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Press Release

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Isis Pharmaceuticals Prices Offering of \$425 Million of 1.00% Convertible Senior Notes

CARLSBAD, Calif., Nov. 12, 2014 /PRNewswire/ -- 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' 2% 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.

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

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