

# 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): **May 8, 2013**

## 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)
- 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 8.01. Other Events.

On May 8, 2013, we entered into an underwriting agreement (the "Underwriting Agreement") with Goldman, Sachs & Co. and J.P. Morgan Securities LLC as representatives of the several underwriters (collectively, the "Underwriters"), relating to the issuance and sale of 9,000,000 shares of our common stock, par value \$0.001 per share. The price to the public in this offering is \$19.00 per share, and the Underwriters have agreed to purchase the shares from us pursuant to the Underwriting Agreement at a price of \$18.05 per share. The net proceeds to us from this offering are expected to be approximately \$162.1 million, after deducting underwriting discounts and commissions but before deducting other estimated offering expenses. The offering is expected to close on or about May 14, 2013, subject to customary closing conditions. In addition, under the terms of the Underwriting Agreement, we have granted the Underwriters an option, exercisable for 30 days, to purchase up to an additional 1,350,000 shares of common stock.

The Underwriting Agreement contains customary representations, warranties and agreements by us, customary conditions to closing, indemnification obligations of Isis and the Underwriters, including for liabilities under the Securities Act of 1933, as amended, other obligations of the parties and termination provisions. The representations, warranties and covenants contained in the Underwriting Agreement were made only for purposes of such agreement and as of specific dates, were solely for the benefit of the parties to such agreement, and may be subject to limitations agreed upon by the contracting parties.

The offering is being made pursuant to our effective registration statement on Form S-3ASR (Registration Statement No. 333-188407) previously filed with the Securities and Exchange Commission and a prospectus supplement thereunder. The Underwriting Agreement is filed as Exhibit 1.1 to this report, and the description of the terms of the Underwriting Agreement is qualified in its entirety by reference to such exhibit. A copy of the opinion of Patrick R. O'Neil relating to the legality of the issuance and sale of the shares in the offering is attached as Exhibit 5.1 hereto.

On May 7, 2013, we issued a press release announcing that we had commenced the offering. On May 8, 2013, we issued a press release announcing that we had priced the offering. Copies of these press releases are attached as Exhibits 99.1 and 99.2 hereto, respectively.

#### Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

- 1.1 Underwriting Agreement, dated May 8, 2013.
- 5.1 Opinion of Patrick R. O'Neil.

23.1	Consent of Patrick R. O'Neil (included in Exhibit 5.1).
99.1	Press Release, dated May 7, 2013, titled "Isis Pharmaceuticals Announces Proposed Public Offering of Common Stock."
99.2	Press Release, dated May 8, 2013, titled "Isis Pharmaceuticals Prices Public Offering of Common Stock."

## FORWARD-LOOKING STATEMENTS

This report includes forward-looking statements regarding Isis' financing plans, including statements related to Isis' offering of common stock and intended use of net proceeds of the offering. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. 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, 2012 and Isis' quarterly report on Form 10-Q for the quarter ended March 31, 2013, which are on file with the SEC. Copies of these and other documents are available from the Company.

## 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: May 9, 2013

By: /s/ B. Lynne Parshall  
**B. LYNNE PARSHALL**  
Chief Operating Officer

## INDEX TO EXHIBITS

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## Isis Pharmaceuticals, Inc.

9,000,000 shares of common stock, par value \$0.001 per share

Underwriting Agreement

May 8, 2013

Goldman, Sachs & Co.,  
 J.P. Morgan Securities LLC  
 As representatives of the several Underwriters  
 named in Schedule I hereto,

c/o Goldman, Sachs & Co.  
 200 West Street  
 New York, New York 10282

c/o J.P. Morgan Securities LLC  
 383 Madison Avenue  
 New York, New York 10179

Ladies and Gentlemen:

Isis Pharmaceuticals, Inc., a Delaware corporation (the "Company"), proposes, subject to the terms and conditions stated herein, to issue and sell to the Underwriters named in Schedule I hereto (the "Underwriters"), for whom you are acting as representatives (the "Representatives"), an aggregate of 9,000,000 shares (the "Firm Securities"), and at the election of the Representatives, up to an aggregate of 1,350,000 additional shares (the "Optional Securities") of common stock of the Company, par value \$0.001 per share ("Stock"). The Firm Securities and the Optional Securities that the Underwriters elect to purchase pursuant to Section 2 hereof are herein collectively called the "Securities". For purposes of this Agreement, a "subsidiary" of the Company will mean any entity the financial statements of which are consolidated with the financial statements of the Company in accordance with generally accepted accounting principles in the United States from time to time ("U.S. GAAP").

1. The Company represents and warrants to, and agrees with, each of the Underwriters that:

- (a) An "automatic shelf registration statement" as defined under Rule 405 under the Securities Act of 1933, as amended (the "Act") on Form S-3 (File No. 333-188407) in respect of the Securities has been filed with the Securities and Exchange Commission (the "Commission") not earlier than three years prior to the date hereof; such registration statement, and any post-effective amendment thereto, became effective on filing; and no stop order suspending the effectiveness of such registration statement or any part thereof has been issued and no proceeding for that purpose has been initiated or threatened by the Commission, and no notice of objection of the Commission to the use of such registration statement or any post-effective amendment thereto pursuant to Rule 401(g)(2) under the Act has been received by the Company (the base prospectus filed as part of such registration

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statement, in the form in which it has most recently been filed with the Commission on or prior to the date of this Agreement, is hereinafter called the "Basic Prospectus"; any preliminary prospectus (including any preliminary prospectus supplement) relating to the Securities filed with the Commission pursuant to Rule 424(b) under the Act is hereinafter called a "Preliminary Prospectus"; the various parts of such registration statement, including all exhibits thereto and including any prospectus supplement relating to the Securities that is filed with the Commission and deemed by virtue of Rule 430B to be part of such registration statement, each as amended at the time such part of the registration statement became effective, are hereinafter collectively called the "Registration Statement"; the Basic Prospectus, as amended and supplemented immediately prior to the Applicable Time (as defined in Section 1(c) hereof), is hereinafter called the "Pricing Prospectus"; the form of the final prospectus relating to the Securities filed with the Commission pursuant to Rule 424(b) under the Act in accordance with Section 5(a) hereof is hereinafter called the "Prospectus"; any reference herein to the Basic Prospectus, the Pricing Prospectus, any Preliminary Prospectus or the Prospectus shall be deemed to refer to and include the documents incorporated by reference therein pursuant to Item 12 of Form S 3 under the Act, as of the date of such prospectus; any reference to any amendment or supplement to the Basic Prospectus, any Preliminary Prospectus or the Prospectus shall be deemed to refer to and include any post-effective amendment to the Registration Statement, any prospectus supplement relating to the Securities filed with the Commission pursuant to Rule 424(b) under the Act and any documents filed under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and incorporated therein, in each case after the date of the Basic Prospectus, such Preliminary Prospectus, or the Prospectus, as the case may be; any reference to any amendment to the Registration Statement shall be deemed to refer to and include any annual report of the Company filed pursuant to Section 13(a) or 15(d) of the Exchange Act after the effective date of the Registration Statement that is incorporated by reference in the Registration Statement; and any "issuer free writing prospectus" as defined in Rule 433 under the Act relating to the Securities is hereinafter called an "Issuer Free Writing Prospectus");

