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): **April 17, 2008**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(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:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o 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 April 17, 2008, Regulus Therapeutics LLC ("Regulus") and GlaxoSmithKline ("GSK") today announced a worldwide strategic alliance to discover, develop and market novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. Regulus is a joint venture between Isis Pharmaceuticals, Inc. and Alnylam Pharmaceuticals, Inc.

Regulus 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 April 17, 2008.

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: April 17, 2008

By: /s/ B. Lynne Parshall

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

INDEX TO EXHIBITS

99.1	Press Release dated April 17, 2008.

GlaxoSmithKline and Regulus Therapeutics Form Strategic Alliance
To Develop MicroRNA Targeted Therapeutics to Treat Inflammatory Diseases

- Companies Announce Significant microRNA Therapeutics Collaboration

Issued – April 17, 2008 , London UK, Philadelphia, PA and Carlsbad, CA GlaxoSmithKline (GSK) and Regulus Therapeutics LLC (Regulus) today announced a worldwide strategic alliance to discover, develop and market novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. Regulus is a joint venture between Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS).

The alliance leverages Regulus' unique expertise and intellectual property position in the discovery and development of microRNA-targeted therapeutics and provides GSK with an option to license product candidates directed at four different microRNA targets with relevance in inflammatory disease. Regulus will be responsible for the discovery and development of the microRNA antagonists through completion of clinical proof of concept, unless GSK chooses to exercise its option earlier. After exercise of the option, GSK will have an exclusive license to drugs developed under each program by Regulus for the relevant microRNA target for further development and commercialization on a worldwide basis. Regulus will have the right to further develop and commercialize any microRNA therapeutics which GSK chooses not to develop or commercialize.

Regulus will receive $20 million in upfront payments from GSK, including a $15 million option fee and a $5 million note (guaranteed by Isis and Alnylam) that will convert into Regulus common stock in the future under certain specified circumstances. Regulus could also be eligible to receive up to $144.5 million in development, regulatory and sales milestone payments for each of the four microRNA-targeted therapeutics discovered and developed as part of the alliance. In addition to the potential of nearly $600 million Regulus could receive in option, license and milestone payments, Regulus

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would also receive tiered royalties up to double digits on worldwide sales of products resulting from the alliance.

"We are focused on finding innovative medicines through both internal efforts and by 'virtualizing' a portion of the inflammatory diseases pipeline. We are very excited to be working with Regulus and exploring the therapeutic opportunities in inflammation offered by targeting microRNAs, an exciting new area of biology," said Jose Carlos Gutierrez-Ramos, Ph.D., Senior Vice President and head of the Immuno-Inflammation Center of Excellence for Drug Discovery of GSK. "When associated with an aberrant inflammatory response, microRNAs represent disease targets whose therapeutic modulation could revolutionize the way we treat immune diseases and provide benefits not readily achievable with today's medicines."

"GSK is an outstanding partner for Regulus, and we look forward to expanding our efforts in inflammation where a new class of therapeutics could offer novel options to treat disease," said Kleanthis G. Xanthopoulos, Ph.D., President and Chief Executive Officer of Regulus. "microRNA therapeutics represent an exciting new frontier for pharmaceutical research, opening many opportunities including those present in inflammation and immune diseases. As a leading microRNA therapeutics company, Regulus has the expertise and access to proprietary antisense technologies, which provide the tools and potential to quickly move therapeutic programs toward the clinic. Through its relationship with Alnylam and Isis, Regulus also has a vast patent estate in microRNAs."

About microRNAs

microRNAs 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. microRNA therapeutics represent a new approach for the treatment of a wide range of human diseases. The inappropriate absence or presence of specific microRNAs in various cells has been shown to be associated with specific human diseases including cancer, viral infection, and metabolic disorders. Targeting

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microRNAs with novel therapeutic agents could result in high-impact and broadly acting treatments for human diseases.

About Regulus Therapeutics LLC

Regulus is a biopharmaceutical company formed to discover, develop and commercialize microRNA therapeutics. Regulus was founded in late 2007 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 microRNA antagonist strategies that work *in vivo* in animal studies (Krutzfeldt *et al. Nature* **438**, 685-689 (2005); Esau *et al. Cell Metab*., **3**, 87-98 (2006)). Isis and Alnylam have also created and consolidated key intellectual property for the development and commercialization of microRNA therapeutics. Regulus maintains facilities in Carlsbad, California. For more information, visit www.regulusrx.com.

About Alnylam Pharmaceuticals, Inc.

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, among 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 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, 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 19 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Ibis Biosciences, Inc., Isis' majority-owned subsidiary, is developing and commercializing the Ibis T5000™ Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. 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/Isis 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 relationship between Regulus and GSK. 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, including those statements that are described as such parties' 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. Such parties' 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 these forward-looking statements reflect the good faith judgment of the management of each such party,

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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 Isis', Alnylam's and Regulus' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2007 and in Alnylam's annual report on Form 10-K for the year ended December 31, 2007, which are on file with the SEC. Copies of this and other documents are available from Isis, Alnylam or Regulus.

About GlaxoSmithKline

GlaxoSmithKline – one of the world's leading research-based pharmaceutical and healthcare companies – is committed to improving the quality of human life by enabling people to do more, feel better and live longer.

About the II CEDD

The Immuno-Inflammation Centre of Excellence for Drug Discovery is dedicated to discovering therapies for inflammatory diseases such as rheumatoid arthritis, inflammatory bowel disease and psoriasis. It is designed to integrate and better coordinate the progression of inflammatory disease medicines from therapeutic hypothesis to clinical proof of concept. It focuses on building an innovative pipeline through both internal efforts and external alliances with other companies and research institutions and will focus on 'virtualizing' a portion of the inflammatory diseases pipeline by forming multiple risk-sharing/reward-sharing alliances.

GlaxoSmithKline Contacts:

UK Media:
Gwenan White (020) 8047 5502
Philip Thomson (020) 8047 5502

US Media:
Nancy Pekarek (215) 751 7709

European Analyst/Investor enquiries:
David Mawdsley (020) 8047 5564
Sally Ferguson (020) 8047 5543

Regulus Therapeutics Contacts:

info@regulusrx.com

Cynthia Clayton (Investors)
Alnylam Pharmaceuticals
617-551-8207

US Analyst/ Investor enquiries:
Frank Murdolo (215) 751 7002
Tom Curry (215) 751 5419

Amy Blackley, Ph.D. (Media)
Isis Pharmaceuticals
760-603-2772