

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): **September 7, 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 September 7, 2007, Isis Pharmaceuticals, Inc. ("Isis") announced the launch of Regulus Therapeutics LLC, a joint venture with Alnylam Pharmaceuticals, Inc. focused on the discovery, development, and commercialization of microRNA (miRNA) therapeutics.

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

This report includes forward-looking statements regarding the future therapeutic and commercial potential of Isis' technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus. 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 this and other documents are available from the Company.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated September 7, 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: September 7, 2007

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

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Contacts

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Isis and Alnylam Launch Regulus Therapeutics, a Joint Venture to Discover, Develop, and Commercialize microRNA Therapeutics

- By Targeting Gene Pathways, microRNA Therapeutics Represent a New Approach for the Treatment of a Broad Range of Human Disease -

- David Baltimore to Join Regulus Board of Directors and Chair Scientific Advisory Board Comprised of Key Pioneers in microRNA Research -

- Companies to Host Conference Call Webcast to Discuss Regulus Therapeutics at 8:30 a.m. ET Friday -

CAMBRIDGE, Mass. and CARLSBAD, Calif., September 7, 2007 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today the launch of Regulus Therapeutics LLC, a joint venture focused on the discovery, development, and commercialization of microRNA (miRNA) therapeutics. Because miRNAs regulate whole networks of genes that can be involved in discrete disease processes, miRNA therapeutics represent a new approach to target the pathways of human disease. Regulus will combine the strengths and assets of Isis' and Alnylam's technologies, know-how, and intellectual property (IP) with strong leadership from a focused management team and Scientific Advisory Board to be chaired by Nobel laureate David Baltimore and include key pioneers in the miRNA field.

Both Isis and Alnylam will grant Regulus exclusive licenses to their IP for miRNA therapeutic applications, as well as certain early fundamental patents in the miRNA field including the "Tuschl III" patent. Alnylam will make an initial investment of \$10 million to balance venture ownership; thereafter Isis and Alnylam will share funding of Regulus. Regulus will be operated as an independent company with an independent Board of Directors and management team. Alnylam and Isis will retain rights to develop and commercialize on pre-negotiated terms miRNA therapeutic products that Regulus decides not to develop either itself or with a partner.

"The emerging biology of microRNAs points to a completely new understanding of cellular mechanisms for regulation of gene expression," said David Baltimore, Ph.D., of California Institute of Technology. "I believe that microRNAs represent previously unexplored disease

targets where pharmacological approaches could lead to the emergence of novel therapies for many human disorders. Accordingly, I'm very excited to join in the formation of Regulus and to help build the leading microRNA therapeutics company."

"The opportunity to antagonize microRNAs could create a new frontier for pharmaceutical research where an entire disease pathway is targeted for intervention, not just a single disease target. Indeed, due to their mechanism of action, we believe microRNA therapeutics could have profound implications for the treatment of a broad range of diseases including cancer, viral infection, and metabolic disorders," said John Maraganore, Ph.D., President and Chief Executive Officer of Alnylam. "Isis' and Alnylam's intellectual property and technologies open the door to these new opportunities and, when combined to form Regulus, create an unmatched effort to establish the leading microRNA therapeutics company."

"We are excited to embark on this venture, which represents an opportunity to invest in a focused expansion of our ongoing microRNA research efforts through Regulus' application of our antisense technology platform to create microRNA therapeutics. Indeed, it is timely to extend our know-how and clinical advances with antisense drugs to the field of microRNAs, an area that stands at the forefront of modern biology," said Stanley Croke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis. "Regulus will be fully enabled with intellectual property, technology, and funding from Isis and Alnylam to create a bold and successful new venture."

Regulus' newly formed Scientific Advisory Board will be chaired by David Baltimore, Ph.D., who will also serve as the first Regulus independent Director, and, subject to relevant institutional approvals, initially will comprise the following members:

- David Baltimore, Ph.D., Professor of Biology at California Institute of Technology and the recipient of the 1975 Nobel Prize in Physiology or Medicine;
- David Bartel, Ph.D., Professor of Biology at MIT and a member of the Whitehead Institute for Biomedical Research;
- Scott Hammond, Ph.D., Assistant Professor of Cell and Developmental Biology at the University of North Carolina School of Medicine;
- Markus Stoffel, M.D., Ph.D., Professor for Metabolic Diseases at the Institute of Molecular Systems Biology, Swiss Federal Institute of Technology (ETH);
- Thomas Tuschl, Ph.D., Associate Professor at the Rockefeller University; and
- Phillip D. Zamore, Ph.D., Gretchen Stone Cook Professor of Biomedical Sciences at the University of Massachusetts Medical School.