- (b) No order preventing or suspending the use of any Preliminary Prospectus or any Issuer Free Writing Prospectus has been issued by the Commission, and each Preliminary Prospectus, at the time of filing thereof, conformed in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder, and did not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with information furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein
- (c) For the purposes of this Agreement, the "Applicable Time" is 5:30 p.m. (Eastern time) on the date of this Agreement; the Pricing Prospectus, as supplemented by the information set forth in Schedule II(b) hereto, taken together (collectively, the "Pricing Disclosure Package") did not, as of the Applicable Time, and will not, as of each Time of Delivery, contain an untrue statement of a material fact or omit to state a material fact necessary in order to make the statements made therein, in the light of the circumstances under which they were made, not misleading; and each

Prospectus or the Prospectus and each such Issuer Free Writing Prospectus, as supplemented by and taken together with the Pricing Disclosure Package as of the Applicable Time, did not include any untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that this representation and warranty shall not apply to statements or omissions made in an Issuer Free Writing Prospectus in reliance upon and in conformity with information furnished in writing to the Company by an Underwriter through the Representatives by or on behalf of an Underwriter expressly for use therein;

- (d) The documents incorporated by reference in the Pricing Disclosure Package and the Prospectus, when they became effective or were filed with the Commission, as the case may be, conformed in all material respects to the requirements of the Act or the Exchange Act, as applicable, and the rules and regulations of the Commission thereunder, and none of such documents contained an untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary to make the statements therein not misleading; any further documents so filed and incorporated by reference in the Prospectus or any further amendment or supplement thereto, when such documents become effective or are filed with the Commission, as the case may be, will conform in all material respects to the requirements of the Act or the Exchange Act, as applicable, and the rules and regulations of the Commission thereunder and will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with information furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein; and no such documents were filed with the Commission since the Commission's close of business on the business day immediately prior to the date of this Agreement and prior to the execution of this Agreement, except as set forth on Schedule II(c) hereto;
- (e) The Registration Statement conforms, and the Prospectus and any further amendments or supplements to the Registration Statement and the Prospectus will conform, in all material respects to the requirements of the Act and the rules and regulations of the Commission thereunder and do not and will not, as of the applicable effective date as to each part of the Registration Statement and as of the applicable filing date as to the Prospectus and any amendment or supplement thereto, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; provided, however, that this representation and warranty shall not apply to any statements or omissions made in reliance upon and in conformity with information furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein;
- (f) (A) (i) At the time of filing the Registration Statement, (ii) at the time of the most recent amendment thereto for the purposes of complying with Section 10(a)(3) of the Act (whether such amendment was by post-effective amendment, incorporated report filed pursuant to Section 13 or 15(d) of the Exchange Act or form of prospectus), and (iii) at the time the Company or any person acting on its behalf (within the meaning, for this clause only, of Rule 163(c) under the Act) made any offer relating to the Securities in reliance on the exemption of Rule 163 under the Act, the Company was a "well-known seasoned issuer" as defined in

Rule 405 under the Act; and (B) at the earliest time after the filing of the Registration Statement that the Company or another offering participant made a bona fide offer (within the meaning of Rule 164(h)(2) under the Act) of the Securities, the Company was not an "ineligible issuer" as defined in Rule 405 under the Act;

- (g) Each of the Company and its subsidiaries (as defined in Rule 405 under the Securities Act) has been duly organized and is validly existing and in good standing as a corporation or other business entity under the laws of its jurisdiction of organization and is duly qualified to do business and in good standing as a foreign corporation or other business entity in each jurisdiction in which its ownership or lease of property or the conduct of its businesses requires such qualification, except where the failure to be so qualified or in good standing would not, in the aggregate, reasonably be expected to have a material adverse effect on the condition (financial or otherwise), results of operations, stockholders' equity, properties, business or prospects of the Company and its subsidiaries taken as a whole or a material adverse effect on the performance by the Company of its obligations under this Agreement or the consummation of any of the transactions contemplated hereby or thereby (a "Material Adverse Effect"); each of the Company and its subsidiaries has all power and authority necessary to own or hold its properties and to conduct the businesses in which it is engaged. The Company does not own or control, directly or indirectly, any corporation, association or other entity other than the subsidiaries listed in the Company's Annual Report on Form 10-K for the most recent fiscal year. None of the subsidiaries of the Company is a "significant subsidiary" (as defined in Rule 405 under the Securities Act);
- (h) Except as described in each of the Pricing Disclosure Package and the Prospectus, neither the Company nor any of its subsidiaries has sustained, since the date of the latest financial statements reviewed or audited by Ernst & Young LLP and included in the Pricing Disclosure Package, any loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, and, since such date, there has not been any change in the total current assets, capital stock or long-term debt of the Company or any of its subsidiaries (other than a change in the number of outstanding shares of Stock due to the issuance of shares upon the exercise of options under the Company's previous or currently existing equity incentive and other similar officer, director or employee benefit plans) or any adverse change, or any development involving a prospective adverse change, in or affecting the condition (financial or otherwise), results of operations, stockholders' equity, properties, management, business or prospects of the Company and its subsidiaries, taken as a whole, in each case except as would not, in the aggregate, reasonably be expected to have a Material Adverse Effect;
- (i) (i) The Company and each of its subsidiaries has good and marketable title in fee simple to all real property and good and marketable title to all personal property owned by them, in each case free and clear of all liens, encumbrances and defects, except such as are described in the Pricing Disclosure Package and the Prospectus and such as do not affect the value of such property and do not interfere with the use made and proposed to be made of such property by the Company or any of its subsidiaries; and (ii) all assets held under lease by the Company or any of its subsidiaries

the case of (i) and (ii), as would not, in the aggregate, reasonably be expected to have a Material Adverse Effect;

