRNAs with drug-like properties. The rapid advancement of RNAi therapeutics is in part due to the pioneering work of Isis in virtually every area of oligonucleotide technology," said John Maraganore, Ph.D., President and Chief Executive Officer of Alnylam.

Isis owns or controls more than 1,500 issued patents pertaining to nucleic acid based therapeutics. These patents have been exclusively licensed to Alnylam for double-stranded RNAi therapeutics and include, but are not limited to:

- The Crooke Patents: U.S. 5,898,031 and 6,107,094 cover compositions, methods, and uses of modified oligonucleotides to inactivate a target mRNA mediated by a double-stranded RNase;
- Phosphorothioate and 2'-o-methyl modifications (Buhr, U.S. Patent No. 6,476,205); and,

2'-Ribose modifications (Cook, U.S. Patent Nos. 5,670,633; 6,005,087; 6,531,584; and 7,138,517).

"Since 2004 we have enjoyed a productive collaboration with Alnylam. Our technology supports both companies' leading drug discovery efforts in this new area of antisense. Working together we have made significant advances in RNAi technology and in creating drugs from this technology platform. Isis has benefited substantially from Alnylam's business development and financial successes. We look forward to additional successes from this valuable strategic relationship," said Stan Crooke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis Pharmaceuticals, Inc. "Our pioneering efforts in developing nucleic acid based drugs have resulted in a very broad and valuable patent estate. The breadth and depth of our patent estate has allowed us to create a number of strategic relationships such as the one we have with Alnylam that ensure our continued leadership in the field. This transaction further underscores the value of our innovation and strategy."

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. 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 Pharmaceuticals' business, its intellectual property portfolio, and the therapeutic and commercial potential of the Company's technologies. 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 March 31, 2007, which are 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" means Isis Pharmaceuticals and its subsidiaries.

SOURCE Isis Pharmaceuticals, Inc.

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