
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): **October 17, 2007 (October 14, 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))
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Item 1.01. Entry into a Material Definitive Agreement.

On October 14, 2007, Isis Pharmaceuticals, Inc. ("Isis") and Drug Royalty Trust 3, successor-in-interest to Drug Royalty USA, Inc., ("DRT 3") agreed to resolve their disputes regarding various alleged competing breaches of their Agreement for Sale and Assignment of Rights ("Agreement") dated December 21, 2004. Isis received a total of \$8 million as the final purchase price installment which was due under the Agreement on October 15, 2007; DRT 3 paid Isis \$7 million on that date subject to the terms of an Amendment to the Agreement and an unaffiliated third party paid Isis \$1 million on that date. This full and final settlement of the dispute did not constitute an admission of any liability by either Isis or DRT 3 but is rather a compromise of disputed claims.

As part of the settlement, Isis and DRT 3 amended the Agreement to reflect the adjustment to the final purchase price installment. Isis has filed a copy of the amendment as an exhibit to this Report, the terms of which are incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

10.1 Amendment No. 1 to Sale Agreement dated October 14, 2007 between Isis and DRT 3.

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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: October 15, 2007

By: /s/ B. Lynne Parshall

INDEX TO EXHIBITS

10.1 Amendment No. 1 to Sale Agreement dated October 14, 2007 between Isis and DRT 3.

AMENDMENT NO. 1 TO SALE AGREEMENT

This Amendment No. 1 (the "Amendment to Sale Agreement") to the Agreement for Sale and Assignment of Rights, dated as of December 21, 2004, by and between ISIS Pharmaceuticals, Inc. ("ISIS") and Drug Royalty USA, Inc., ("DRC") (the "Sale Agreement") is entered into as of October 14, 2007 (the "Effective Date"), by and between ISIS and Drug Royalty Trust 3, a statutory trust formed under the Delaware Statutory Trust Act, as successor-in-interest to DRC ("DRT"). Except as expressly set forth herein, all capitalized terms shall have the meaning set forth in the Sale Agreement.

RECITALS

WHEREAS, as a result of a dispute that arose between the Parties, the Parties now desire to amend the Sale Agreement as set forth in this Amendment No. 1 to Sale Agreement in full and final settlement of such dispute.

NOW THEREFORE, DRT and ISIS hereby agree to amend the Sale Agreement as follows:

1. Delete Section 1.2(a)(iii) and insert in its place the following:

"(iii) seven million US dollars (US\$7,000,000) due and payable on October 15, 2007 ("**Third Payment Date**")."

Except as expressly amended and supplemented hereby, all other terms of the Sale Agreement shall remain in full force and effect except that this \$7,000,000 payment shall not be subject to and/or contingent upon ISIS fulfilling its obligation to bring the Opposition Prior Art to the attention of the European Patent Office as required by the terms of the Sale Agreement.

IN WITNESS WHEREOF, the parties hereto have caused this Amendment No. 1 to Sale Agreement to be executed in duplicate by their duly authorized representatives.

ISIS PHARMACEUTICALS, INC.

DRUG ROYALTY CORPORATION, INC,
AS MANAGER OF DRUG ROYALTY
TRUST 3

BY: /s/ B. Lynne Parshall

BY: /s/ Behzad Khosrowshahi

NAME: B. Lynne Parshall

NAME: Behzad Khosrowshahi

TITLE: EVP & CFO

TITLE: President & CFO