- (j) The Company has an authorized capitalization as set forth in each of the Pricing Disclosure Package and the Prospectus on the dates indicated therein, and all of the issued shares of capital stock of the Company have been duly authorized and validly issued, are fully paid and non-assessable, conform in all material respects to the description thereof contained in each of the Pricing Disclosure Package and the Prospectus and were issued in compliance with federal and state securities laws and not in violation of any preemptive right, resale right, right of first refusal or similar right. All of the Company's options, warrants and other rights to purchase or exchange any securities for shares of the Company's capital stock have been duly authorized and validly issued, conform to the description thereof contained in each of the Pricing Disclosure Package and the Prospectus and were issued in compliance with federal and state securities laws. There are no outstanding options to purchase, or any rights or warrants to subscribe for, or any securities or obligations convertible into, or any contracts or commitments to issue or sell, any shares of the Company's capital stock, any shares of capital stock of any subsidiary, or any such warrants, convertible securities or obligations, except as set forth in the Pricing Disclosure Package and the Prospectus and except for shares of Company capital stock and options to purchase shares of Company capital stock granted under, or contracts or commitments pursuant to, the Company's previous or currently existing equity incentive and other similar officer, director or employee benefit plans. There is no and has been no policy or practice of the Company to intentionally coordinate the grant of options to employees with the release or other public announcement of material information regarding the Company or its results of operations or prospects to minimize the exercise price of such options. All of the issued shares of capital stock of each subsidiary of the Company have been duly authorized and validly issued, are fully paid and non-assessable and are owned directly or indirectly by the Company, free and clear of all liens, encumbrances, equities or claims, except for such liens, encumbrances, equities or claims as would not, in the aggregate, reasonably be expected to have a Material Adverse Effect;
- (k) Except as identified in the Pricing Disclosure Package and the Prospectus, there are no contracts, agreements or understandings between the Company and any person granting such person the right to require the Company to file a registration statement under the Securities Act with respect to any securities of the Company owned or to be owned by such person or to require the Company to include such securities in any securities being registered pursuant to the Registration Statement or any other registration statement filed by the Company under the Securities Act;
- (l) The Company has all requisite corporate power to execute, deliver and perform its obligations under this Agreement. This Agreement has been duly and validly authorized, executed and delivered by the Company;
- (m) The Securities have been duly and validly authorized and, when issued and delivered against payment therefor as provided herein, will be duly and validly issued and fully paid and non-assessable and will conform in all material respects to the description of the Securities contained in the Pricing Disclosure Package and the Prospectus;
- (n) Prior to the date hereof, the Company and its affiliates have not taken, directly or indirectly, any action (A) designed to or that has constituted or that reasonably can be expected to cause or result in the stabilization or manipulation of the price of any security of the

Company in connection with the offering of the Securities to facilitate the sale or resale of such securities or (B) prohibited by Regulation M under the Exchange Act;

- (o) The issue and sale of the Securities and the compliance by the Company with this Agreement, the application of the net proceeds from the sale of the Securities as described under "Use of Proceeds" in each of the Pricing Disclosure Package and the Prospectus and the consummation of the transactions contemplated hereby and thereby, will not (i) conflict with or result in a breach or violation of any of the terms or provisions of, impose any lien, charge or encumbrance upon any property or assets of the Company or its subsidiaries, or constitute a default under, any indenture, mortgage, deed of trust, loan agreement, license, lease or other agreement or instrument to which the Company or any of its subsidiaries is a party or by which the Company or any of its subsidiaries is bound or to which any of the property or assets of the Company or any of its subsidiaries is subject, (ii) result in any violation of the provisions of the charter or by-laws or similar organizational document of the Company or any of its subsidiaries or (iii) result in any violation of any statute or any judgment, order, decree, rule or regulation of any court or arbitrator or federal, state, local or foreign governmental agency or regulatory authority having jurisdiction over the properties or assets of the Company or any of its subsidiaries or any of their properties or assets ("Governmental Authority"), except, with respect to clauses (i) and (iii), conflicts, breaches, violations, impositions, charges or defaults that would not reasonably be expected to have a Material Adverse Effect;
- (p) No consent, approval, authorization or order of, or filing, registration or qualification with any Governmental Authority is required for the issue and sale of the Securities, the execution, delivery and performance by the Company of its obligations under this Agreement, the application of the net proceeds from the sale of the Securities as described under "Use of Proceeds" in each of the Pricing Disclosure Package and the Prospectus and the consummation of the transactions contemplated hereby and thereby, except for such consents, approvals, authorizations, orders, filings, registrations or qualifications as have been obtained under the Act or may be required under state securities or Blue Sky laws in connection with the purchase and distribution of the Securities by the Underwriters and listing of the Securities on the NASDAQ Global Market;
- (q) Neither the Company nor any of its subsidiaries (i) is in violation of its charter or by-laws (or similar organizational documents), (ii) is in default, and no event has occurred that, with notice or lapse of time or both, would constitute such a default, in the due performance or observance of any term, covenant, condition or other obligation contained in any indenture, mortgage, deed of trust, loan agreement, license or other agreement or instrument to which it is a party or by which it is bound or to which any of its properties or assets is subject or (iii) is in violation of any statute or any order, rule or regulation of any Governmental Authority or has failed to obtain any license, permit, certificate, franchise or other governmental authorization or permit necessary to the ownership of its property or to the conduct of its business, except in the case of clauses (ii) and (iii), to the extent any such conflict, breach, violation or default would not, in the aggregate, reasonably be expected to have a Material Adverse Effect;

- (r) The statements set forth in each of the Pricing Disclosure Package and the Prospectus under the caption “Description of Capital Stock,” insofar as they purport to constitute a summary of the terms of the Securities and the provisions of the laws and documents referred to therein and under the captions “Material U.S. Federal Income Tax

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Considerations,” and “Underwriting,” insofar as they purport to describe the provisions of the laws and documents referred to therein, are accurate in all material respects; *except* that the Company makes no such representation or warranty under this Section 1(r) in each case to the extent, but only to the extent, that such statement was made in the Pricing Disclosure Package or the Prospectus in reliance upon and in conformity with written information furnished to the Company by such Underwriter through the Representatives expressly for use therein.

- (s) The statistical and market-related data included under the captions “Business” in the Company’s annual report on Form 10-K for the year ended December 31, 2012 and in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in the Company’s annual report on Form 10-K for the year ended December 31, 2012 and in the Company’s quarterly reports on Form 10-Q for the three months ended March 31, 2013 incorporated by reference in the Pricing Disclosure Package and the consolidated financial statements of the Company and its subsidiaries included in the Pricing Disclosure Package are based on or derived from sources which the Company reasonably believes are reliable and accurate, and such data agree with the sources from which they are derived in all material respects;
- (t) Except as described in the Pricing Disclosure Package and the Prospectus, there are no legal or governmental proceedings pending to which the Company or any of its subsidiaries is a party or of which any property or assets of the Company or any of its subsidiaries is the subject that would, in the aggregate, reasonably be expected to have a Material Adverse Effect; and to the Company’s knowledge, no such proceedings are threatened in writing or contemplated by Governmental Authorities or others;
- (u) There are no legal or governmental proceedings or contracts or other documents that would be required to be described in a registration statement of the Company under the Act or, in the case of documents, required to be filed as exhibits to such registration statement pursuant to Item 601(10) of Regulation S-K that have not been described or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus. Neither the Company nor any of its subsidiaries has knowledge that any other party to any such contract, agreement or arrangement has any intention not to render full performance as contemplated by the terms thereof. The statements made or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus insofar as they purport to constitute summaries of the terms of statutes, rules or regulations, legal or governmental proceedings or contracts and other documents, constitute accurate summaries of the terms of such statutes, rules and regulations, legal and governmental proceedings and contracts and other documents in all material respects;
- (v) Neither the Company nor any subsidiary is, and after giving effect to the offer and sale of the Securities and the application of the net proceeds therefrom as described under “Use of Proceeds” in each of the Pricing Disclosure Package and the Prospectus will be required to register as, (i) an “investment company” or a company “controlled” by an “investment company” within the meaning of the United States Investment Company Act of 1940, as amended (the “Investment Company Act”), and the rules and regulations of the Commission thereunder or (ii) a “business development company” (as defined in Section 2(a)(48) of the Investment Company Act);
- (w) Neither the Company nor its affiliates nor any other person acting on behalf of the Company has sold or issued any securities that would be integrated with the offering of the Securities

