

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): **November 15, 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 October 15, 2008, Isis Pharmaceuticals, Inc. ("Isis") and RBS Asset Finance, Inc. ("RBS") originally entered into a Loan Agreement related to an equipment financing. On November 15, 2010 Isis and RBS amended the Loan Agreement to extend the time Isis has to draw funding under the agreement through July 27, 2011 (such agreement, as amended, the "Loan Agreement").

On November 15, 2010, Isis drew approximately \$1.6 million in additional principal under the Loan Agreement, bringing the total amount of principal borrowed by Isis under the Loan Agreement to \$16.7 million.

Under the Loan Agreement, Isis may borrow up to \$18.4 million in principal to finance the purchase of equipment. Each loan under the Loan Agreement will have a term of approximately 3 years, with principal and interest payable monthly. Interest on amounts Isis borrows under the Loan Agreement will be calculated based upon the 3 year interest rate swap at the time of each loan plus 4%. As collateral, RBS will have a security interest in the equipment purchased under the Loan Agreement.

Under the Loan Agreement, each of the following events are events of default, which may result in acceleration of the amounts payable under the Loan Agreement:

- Isis fails to timely pay amounts due under the Loan Agreement;
- Isis fails to perform or observe its material obligations under the Loan Agreement or another agreement with RBS, and such failure continues after a reasonable notice and cure period;
- Isis defaults under any of its other debt having a principal amount in excess of \$10 million;
- Isis fails to pay a judgment or order to pay money that is excess of \$10 million, unless covered by Isis' insurance or under appeal by Isis;
- The occurrence of a change of control of Isis, where the acquiring entity does not satisfy specified minimum credit criteria; or
- Isis becomes insolvent or enters bankruptcy proceedings.

Isis' jointly owned subsidiary, Regulus Therapeutics Inc. ("Regulus") has a separate \$1 million equipment financing agreement with RBS on the same terms as the Loan Agreement. Isis has guaranteed Regulus' repayment obligations under this agreement.

Item 2.03. Creation of a Direct Financial Obligation or an Obligation under an Off-Balance Sheet Arrangement of a Registrant.

Reference is made to the disclosures set forth in Item 1.01 above, and are incorporated herein by reference.

In this report, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals.

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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: November 15, 2010

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL

Chief Financial Officer and Chief Operating Officer

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