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 10, 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)
- 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.

The information set forth in Item 8.01 of this Current Report on Form 8-K is incorporated herein by reference.

Item 3.02. Unregistered Sales of Equity Securities.

The information set forth in Item 8.01 of this Current Report on Form 8-K is incorporated herein by reference.

Item 8.01. Other Events.

On November 11, 2014, Isis Pharmaceuticals, Inc. (the "Company") entered into a purchase agreement (the "Purchase Agreement") with J.P. Morgan Securities LLC, Stifel, Nicolaus & Company Incorporated and BMO Capital Markets Corp., as representatives (the "Representatives") of the several initial purchasers listed in Schedule I thereto (collectively, the "Initial Purchasers"), relating to the sale by the Company of \$425.0 million aggregate principal amount of the Company's 1.00% Convertible Senior Notes due 2021 in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended (the "Securities Act"). The Company expects this offering (the "Note Offering") to close on November 17, 2014, subject to the satisfaction of customary closing conditions. In addition, under the terms of the Purchase Agreement, the Company granted the Initial Purchasers a 30-day option to purchase up to an additional \$75.0 million aggregate principal amount of 1.00% Convertible Senior Notes due 2021, solely to cover overallotments, if any.

The Company estimates the net proceeds it will receive from the Note Offering will be approximately \$413.9 million (or approximately \$487.0 million if the Initial Purchasers exercise their option to purchase additional notes in full), after deducting the Initial Purchasers' discount and estimated offering expenses payable by the Company. All of the net proceeds of the Note Offering will be applied toward the repurchase of the Company's 2 ¾% Convertible Senior Notes due 2019 (the "2019 Notes"). Concurrently with the Note Offering, the Company is repurchasing approximately \$140.0 million principal amount of 2019 Notes through individually negotiated transactions with holders of such 2019 Notes. These repurchases could have the effect of raising or maintaining the market price of the Company's common stock above levels that would otherwise have prevailed, or preventing or retarding a decline in the market price of its common stock. If the Initial Purchasers exercise their over-allotment option in full following the Note Offering, the Company intends to use the net proceeds from any such exercise to develop select drugs in its pipeline to later stages of development prior to partnering, to further develop and potentially commercialize the drugs in its lipid franchise, and for general corporate and working capital purposes. Until any such net

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The Notes will be general unsecured senior obligations of the Company and will bear interest at a fixed rate of 1.00% per year, payable semiannually in arrears on May 15 and November 15 of each year, beginning on May 15, 2015. The Notes will be convertible under certain circumstances prior to the close of business on the business day immediately preceding July 1, 2021, and will be convertible on or after July 1, 2021 irrespective of these conditions. The Company will settle conversions of the Notes by paying or delivering, as the case may be, cash, shares of its common stock or a combination of cash and shares of its common stock, at its election. The conversion rate will initially be 14.9685 shares of common stock per \$1,000 principal amount of Notes (equivalent to an initial conversion price of approximately \$66.81 per share of common stock). The conversion rate and the corresponding conversion price will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, the Company will increase the conversion rate for a holder who elects to convert its Notes in connection with such a corporate event in certain circumstances. The Company may not redeem the Notes prior to maturity, and no sinking fund is provided for the Notes. If the Company undergoes a fundamental change (as defined in the indenture relating to the Notes), holders may require the Company to purchase for cash all or any portion of their Notes at a purchase price equal to 100% of the principal amount of the Notes to be purchased, plus accrued and unpaid interest to, but excluding, the fundamental change purchase date. The Notes will mature on November 15, 2021, unless earlier converted or purchased.

For a period of 90 days from November 11, 2014, neither the Company nor any of its directors or executive officers will, without the prior consent of the Representatives, subject to limited exceptions (including but not limited to sales under existing Rule 10b5-1 trading plans), offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of any shares of the Company's common stock, or any securities convertible into, or exercisable or exchangeable for or that represent the right to receive shares of the Company's common stock, or enter into any swap or other agreement that transfers any of the economic consequences of ownership of the Company's common stock or any such other securities.

On November 10, 2014, the Company issued a press release titled "Isis Pharmaceuticals Announces Proposed Offering of \$425 Million of Convertible Senior Notes" (the "Launch Press Release") announcing the launch of the Note Offering. A copy of the Launch Press Release is attached hereto as Exhibit 99.1 and incorporated by reference herein.