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contemplated by this Agreement pursuant to the Act, the rules and regulations thereunder or the interpretations thereof by the Commission;

- (x) The historical financial statements (including the related notes and supporting schedules) included or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus present fairly in all material respects the financial condition, results of operations and cash flows of the entities purported to be shown thereby, at the dates and for the periods indicated, and have been prepared in conformity with U.S. GAAP applied on a consistent basis throughout the periods involved. The other financial information and data included or incorporated by reference in the Prospectus are, in all material respects, accurately presented and prepared on a basis consistent with such financial statements and the books and records of the Company. The interactive data in eXtensible Business Reporting Language incorporated by reference in the Pricing Disclosure Package and the Prospectus fairly present the information called for in all material respects and has been prepared in all material respects in accordance with the Commission’s rules and guidelines applicable thereto;
- (y) (i) The Company and each of its subsidiaries have established and maintain disclosure controls and procedures (as such term is defined in Rule 13a-15 under the Exchange Act), (ii) such disclosure controls and procedures are designed to ensure that the information required to be disclosed by the Company in the reports they file or submit under the Exchange Act (assuming the Company was required to file or submit such reports under the Exchange Act) is accumulated and communicated to management of the Company and its subsidiaries, including their respective principal executive officers and principal financial officers, as appropriate, to allow timely decisions regarding required disclosure to be made; and (iii) such disclosure controls and procedures are effective in all material respects to perform the functions for which they were established;
- (z) The Company and each of its subsidiaries (i) make and keep accurate books and records and (ii) maintain and have maintained effective internal control over financial reporting as defined in Rule 13a-5 under the Exchange Act and a system of internal accounting controls sufficient to provide reasonable assurance that (A) transactions are executed in accordance with management’s general or specific authorization, (B) transactions are recorded as necessary to permit preparation of its financial statements in conformity with U.S. GAAP and to maintain accountability for its assets, (C) access to its assets is permitted only in accordance with management’s general or specific authorization, (D) the reported accountability for its assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences and (E) the interactive data in eXtensible Business Reporting Language incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus fairly present the information called for in all material respects and is prepared in all material respects in accordance with the Commission’s rules and guidelines applicable thereto;

- (aa) Ernst & Young LLP, who have certified certain financial statements of the Company, whose report appears or is incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus are independent public accountants as required by the Act and the rules and regulations thereunder;
- (bb) Since the date of the most recent balance sheet of the Company and its consolidated subsidiaries reviewed or audited by Ernst & Young LLP and the audit committee of the board of directors of the Company, (i) the Company has not been advised of (A) any significant

8

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deficiencies in the design or operation of internal controls that would adversely affect the ability of the Company or any of its subsidiaries to record, process, summarize and report financial data, or any material weaknesses in internal controls or (B) any fraud, whether or not material, that involves management or other employees who have a significant role in the internal controls of the Company and each of its subsidiaries, and (ii) since that date, there have been no significant changes in internal controls or in other factors that would significantly affect internal controls, including any corrective actions with regard to significant deficiencies and material weaknesses;

- (cc) Since the date as of which information is given in the Pricing Disclosure Package and except as otherwise described in the Pricing Disclosure Package and the Prospectus, the Company has not (i) issued or granted any securities (except pursuant to the Company's previous or currently existing equity incentive and other similar officer, director or employee benefit plans), (ii) incurred any liability or obligation, direct or contingent, other than liabilities and obligations that were incurred in the ordinary course of business, (iii) entered into any material transaction not in the ordinary course of business or (iv) declared or paid any dividend on its capital stock;
- (dd) "Intellectual Property" means all patents, patent applications, inventions, trademarks, service marks, trade names, trademark registrations, service mark registrations, copyrights, licenses, know-how, software, systems and technology (including trade secrets and other unpatented and/or unpatentable proprietary or confidential information, systems or procedures) or other intellectual property, including, without limitation, all of the intellectual property described in the Pricing Disclosure Package and the Prospectus as being owned or licensed by the Company and its subsidiaries. The Company and each of its subsidiaries own or possess adequate rights to use all Intellectual Property necessary for the conduct of their respective businesses, except where the failure to own or possess such Intellectual Property would not, individually or in the aggregate, have a Material Adverse Effect. The Company and its subsidiaries have no reason to believe that the conduct of their respective businesses will conflict with, and have not received any notice of any claim of conflict with, any such rights of others, except where such conflict or claims of conflict would not, individually or in the aggregate, have a Material Adverse Effect. Except as disclosed in the Pricing Disclosure Package and the Prospectus, (A) there is no infringement, misappropriation or violation by third parties of any such Intellectual Property, except as such infringement, misappropriation or violation would not result in a Material Adverse Effect; (B) there is no pending or, to the knowledge of the Company and its subsidiaries, threatened action, suit, proceeding or claim by others challenging the rights of the Company and its subsidiaries in or to any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim which would have a Material Adverse Effect; (C) the Intellectual Property owned by the Company and its subsidiaries and, to the knowledge of the Company, the Intellectual Property licensed to the Company and its subsidiaries has not been adjudged invalid or unenforceable, in whole or in part, and there is no pending or threatened in writing action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim which would have a Material Adverse Effect; (D) there is no pending or threatened action, suit, proceeding or claim by others that the Company or its subsidiaries infringe, misappropriate or otherwise violate any Intellectual Property or other proprietary rights of others, the Company and its subsidiaries have not received any written notice of such claim and the Company is unaware of any other

