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 26, 2014

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.)

2855 Gazelle Court Carlsbad, CA 92010

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

On November 26, 2014, Isis Pharmaceuticals, Inc. (the "Company") issued \$15.0 million aggregate principal amount of the Company's 1.00% Convertible Senior Notes due 2021 (the "Option Notes") to J.P. Morgan Securities LLC, Stifel, Nicolaus & Company, Incorporated and BMO Capital Markets Corp. (collectively, the "Initial Purchasers") in connection with the final exercise of the Initial Purchasers' option to purchase additional notes solely to cover over-allotments. The Option Notes, together with the \$485.0 million aggregate principal amount of the Company's 1.00% Convertible Senior Notes due 2021 that were previously issued (collectively, the "Notes"), were issued in connection with a private offering (the "Note Offering") to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended, and were issued pursuant to the Indenture dated as of November 17, 2014 by and between the Company and Wells Fargo Bank, National Association, as trustee. The Company estimates the aggregate net proceeds it will receive from the Note Offering will be approximately \$487.0 million, after deducting the Initial Purchasers' discount and estimated offering expenses payable by the Company.

The information set forth in Item 1.01 of the Company's Current Report on Form 8-K filed November 21, 2014 is hereby incorporated by reference.

Item 3.02. Unregistered Sales of Equity Securities.

The information set forth in Item 2.03 of this Current Report on Form 8-K and in Item 1.01 of the Company's Current Report on Form 8-K filed November 21, 2014 is hereby incorporated by reference.

Item 9.01. Financial Statements and Exhibits.

- (d) Exhibits.
 - 4.1 Indenture dated as of November 17, 2014 by and between Isis Pharmaceuticals, Inc. and Wells Fargo Bank, National Association, as trustee (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed November 21, 2014).
 - 4.2 Form of 1.00% Convertible Senior Note due 2021 (incorporated by reference to Exhibit 4.2 to the Company's Current Report on Form 8-K filed November 21, 2014).

Forward-Looking Statements

This Current Report on Form 8-K includes forward-looking statements regarding the Company's financing plans, including statements related to the Note Offering and the Company's intended use of net proceeds of the Note Offering. Such statements are subject to certain risks and uncertainties including, without limitation, risks related to the fact that the Company's management will have broad discretion in the use of the proceeds from the remainder of the net proceeds from the Note Offering (after giving effect to the repurchase of the 2 ¾% Convertible Senior Notes due 2019). The Company's 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 the Company's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by the Company. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning the Company's programs are described in additional detail in the Company's annual report on Form 10-K for the year ended December 31, 2013 and its most recent quarterly report on Form 10-Q for the quarter ended September 30, 2014, which are on file with the Securities and Exchange Commission.

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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: December 3, 2014

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL

Senior Vice President, Legal and
General Counsel

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