On November 12, 2014, the Company issued another press release titled "Isis Pharmaceuticals Prices Offering of \$425 Million of 1.00% Convertible Senior Notes" (the "Pricing Press Release") announcing the pricing of the Note Offering. A copy of the Pricing Press Release is attached hereto as Exhibit 99.2 and incorporated by reference herein.

This Current Report on Form 8-K does not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall it constitute an offer to sell, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful. Any offers of the securities would be made only by means of a confidential offering memorandum. These securities have not been registered under the Securities Act or any state securities laws and, unless so registered, may not be offered or sold in the United States or to U.S. persons except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and applicable state laws.

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Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Launch Press Release dated November 10, 2014.

99.2 Pricing Press Release dated November 12, 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 market and other general economic conditions, whether the Company will be able to satisfy the conditions required to close any sale of the Notes, the fact that the Company's management will have broad discretion in the use of the proceeds from any sale of the Notes and the Company's ability to successfully repurchase its 2019 Notes. 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: November 13, 2014 By: /s/ Elizabeth L. Hougen

ELIZABETH L. HOUGEN
Senior Vice President, Finance and

Chief Financial Officer

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INDEX TO EXHIBITS

99.1	Launch Press Release dated November 10, 2014.
99.2	Pricing Press Release dated November 12, 2014.

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ISIS PHARMACEUTICALS ANNOUNCES PROPOSED OFFERING OF \$425 MILLION OF CONVERTIBLE SENIOR NOTES

CARLSBAD, Calif., November 10, 2014 — Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it intends to offer, subject to market and other considerations, \$425.0 million aggregate principal amount of Convertible Senior Notes due 2021 (the "Convertible Notes") in a private placement. Isis also intends to grant to the initial purchasers of the Convertible Notes a 30-day option to purchase up to an additional \$63.75 million aggregate principal amount of the Convertible Notes, solely to cover over-allotments, if any.

Concurrently with this offering, Isis intends to use a portion of the net proceeds of the offering to repurchase up to \$140.0 million principal amount of its outstanding 23% Convertible Senior Notes due 2019 (the "2019 Notes") through individually negotiated transactions with holders of such 2019 Notes. Any repurchase of the 2019 Notes could have the effect of raising or maintaining the market price of Isis' common stock above levels that would otherwise have prevailed or preventing or retarding a decline in the market price of its common stock. In addition, following this offering, Isis intends to use the remainder of the net proceeds to develop select drugs in its pipeline to later stages of development prior to partnering, to further develop and potentially commercialize the drugs in its lipid franchise and for general corporate and working capital purposes.

The Convertible Notes will be general unsecured senior obligations of Isis and will accrue interest payable semiannually in arrears. The Convertible Notes will be convertible under certain circumstances, and Isis will settle conversions of the Convertible Notes by paying or delivering, as the case may be, cash, shares of its common stock or a combination of cash and shares of its common stock, at its election. The interest rate, conversion rate and other terms of the Convertible Notes will be determined at the time of pricing of the offering.

The offering is being made only to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended. Neither the Convertible Notes nor any shares of Isis' common stock issuable upon conversion of the Convertible Notes have been or are expected to be registered under the Securities Act or under any state securities laws and, unless so registered, may not be offered or sold in the United States or to U.S. persons except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and applicable state securities laws. This press release does not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall it constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale is unlawful.

This press release includes forward-looking statements regarding Isis' financing plans, including statements related to Isis' offering of the Convertible Notes and the intended use of net proceeds of the offering. Such statements are subject to certain risks and uncertainties including, without limitation, risks related to whether Isis will consummate the offering of the Convertible Notes on the expected terms, or at all, market and other general economic conditions, whether Isis will be able to satisfy the conditions required to close any sale of the Convertible Notes, the fact that Isis' management will have broad discretion in the use of the proceeds from any sale of the Convertible Notes and Isis' ability to successfully repurchase any of its 2019 Notes on acceptable terms, or at all. Isis' 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 Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2013 and its most recent quarterly report on Form 10-Q, which are on file with the SEC.

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc.