9

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facts which would form a reasonable basis for any such claim which would have a Material Adverse Effect; and (E) to the Company's knowledge, no employee of the Company or a subsidiary of the Company is in or has ever been in violation of any term of any employment contract, patent disclosure agreement, invention assignment agreement, non-competition agreement, non-solicitation agreement, nondisclosure agreement or any restrictive covenant to or with a former employer, where the basis of such violation relates to (i) such employee's employment with the Company or a subsidiary of the Company, or (ii) actions undertaken by the employee while employed with the Company or a subsidiary of the Company, except (in the case of (i) and (ii)) for such violations as would not have a Material Adverse Effect. To the Company's knowledge, all material technical information developed by and belonging to the Company and its subsidiaries which has not been patented has been kept confidential, except as would not have a Material Adverse Effect. The Company is not a party to or bound by any options, licenses or agreements with respect to the Intellectual Property that are required to be described in a registration statement filed under the Act or would be required to be filed as exhibits to a registration statement of the Company pursuant to Item 601(10) of Regulation S-K that have not been described or incorporated by reference in the Registration Statement, the Pricing Disclosure Package and the Prospectus;

- (ee) Except as described in the Pricing Disclosure Package and the Prospectus, the Company and each of its subsidiaries: (A) are and at all times have been in full compliance with all statutes, rules, regulations, or guidances applicable to the ownership, testing, development, manufacture, packaging, processing, use, distribution, marketing, labeling, promotion, sale, offer for sale, storage, import, export or disposal of any product or product candidate manufactured or distributed by the Company and its subsidiaries ("Applicable Laws"); (B) have not received any U.S. Food and Drug Administration ("FDA") Form 483, notice of adverse finding, warning letter, untitled letter or other correspondence or notice from the FDA or any other Governmental Authority alleging or asserting noncompliance with any Applicable Laws or any licenses, certificates, approvals, clearances, authorizations, permits and supplements or amendments thereto required by any such Applicable Laws ("Authorizations"); (C) possess all Authorizations and such Authorizations are valid and in full force and effect and are not in violation of any term of any such Authorizations; (D) have not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Authority or third party alleging that any product operation or activity is in violation of any Applicable Laws or Authorizations and have no knowledge that any such Governmental Authority or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding; (E) have not received notice that any Governmental Authority has taken, is taking or intends to take action to limit, suspend, modify or revoke any Authorizations and have no knowledge that any such Governmental Authority is considering such action; (F) have filed, obtained, maintained or submitted all reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Authorizations and represent that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and correct on the date filed (or were corrected or supplemented by a

subsequent submission), except where the failure to so file, obtain, maintain or submit would not reasonably be expected to have a Material Adverse Effect; and (G) have not, either voluntarily or involuntarily, initiated, conducted, or issued or caused to be initiated, conducted or issued, any recall, market withdrawal or replacement, safety alert, post-sale warning, “dear doctor” letter, or other

notice or action relating to the alleged lack of safety or efficacy of any of its product or any alleged product defect or violation and, to the Company’s knowledge, no third party has initiated, conducted or intends to initiate any such notice or action;

- (ff) The studies, tests and preclinical and clinical trials conducted by or on behalf of the Company and each of its subsidiaries or with respect to the Company’s, or its subsidiaries’ products or product candidates were and, if still pending, are being conducted in all material respects in accordance with experimental protocols, procedures and controls pursuant to accepted professional scientific standards and all Applicable Laws and Authorizations, including, without limitation, the Federal Food, Drug and Cosmetic Act and the rules and regulations promulgated thereunder; the descriptions of the results of such studies, tests and trials contained in the Pricing Disclosure Package and the Prospectus are accurate and complete in all material respects and fairly present the data derived from such studies, tests and trials; except to the extent disclosed in the Pricing Disclosure Package and the Prospectus, the Company is not aware of any studies, tests or trials, the results of which the Company believes reasonably refute the study, test, or trial results described or referred to in the Pricing Disclosure Package and the Prospectus when viewed in the context in which such results are described and the clinical state of development; and neither the Company and its subsidiaries, nor, to the knowledge of the Company, any of the Company’s or its subsidiaries’ collaboration partners have received any notices or correspondence from any Governmental Authority requiring the termination, suspension or material modification of any studies, tests or preclinical or clinical trials conducted by or on behalf of the Company or its subsidiaries or with respect to the Company’s, or its subsidiaries’ products or product candidates. All of the descriptions in the Pricing Disclosure Package and the Prospectus of the legal and governmental procedures and requirements of the FDA or any foreign, state or local governmental body exercising comparable authority are accurate in all material respects;
- (gg) The Company and each of its subsidiaries have such permits, licenses, patents, franchises, certificates of need and other approvals or authorizations of such Governmental Authorities (“Permits”) as are necessary under applicable law to own their properties and conduct their businesses in the manner described in the Pricing Disclosure Package and the Prospectus, except for any of the foregoing that would not, in the aggregate, reasonably be expected to have a Material Adverse Effect or except as described in the Pricing Disclosure Package and the Prospectus; each of the Company and its subsidiaries has fulfilled and performed all of its obligations with respect to the Permits, and no event has occurred that allows, or after notice or lapse of time would allow, revocation or termination thereof or results in any other impairment of the rights of the holder or any such Permits, except for any of the foregoing that would not reasonably be expected to have a Material Adverse Effect or except as described in the Pricing Disclosure Package;
- (hh) (i) Each “employee benefit plan” (within the meaning of Section 3(3) of the Employee Retirement Security Act of 1974, as amended (“ERISA”)) for which the Company or any member of its “Controlled Group” (defined as any organization which is a member of a controlled group of corporations within the meaning of Section 414 of the Internal Revenue Code of 1986, as amended (the “Code”)) would have any liability (each a “Plan”) has been maintained in material compliance with its terms and with the requirements of all applicable statutes, rules and regulations including ERISA and the Code; (ii) with respect to each Plan subject to Title IV of ERISA (a) no “reportable event” (within the meaning of Section 4043(c)

of ERISA) has occurred or is reasonably expected to occur, (b) no “accumulated funding deficiency” (within the meaning of Section 302 of ERISA or Section 412 of the Code), whether or not waived, has occurred or is reasonably expected to occur, (c) the fair market value of the assets under each Plan exceeds the present value of all benefits accrued under such Plan (determined based on those assumptions used to fund such Plan) and (d) neither the Company or any member of its Controlled Group has incurred, or reasonably expects to incur, any liability under Title IV of ERISA (other than contributions to the Plan or premiums to the Pension Benefit Guaranty Corporation in the ordinary course and without default) in respect of a Plan (including a “multiemployer plan,” within the meaning of Section 4001(c)(3) of ERISA); and (iii) each Plan that is intended to be qualified under Section 401(a) of the Code is so qualified and nothing has occurred, whether by action or by failure to act, which would cause the loss of such qualification;