Conference Call Information

Alnylam and Isis will host a conference call on September 7, 2007 at 8:30 a.m. ET to discuss the formation and launch of Regulus Therapeutics. The call may be accessed by dialing 800-901-5231 (domestic) or 617-786-2961 (international) five minutes prior to the start time, and providing the passcode

44818346. A replay of the call will be available from 10:30 a.m. ET September 7, 2007 until September 13, 2007. To access the replay, please dial 888-286-8010 (domestic) or 617-801-6888 (international), and provide the passcode 11989900. A live audio webcast of the call will be available on Isis' website at www.isispharm.com and on the "Investors" section of the Alnylam's website, www.alnylam.com, and on Regulus' website at www.regulusrx.com. An archive of the webcast will be available on the both companies' websites approximately two hours after the event.

About microRNA

microRNAs (miRNAs) are a recently discovered class of genetically encoded small RNAs, approximately 20 nucleotides in length, and are believed to regulate the expression of a large number of human genes. miRNA therapeutics represent a new approach for the treatment of a broad range of human disease. When inappropriately encoded, miRNAs represent potential disease targets whose selective antagonism can result in the correction of an entire disease pathway in a manner unachievable by today's medicines. In fact, the inappropriate absence or presence of specific miRNA molecules in various cells has been shown to be associated with specific human diseases including cancer, viral infection, and metabolic disorders.

About Regulus

Regulus Therapeutics LLC is a biopharmaceutical company formed to discover, develop and commercialize miRNA therapeutics. The company was created as a joint venture between Alnylam Pharmaceuticals, a leader in RNAi therapeutics, and Isis Pharmaceuticals, a leader in antisense technologies and therapeutics. Isis and Alnylam scientists and collaborators were the first to discover miRNA antagonist strategies that work *in vivo* in animal studies (Krutzfeldt *et al.* (2005) *Nature* **438**, 685-689; Esau *et al.* (2006) *Cell Metab.*, **3**, 87-98). Isis and Alnylam have also created and consolidated key IP believed by the companies to be required for development and commercialization of miRNA therapeutics. The company, founded in 2007, maintains facilities in Carlsbad, California. For more information, visit www.regulusrx.com.

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; its most advanced program is in Phase II human clinical trials for the treatment of respiratory syncytial virus (RSV) infection. In addition, the company is developing RNAi therapeutics for the treatment of influenza, hypercholesterolemia, and liver cancers, amongst other diseases. 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 Merck, Medtronic, Novartis, Biogen Idec, and Roche. The company, founded in 2002, maintains headquarters in Cambridge, Massachusetts. For more information, visit 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 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.

Alnylam Forward-Looking Statements

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including statements concerning the potential of miRNA therapeutics and the importance of Alnylam's IP, know-how, and other technology in the discovery, development and commercialization of miRNA therapeutics, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including risks related to: Alnylam's approach to discover and develop novel drugs, which is unproven and may never lead to marketable products; Alnylam's ability to attract and retain highly qualified employees; obtaining, maintaining and protecting intellectual property utilized by Alnylam's products; Alnylam's ability to enforce its patents against infringers and to defend its patent portfolio against challenges from third parties; Alnylam's ability to obtain additional funding to support its business activities; Alnylam's dependence on third parties for development, manufacture, marketing, sales and distribution of products; the successful development of Alnylam's product candidates, all of which are in early stages of development; obtaining regulatory approval for products; competition from others using technology similar to Alnylam's and others developing products for similar uses; Alnylam's dependence on collaborators; and Alnylam's short operating history; as well as those risks more fully discussed in the "Risk Factors" section of its most recent quarterly report on Form 10-Q on file with the Securities and Exchange Commission. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam does not assume any obligation to update any forward-looking statements.

Isis Forward Looking Statements

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