

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): **June 21, 2010**

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 1.01. Entry into a Material Definitive Agreement.

On June 22, 2010, Isis Pharmaceuticals, Inc. ("Isis") and Alnylam Pharmaceuticals, Inc. ("Alnylam") announced that Regulus Therapeutics Inc. ("Regulus") entered into a global, strategic alliance with sanofi-aventis to discover, develop, and commercialize microRNA therapeutics.

Alnylam and Isis formed Regulus in 2007, with each company currently owning approximately 50% of the preferred stock.

Isis and Alnylam 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 June 22, 2010.

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: June 22, 2010

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer,
Chief Financial Officer and Director

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99.1 Press Release dated June 22, 2010.

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Isis and Alnylam Provide Update on Regulus' Strategic Alliance with Sanofi-Aventis

Press Release Source: Alnylam Pharmaceuticals, Inc. On Tuesday June 22, 2010, 6:05 am

CAMBRIDGE, Mass. and CARLSBAD, Calif.—(BUSINESS WIRE)—Alnylam Pharmaceuticals, Inc. (Nasdaq: **ALNY - News**):

- *New Partnership Validates Alnylam and Isis Strategy for Shareholder Value Creation*
- *Regulus, Alnylam and Isis to Host Conference Call Webcast to Discuss Regulus-Sanofi-aventis Collaboration on June 22, 2010 at 8:30 a.m. ET (5:30 a.m. PT)*

Alnylam Pharmaceuticals, Inc. (Nasdaq: **ALNY - News**) and Isis Pharmaceuticals, Inc. (Nasdaq: **ISIS - News**) announced today that, as a result of the newly formed alliance Regulus has established with sanofi-aventis, each company will receive a payment of \$1.8 million from Regulus. This represents 7.5% of the \$25 million upfront payment from sanofi-aventis to Regulus. In addition, Alnylam and Isis are each eligible to receive a similar percentage of potential future success-based milestone payments from the alliance.

“We and Isis congratulate Regulus on forming this important new alliance with sanofi-aventis. Regulus stands as the leader in the emerging field of microRNA therapeutics, and this new partnership reflects the high level of interest across the pharmaceutical industry for innovative medicines based on this new biology,” said John Maraganore, Ph.D., Chief Executive Officer of Alnylam and Chairman of the Board of Regulus. “Regulus is also representative of Alnylam’s strategy to actively pursue new business opportunities across the broader dimensions of RNA biology and technology. In the case of the new partnership between Regulus and sanofi-aventis, the agreement will enable substantial funding for the advancement of microRNA therapeutics, while Alnylam maintains its significant ownership level to the benefit of our shareholders.”

“In Regulus, Isis and Alnylam have created a focused company that leverages the collective expertise and intellectual property of both companies in the exciting field of microRNA therapeutics. We believe that this approach provides Regulus with a clear and unmatched advantage in developing microRNA therapeutics, including the ability to form industry-leading partnerships that access capabilities and funding. Certainly, the newly formed relationship between Regulus and sanofi-aventis exemplifies the high pharmaceutical interest in microRNAs and Regulus’ leadership within that field,” said Stanley T. Crooke, M.D., Ph.D., Isis Pharmaceuticals Chairman and CEO and member of the Board of Directors of Regulus. “Not only have we created the leading microRNA company, but we are also able to share early in its successes and reap the benefits of our innovation. We believe that this type of deal brings significant value to our shareholders and further validates the strategy behind the unique business model that we have developed at Isis.”

Regulus entered into a global, strategic alliance with sanofi-aventis to discover, develop, and commercialize microRNA therapeutics. The alliance represents the largest microRNA partnership formed to date, valued at potentially over \$750 million, and includes a \$25 million upfront fee, a \$10 million future equity investment subject to mutual agreement on company valuation, and annual research support for three years with the option to extend two additional years. In addition, Regulus is eligible to receive royalties on microRNA therapeutic products commercialized by sanofi-aventis. Sanofi-aventis will support 100% of the costs of clinical development and commercialization of each program. The alliance will initially focus on the therapeutic area of fibrosis. Regulus and sanofi-aventis will collaborate on up to four microRNA targets, including Regulus’ lead fibrosis program targeting microRNA-21. sanofi-aventis also receives an option for a broader technology alliance that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this three-year option is worth up to an additional \$50 million to Regulus. Alnylam and Isis are each eligible to receive 7.5% of all potential milestone payments, in addition to royalties on product sales.

Alnylam Pharmaceuticals and Isis Pharmaceuticals formed Regulus in 2007, with each company currently owning approximately 50% of the preferred stock.

Conference Call Information

Regulus, Alnylam and Isis will hold a conference call to discuss Regulus’ alliance with sanofi-aventis on June 22, 2010 at 8:30 a.m. ET. To access the call, please dial 866-314-5050 (domestic) or 617-213-8051 (international) five minutes prior to the start time and provide the passcode 26980506. A replay of the call will be available beginning at 11:30 a.m. ET on June 22, 2010. To access the replay, please dial 888-286-8010 (domestic) or 617-801-6888 (international), and provide the passcode 97121953.

A live audio webcast of the call will also be available on the “Investors” section of Alnylam’s website, <http://www.alnylam.com> and Isis’ website, <http://www.isispharm.com>. An archived webcast will be available on the Alnylam and Isis website approximately two hours after the event.

About Alnylam Pharmaceuticals

Alnylam is a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. The company is applying its therapeutic expertise in RNAi to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Alnylam is leading the translation of RNAi as a new class of innovative medicines with peer-reviewed research efforts published in the world’s top scientific journals including *Nature*, *Nature Medicine*, and *Cell*. The company is leveraging these capabilities to build a broad pipeline of RNAi therapeutics for the treatment of a wide range of disease areas, including respiratory syncytial virus (RSV), liver cancers, TTR-mediated amyloidosis (ATTR), hypercholesterolemia, and Huntington’s disease. In addition, Alnylam formed Alnylam Biotherapeutics, a division of the company focused on the development of RNAi technologies for application in manufacturing processes for biotherapeutic products, including recombinant proteins and monoclonal antibodies. The company’s leadership position in fundamental patents, technology, and know-how relating to RNAi has enabled it to form major alliances with leading companies including Medtronic, Novartis, Biogen Idec, Roche, Takeda, Kyowa Hakko Kirin, and Cubist. Alnylam and Isis are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development, and commercialization of microRNA therapeutics. Founded in 2002, Alnylam maintains headquarters in Cambridge, Massachusetts. For more information, please visit <http://www.alnylam.com>.

About Isis Pharmaceuticals

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 Alnylam 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 <http://www.isispharm.com>.

Forward-Looking Statements

This press release includes forward-looking statements regarding the future therapeutic and commercial potential of Isis', Alnylam's and Regulus' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding expectations around the newly formed alliance between Regulus and sanofi-aventis, the therapeutic potential of targeting microRNA-21 and the potential for future payments to Isis and Alnylam under this alliance. Any statement describing Isis', Alnylam's or Regulus' 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. Such parties' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause their results to differ materially from those expressed or implied by such forward-looking statements. Although these forward-looking statements reflect the good faith judgment of the management of each such party, these statements are based only on facts and factors currently known by Isis, Alnylam or Regulus, as the case may be. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Regulus', Isis', and Alnylam's programs are described in additional detail in each of Isis' and Alnylam's annual report on Form 10-K for the year ended December 31, 2009 and their most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from either Isis or Alnylam.