- (ii) Neither the Company nor any subsidiary is in violation of or has received notice of any violation with respect to any federal or state law relating to discrimination in the hiring, promotion or pay of employees, nor any applicable federal or state wage and hour laws, nor any state law precluding the denial of credit due to the neighborhood in which a property is situated, the violation of any of which would reasonably be expected to have a Material Adverse Effect;
- (jj) Except as described in the Pricing Disclosure Package and the Prospectus, no labor disturbance by the employees of the Company or any of its subsidiaries exists or, to the knowledge of the Company, is imminent that would reasonably be expected to have a Material Adverse Effect, and the Company is not aware of any existing or imminent labor disturbance by, or dispute with, the employees of any of the Company’s or any of the Company’s subsidiaries’ collaborative partners, principal suppliers, contractors or customers that would reasonably be expected to have a Material Adverse Effect;
- (kk) The Company and each of its subsidiaries have filed all federal, state, local and foreign income and franchise tax returns required to be filed through the date hereof, subject to permitted extensions, such tax returns are true and complete in all material respects, all taxes due thereon have been paid, and no material tax deficiency has been determined adversely to the Company or any of its subsidiaries, nor does the Company have any knowledge of any tax deficiencies that would, in the aggregate, reasonably be expected to have a Material Adverse Effect;
- (ll) There are no transfer taxes or other similar fees or charges under Federal law or the laws of any state, or any political subdivision thereof, required to be paid in connection with the execution and delivery of this Agreement or the issuance by the Company or sale by the Company of the Securities;



- (mm) The Company and each of its subsidiaries (i) are, and at all times prior hereto were, in compliance with all laws, regulations, ordinances, rules, orders, judgments, decrees, permits or other legal requirements of any Governmental Authority, including without limitation any international, national, state, provincial, regional, or local authority, relating to the protection of human health or safety, the environment, or natural resources, or to hazardous or toxic substances or wastes, pollutants or contaminants (“Environmental Laws”) applicable to such entity, which compliance includes, without limitation, obtaining, maintaining and complying with all permits and authorizations and approvals required by Environmental Laws to conduct their respective businesses, and (ii) have not received written notice of any actual or alleged violation of Environmental Laws, or of any potential liability for or other obligation

12

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concerning the presence, disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, except in the case of clause (i) or (ii) where such non-compliance, violation, liability, or other obligation would not, in the aggregate, reasonably be expected to have a Material Adverse Effect. Except as described in the Pricing Disclosure Package and the Prospectus, (A) there are no proceedings that are pending, or known to be contemplated, against the Company or any of its subsidiaries under Environmental Laws in which a Governmental Authority is also a party, other than such proceedings regarding which it is reasonably believed no monetary sanctions of \$250,000 or more will be imposed, (B) the Company and its subsidiaries are not aware of any issues regarding compliance with Environmental Laws, or liabilities or other obligations under Environmental Laws or concerning hazardous or toxic substances or wastes, pollutants or contaminants, that would reasonably be expected to have a Material Adverse Effect, and (C) none of the Company and its subsidiaries anticipates material capital expenditures relating to Environmental Laws;

- (nn) Except such as are described in the Pricing Disclosure Package and the Prospectus, the Company and each of its subsidiaries carry, or are covered by, insurance from insurers of recognized financial responsibility in such amounts and covering such risks as, based on the Company’s internal assessments, is adequate for the conduct of their respective businesses and the value of their respective properties and as is customary for companies engaged in similar businesses in similar industries. All policies of insurance of the Company and its subsidiaries are in full force and effect; the Company and its subsidiaries are in compliance with the terms of such policies in all material respects; and neither the Company nor any of its subsidiaries has received notice from any insurer or agent of such insurer that capital improvements or other expenditures are required or necessary to be made in order to continue such insurance; there are no claims by the Company or any of its subsidiaries under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause; and neither the Company nor any such subsidiary has any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not reasonably be expected to have a Material Adverse Effect;
- (oo) The operations of the Company and its subsidiaries are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Authority (collectively, the “Money Laundering Laws”) and no action, suit or proceeding by or before any Governmental Authority involving the Company or any of its subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened, except, in each case, as would not reasonably be expected to have a Material Adverse Effect;
- (pp) Neither the Company nor any of its subsidiaries nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company or any of its subsidiaries is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department (“OFAC”); and the Company will not directly or indirectly use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other person or entity, for the purpose of

13

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financing the activities of any person currently subject to any U.S. sanctions administered by OFAC;

- (qq) Neither the Company nor any of its subsidiaries, nor, to the knowledge of the Company, any director, officer, agent, employee or other person acting on behalf of the Company or any of its subsidiaries, has (i) used any corporate funds for any unlawful contribution, gift, entertainment or other unlawful expense relating to political activity; (ii) made any direct or indirect unlawful payment to any foreign or domestic government official or employee from corporate funds; (iii) violated or is in violation of any provision of the Foreign Corrupt Practices Act of 1977; or (iv) made any bribe, rebate, payoff, influence payment, kickback or other unlawful payment;
- (rr) No subsidiary of the Company is currently prohibited, directly or indirectly, from paying any dividends to the Company, from making any other distribution on such subsidiary’s capital stock, from repaying to the Company any loans or advances to such subsidiary from the Company or from transferring any of such subsidiary’s property or assets to the Company or any other subsidiary of the Company, except as described in the Pricing Disclosure Package;
- (ss) There is and has been no failure on the part of the Company and any of the Company’s directors or officers, in their capacities as such, to comply in all material respects with the provisions of the Sarbanes-Oxley Act of 2002 and the rules and regulations promulgated in connection therewith;
- (tt) The Company is not aware of any relationship, direct or indirect, that is required to be described in a registration statement of the Company pursuant to Item 404 of Regulation S-K, exists between or among the Company, on the one hand, and the directors, officers, stockholders, customers or suppliers of the Company, on the other hand, that has not been described in the Registration Statement, the Pricing Disclosure Package and the Prospectus;
- (uu) Each forward-looking statement (within the meaning of Section 27A of the 1933 Act and Section 21E of the 1934 Act) contained or incorporated by reference in the Pricing Disclosure Package and the Prospectus has been made with a reasonable basis, at the time it was made, or has been disclosed in good faith, at the time it was disclosed; and

- (vv) On and immediately after each Time of Delivery, each of the Company and its subsidiaries (after giving effect to the issuance of the Securities and to the other transactions related thereto as described in each of the Pricing Disclosure Package and the Prospectus) will be Solvent. As used in this paragraph, the term “Solvent” means, with respect to a particular date, that on such date (i) the present fair market value (or present fair saleable value) of the assets of each of the Company and its subsidiaries is not less than the total amount required to pay the probable liabilities on its total existing debts and liabilities (including contingent liabilities) as they become absolute and matured, (ii) each of the Company and its subsidiaries is able to realize upon its assets and pay its debts and other liabilities, contingent obligations and commitments as they mature and become due in the normal course of business, (iii) assuming the sale of the Securities as contemplated by this Agreement and each of the Pricing Disclosure Package and the Prospectus, neither the Company nor its subsidiaries is incurring debts or liabilities beyond its ability to pay as such debts and liabilities mature; and (iv) neither the Company nor its subsidiaries is engaged in any business or

14

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transaction, and neither of them is about to engage in any business or transaction, for which its property would constitute unreasonably small capital after giving due consideration to the prevailing practice in the industry in which each of the Company and its subsidiaries is engaged. In computing the amount of such contingent liabilities at any time, it is intended that such liabilities will be computed at the amount that, in the light of all the facts and circumstances existing at such time, represents the amount that can reasonably be expected to become an actual or matured liability.