Isis Pharmaceuticals' Contacts:

D. Wade Walke, Ph.D. Executive Director, Corporate Communications and Investor Relations 760-603-2741 Amy Blackley, Ph.D. Associate Director, Corporate Communications 760-603-2772

ISIS PHARMACEUTICALS PRICES OFFERING OF \$425 MILLION OF 1.00% CONVERTIBLE SENIOR NOTES

CARLSBAD, Calif., November 12, 2014 — Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the pricing of its offering of \$425.0 million aggregate principal amount of Convertible Senior Notes due 2021 (the "Convertible Notes") in a private placement. Isis also granted the initial purchasers of the Convertible Notes a 30-day option to purchase up to an additional \$75.0 million aggregate principal amount of the Convertible Notes, solely to cover over-allotments, if any. The sale of the Convertible Notes is expected to close on November 17, 2014, subject to customary closing conditions.

Isis expects that the net proceeds from this offering will be approximately \$413.9 million (or approximately \$487.0 million if the initial purchasers exercise their over-allotment option in full), after deducting discounts to the initial purchasers and estimated offering expenses payable by Isis. All of the net proceeds of the offering will be applied toward the repurchase of Isis' 2¾% Convertible Senior Notes due 2019 (the "2019 Notes"). Concurrently with this offering, Isis is repurchasing approximately \$140.0 million principal amounts of the 2019 Notes through individually negotiated transactions with holders of such 2019 Notes. These repurchases could have the effect of raising or maintaining the market price of Isis' common stock above levels that would otherwise have prevailed or preventing or retarding a decline in the market price of its common stock.

If the initial purchasers exercise their over-allotment option in full, following this offering, Isis intends to use the net proceeds from any such exercise to develop select drugs in its pipeline to later stages of development prior to partnering, to further develop and potentially commercialize the drugs in its lipid franchise and for general corporate and working capital purposes.

The Convertible Notes will bear interest at a fixed rate of 1.00% per year, payable semiannually in arrears on May 15 and November 15 of each year, beginning on May 15, 2015. The Convertible Notes will mature on November 15, 2021, unless earlier purchased or converted.

The Convertible Notes are convertible, at the option of the holders at any time prior to the close of business on the business day immediately preceding July 1, 2021 only under satisfaction of specified conditions and during specified periods. On or after July 1, 2021 until the close of business on the second scheduled trading day preceding the maturity date, holders may convert their Convertible Notes at their option at the conversion rate then in effect at any time irrespective of these conditions. Isis will settle conversions of the Convertible Notes by paying or delivering, as the case may be, cash, shares of its common stock or a combination of cash and shares of its common stock, at its election.

The conversion rate will initially be 14.9685 shares of common stock per \$1,000 principal amount of Convertible Notes (equivalent to an initial conversion price of approximately \$66.81 per share of common stock). The conversion rate and the corresponding conversion price will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, Isis will increase the conversion rate for a holder who elects to convert its Convertible Notes in connection with such a corporate event in certain circumstances.

The Convertible Notes will not be redeemable prior to maturity. If Isis undergoes a fundamental change (as defined in the indenture relating to the Convertible Notes), holders may require Isis to purchase for cash all or part of their Convertible Notes at a purchase price equal to 100% of the principal amount of the Convertible Notes to be purchased, plus accrued and unpaid interest to, but excluding, the fundamental change purchase date.

The offering is being made only to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended (the "Securities Act"). Neither the Convertible Notes nor any shares of Isis' common stock issuable upon conversion of the Convertible Notes have been or are expected to be registered under the Securities Act or under any state securities laws and, unless so registered, may not be offered or sold in the United States or to U.S. persons except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and applicable state securities laws. This press release does not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall it constitute an offer, solicitation or sale in any jurisdiction in which such offer, solicitation or sale is unlawful.

This press release includes forward-looking statements regarding Isis' financing plans, including statements related to Isis' offering of the Convertible Notes and the intended use of net proceeds of the offering. Such statements are subject to certain risks and uncertainties including, without limitation, risks related to market and other general economic conditions, whether Isis will be able to satisfy the conditions required to close any sale of the Convertible Notes, the fact that Isis' management will have broad discretion in the use of the proceeds from any sale of the Convertible Notes and Isis' ability to complete the repurchase of any of its 2019 Notes. Isis' 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 Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2013 and its most recent quarterly report on Form 10-Q, which are on file with the Securities and Exchange Commission.

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