

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K/A

(Amendment No. 2)

CURRENT REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): **October 15, 2008;**
amended March 27, 2009; and
amended September 30, 2009

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") entered into a Loan Agreement related to an equipment financing, and on September 30, 2009 Isis and RBS amended the Loan Agreement to increase the aggregate maximum amount of principal Isis can draw under the agreement (such agreement, as amended, the "Loan Agreement"). Under the Loan Agreement, Isis and its subsidiaries may borrow up to \$19.4 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.

In October 2008, Isis initially drew approximately \$7.2 million in principal under the Loan Agreement.

On March 27, 2009, Isis drew approximately \$2.7 million in additional principal under the Loan Agreement.

On September 30, 2009, Isis drew approximately \$3.7 million in additional principal 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.

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 and its subsidiaries.

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2

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: October 1, 2009

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL

Chief Operating Officer,

Chief Financial Officer and Director

3