2. Subject to the terms and conditions herein set forth, (a) the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at a purchase price per share of \$18.05 (the “Purchase Price”) the number of Firm Securities set forth opposite the name of such Underwriters in Schedule I hereto, and (b) in the event and to the extent that the Underwriters shall exercise the election to purchase Optional Securities as provided below, the Company agrees to issue and sell to each of the Underwriters, and each of the Underwriters agrees, severally and not jointly, to purchase from the Company, at the Purchase Price set forth in clause (a) of this Section 2, that portion of the number of Optional Securities as to which such election shall have been exercised (to be adjusted by you so as to eliminate fractional shares), determined by multiplying such number of Optional Securities by a fraction, the numerator of which is the maximum number of Optional Securities that such Underwriter is entitled to purchase as set forth opposite the name of such Underwriter in Schedule I hereto and the denominator of which is the maximum number of Optional Securities that all of the Underwriters are entitled to purchase hereunder.

The Company hereby grants to the Underwriters the right to purchase at their election up to 1,350,000 Optional Securities, at the Purchase Price set forth in clause (a) of the first paragraph of this Section 2 for the sole purpose of covering sales in excess of the number of Firm Securities, provided that the Purchase Price per Optional Share shall be reduced by an amount per share equal to any dividends or distributions declared by the Company and payable on the Firm Securities but not payable on the Optional Securities. Any such election to purchase Optional Securities may be exercised only by written notice from the Representatives to the Company, given within a period of 30 calendar days from the date of this Agreement, setting forth the aggregate number of Optional Securities to be purchased and the date on which such Optional Securities are to be delivered, as determined by the Representatives but in no event earlier than the First Time of Delivery (as defined in Section 4 hereof) or, unless you and the Company otherwise agree in writing, earlier than one or later than 10 business days after the date of such notice.

3. Upon the authorization by you of the release of the Securities, the several Underwriters propose to offer the Securities for sale upon the terms and conditions set forth in this Agreement and the Prospectus.
4. (a) The Securities to be purchased by each Underwriter hereunder will be represented by one or more definitive global Securities in book-entry form which will be deposited by or on behalf of the Company with The Depository Trust Company (“DTC”) or its designated custodian. The Company will deliver the Securities to the Representatives, for the account of each Underwriter, against payment by or on behalf of such Underwriter of the purchase price therefor by wire transfer to the Company in Federal (same day) funds, by causing DTC to credit the Securities to the account of Goldman, Sachs & Co. at DTC. The Company will cause the certificates representing the Securities to be made available to Goldman, Sachs & Co. for checking at least twenty-four hours prior to the Time of Delivery (as defined below) at

15

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the office of Davis Polk & Wardwell LLP, 1600 El Camino Real, Menlo Park, California 94025 (the “Closing Location”). The time and date of such delivery and payment shall be, with respect to the Firm Securities, 9:30 a.m., New York City time, on May 14, 2013 or such other time and date as the Representatives and the Company may agree upon in writing, and with respect to the Optional Securities, 9:30 a.m. New York City time, on the date specific by you in the written notice given by you of the Underwriters’ election to purchase such Optional Securities, or such other time and date as the Representatives and the Company may agree upon in writing; *provided, however*, that such delivery date must be at least three New York Business Days (as defined below) after such written notice is given and may not be earlier than the First Time of Delivery (as defined below) nor later than ten New York Business Days (as defined below) after the date of such notice; *provided further*, that solely with respect to an Optional Securities written notice that is delivered prior to the First Time of Delivery, the related Time of Delivery (as defined below) must be at least one New York Business Day after the written notice is given. Such time and date for delivery of the Firm Securities are herein called the “First Time of Delivery”, any such time and date for delivery of the Optional Securities, if not the First Time of Delivery, are herein called a “Subsequent Time of Delivery”, and each such time and date for delivery are herein called a “Time of Delivery”.

- (b) The documents to be delivered at any Time of Delivery by or on behalf of the parties hereto pursuant to Section 8 hereof, including the cross-receipt for the Securities and any additional documents requested by the Underwriters pursuant to Section 8(m) hereof, will be delivered at such time and date at the Closing Location, and the Securities will be delivered at DTC (or its designated custodian), all at such Time of Delivery. A meeting will be held at the Closing Location at 5:00 p.m., New York City time, on the New York Business Day next preceding such Time of Delivery, at which meeting the final drafts of the documents to be delivered pursuant to the preceding sentence will be available for review by the parties hereto. For the purposes of this Section 4, “New York Business Day” shall mean each Monday, Tuesday, Wednesday, Thursday and Friday which is not a day on which banking institutions in New York are generally authorized or obligated by law or executive order to close.

5. The Company agrees with each of the Underwriters:

- (a) To prepare the Prospectus in a form approved by you and to file such Prospectus pursuant to Rule 424(b) under the Act not later than the Commission's close of business on the second business day following the execution and delivery of this Agreement; to make no further amendment or any supplement to the Registration Statement, the Basic Prospectus or the Prospectus prior to the last Time of Delivery which shall be disapproved by you promptly after reasonable notice thereof; to advise you, promptly after it receives notice thereof, of the time when any amendment to the Registration Statement has been filed or becomes effective or any amendment or supplement to the Prospectus has been filed and to furnish you with copies thereof; to file promptly all other material required to be filed by the Company with the Commission pursuant to Rule 433(d) under the Act; to file promptly all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act subsequent to the date of the Prospectus and for so long as the delivery of a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is required in connection with the offering or sale of the Securities; to advise you, promptly after it receives notice thereof, of the issuance by the Commission of any stop order or of any order

16

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preventing or suspending the use of any Preliminary Prospectus or other prospectus in respect of the Securities, of any notice of objection of the Commission to the use of the Registration Statement or any post-effective amendment thereto pursuant to Rule 401(g)(2) under the Act, of the suspension of the qualification of the Securities for offering or sale in any jurisdiction, of the initiation or threatening of any proceeding for any such purpose, or of any request by the Commission for the amending or supplementing of the Registration Statement or the Prospectus or for additional information; and, in the event of the issuance of any stop order or of any order preventing or suspending the use of any Preliminary Prospectus or other prospectus or suspending any such qualification, to promptly use its best efforts to obtain the withdrawal of such order; and in the event of any such issuance of a notice of objection, promptly to take such steps including, without limitation, amending the Registration Statement or filing a new registration statement, at its own expense, as may be necessary to permit offers and sales of the Securities by the Underwriters (references herein to the Registration Statement shall include any such amendment or new registration statement);

