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): **February 25, 2010**

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.

HCV Collaboration between Regulus and GSK

On February 25, 2010, Regulus Therapeutics Inc. announced the establishment of a new collaboration with GlaxoSmithKline (GSK) to develop and commercialize microRNA therapeutics targeting microRNA-122 in all fields with Hepatitis C Viral infection (HCV) as the lead indication. Under the terms of the new collaboration, Regulus will receive additional upfront and early-stage milestone payments with the potential to earn more than $150 million in miR-122-related combined payments, and tiered royalties up to double digits on worldwide sales of products.

The collaboration provides GSK with access to Regulus' comprehensive and robust intellectual property estate. Regulus exclusively controls patent rights covering miR-122 antagonists and their use as HCV therapeutics in the United States, Europe, and Japan, including but not limited to the patent families which encompass: the 'Sarnow' patent pertaining to the method of use of anti-miR-122 to inhibit HCV replication, the 'Esau' patent application claiming the use of anti-miRs targeting miR-122 as inhibitory agents, the 'Tuschl III' patent claiming composition of matter for miR-122 and complementary oligonucleotides, and the 'Manoharan' patent claiming antagomirs, including antagomirs targeting miR-122.

Under the terms of the HCV collaboration, Regulus will receive $8 million from GSK, including a $3 million license 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. In addition, Regulus is eligible to receive several near-term significant payments associated with the advancement of an HCV drug, plus additional milestones payments and double-digit royalties consistent with the existing immuno-inflammatory diseases alliance terms. The original immuno-inflammatory diseases alliance was initiated in April 2008 and included a $20 million upfront payment from GSK to Regulus, including a $15 million option fee and a $5 million convertible promissory note, plus up to $144.5 million in discovery, development, regulatory and sales milestone payments for each of the four microRNA-targeted therapeutics discovered and developed by Regulus as part of the alliance. Last year, Regulus achieved the first milestone from the immuno-inflammatory alliance. Because GSK has selected Regulus' miR-122 for the new collaboration, the number of immuno-inflammatory programs GSK has an option to license under the 2008 immuno-inflammatory alliance has been reduced from four to three.

As part of the HCV collaboration, Regulus granted GSK a limited license to develop and commercialize the miR-122 antagonist SPC 3649, if GSK acquires rights to this compound. Regulus will receive development and regulatory milestones as well as royalties if GSK develops and commercializes SPC 3649.

Regulus is a company founded and jointly owned by Isis Pharmaceuticals, Inc. and Alnylam Pharmaceuticals, Inc.

New Accounting Standard Related to Regulus

Beginning in the first quarter of 2010, as a result of a new accounting standard, Isis will no longer include Regulus' revenue and operating expenses in its operating results. Instead Isis will include its share of Regulus' operating results on a separate line in the other income section of its Statement of Operations called "Equity in loss of Regulus Therapeutics Inc." On the balance sheet, Isis will present its share of Regulus' net assets on a separate line in the non-current assets section called "Investment in Regulus Therapeutics Inc.," which means that Isis will no longer include Regulus' cash in its cash balance.

Forward-Looking Statements

This report includes forward-looking statements regarding the future therapeutic and commercial potential of Regulus', Alnylam's, and Isis' business plans, technologies and intellectual property related to microRNA therapeutics being discovered and developed by Regulus, including statements regarding expectations around the relationship between GSK and Regulus. Any statement describing Regulus', Alnylam's, and 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 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 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 Regulus', Alnylam's, and Isis' management 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', Alnylam's, and Isis' programs are described in additional detail in Alnylam's and Isis' annual reports on Form 10-K for the year ended December 31, 2008, and their most recent quarterly reports on Form 10-Q which are on file with the SEC. Copies of these and other documents are available from Alnylam or Isis.

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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: February 25, 2010

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Chief Operating Officer,
Chief Financial Officer and Director