- (b) If required by Rule 430B(h) under the Act, to prepare a form of prospectus in a form approved by you and to file such form of prospectus pursuant to Rule 424(b) under the Act not later than may be required by Rule 424(b) under the Act; and to make no further amendment or supplement to such form of prospectus which shall be disapproved by you promptly after reasonable notice thereof;
- (c) If by the third anniversary (the "Renewal Deadline") of the initial effective date of the Registration Statement, any of the Securities remain unsold by the Underwriters, the Company will file, if it has not already done so and is eligible to do so, a new automatic shelf registration statement relating to the Securities, in a form satisfactory to you. If at the Renewal Deadline the Company is no longer eligible to file an automatic shelf registration statement, the Company will, if it has not already done so, file a new shelf registration statement relating to the Securities, in a form satisfactory to you and will use its best efforts to cause such registration statement to be declared effective within 180 days after the Renewal Deadline. The Company will take all other action necessary or appropriate to permit the public offering and sale of the Securities to continue as contemplated in the expired registration statement relating to the Securities. References herein to the Registration Statement shall include such new automatic shelf registration statement or such new shelf registration statement, as the case may be;
- (d) Promptly from time to time to take such action as you may reasonably request to qualify the Securities for offering and sale under the securities laws of such jurisdictions as you may request and to comply with such laws so as to permit the continuance of sales and dealings therein in such jurisdictions for as long as may be necessary to complete the distribution of the Securities, provided that in connection therewith the Company shall not be required to qualify as a foreign corporation or to file a general consent to service of process in any jurisdiction;
- (e) Prior to 10:00 a.m., New York City time, on the New York Business Day next succeeding the date of this Agreement and from time to time, to furnish the Underwriters with written and electronic copies of the Prospectus in New York City in such quantities as you may reasonably request, and, if the delivery of a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is required at any time prior to the expiration of nine months after the time of issue of the Prospectus in connection with the offering or sale of the

17

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Securities and if at such time any event shall have occurred as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made when such Prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) is delivered, not misleading, or, if for any other reason it shall be necessary during such same period to amend or supplement the Prospectus or to file under the Exchange Act any document incorporated by reference in the Prospectus in order to comply with the Act or the Exchange Act, to notify you and upon your request to file such document and to prepare and furnish without charge to each Underwriter and to any dealer in securities as many written and electronic copies as you may from time to time reasonably request of an amended Prospectus or a supplement to the Prospectus which will correct such statement or omission or effect such compliance; and in case any Underwriter is required to deliver a prospectus (or in lieu thereof, the notice referred to in Rule 173(a) under the Act) in connection with sales of any of the Securities at any time nine months or more after the time of issue of the Prospectus, upon your request but at the expense of such Underwriter, to prepare and deliver to such Underwriter as many written and electronic copies as you may request of an amended or supplemented Prospectus complying with Section 10(a)(3) of the Act;

- (f) To make generally available to its securityholders as soon as practicable, but in any event not later than sixteen months after the effective date of the Registration Statement (as defined in Rule 158(c) under the Act), an earnings statement of the Company and its subsidiaries (which need not be audited) complying with Section 11(a) of the Act and the rules and regulations of the Commission thereunder (including, at the option of the Company, Rule 158);
- (g) During the period beginning from the date hereof and continuing until the date 90 days after the date of this Agreement, not to, without the prior written consent of the Representatives, (i) offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, or file with the Commission a registration statement under the Act relating to any securities of the Company that are substantially similar to the Securities, including but not limited to any securities that are convertible into, exercisable or exchangeable for, or that represent the right to receive, Stock or any such substantially similar securities, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing or (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Stock or any such other securities, whether any such transaction is to be settled by delivery of Stock or such

other securities, in cash or otherwise (other than (v) the Securities, (w) pursuant to equity incentive plans existing on, or pursuant to the terms of securities convertible, exercisable or exchangeable for Stock or other substantially similar securities outstanding as of, the date of this Agreement, (x) pursuant to the terms of securities exercisable for Stock issued after the date of this Agreement pursuant to equity incentive plans existing on the date of this Agreement, (y) registration statements on Form S-8 or any successor form, or (z) the entry into an agreement providing for the issuance of, or the actual issuance of, shares of Stock or securities that are convertible into, exercisable or exchangeable for, or that represent the right to receive Stock, in connection with one or more license agreements, collaboration agreements or joint ventures; *provided* that in the case of clause (z), the aggregate number of shares of Stock that the Company may issue or sell or agree to issue or agree to sell shall not exceed 10% of the total number of shares of Stock

issued and outstanding as of the date of this Agreement, and that the Company shall (1) cause each recipient of such securities to execute and deliver to the Representatives, on or prior to the issuance of such securities, a lock-up agreement in the form attached hereto as Exhibit A covering the remainder of the applicable Lock-up Period (as defined therein), and (2) enter stop transfer instructions with the Company's transfer agent and registrar on such securities, which the Company agrees it will not waive or amend without the prior written consent of the Representatives).

- (h) To pay the required Commission filing fees relating to the Securities within the time required by Rule 456(b)(1) under the Act without regard to the proviso therein and otherwise in accordance with Rules 456(b) and 457(r) under the Act;
- (i) To use the net proceeds received by it from the sale of the Securities pursuant to this Agreement in the manner specified in the Pricing Disclosure Package under the caption "Use of Proceeds";
- (j) To use its best efforts to list, subject to notice of issuance, the Securities on NASDAQ;
- (k) The Company and its affiliates will not take, directly or indirectly, any action prohibited by Regulation M under the Exchange Act (other than the Underwriters, as to whom the Company makes no agreement); and
- (l) Upon request of any Underwriter, to furnish, or cause to be furnished, to such Underwriter an electronic version of the Company's trademarks, servicemarks and corporate logo for use on the website, if any, operated by such Underwriter for the purpose of facilitating the on-line offering of the Securities (the "License"); provided, however, that the License shall be used solely for the purpose described above, is granted without any fee and may not be assigned or transferred.

6.

- (a) (i) The Company represents and agrees that, without your prior consent, it has not made and will not make any offer relating to the Securities that would constitute an Issuer Free Writing Prospectus;
- (ii) each Underwriter represents and agrees that, without the prior consent of the Company and the Representatives, other than one or more term sheets relating to the Securities containing customary information and conveyed to purchasers of securities, it has not made and will not make any offer relating to the Securities that would constitute a "free writing prospectus," as defined in Rule 405 under the Act (any such offer (other than any such term sheets), is hereinafter referred to as a "Underwriter Supplemental Disclosure Document"); and
- (iii) any Issuer Free Writing Prospectus or Underwriter Supplemental Disclosure Document the use of which has been consented to by the Company and the Representatives is listed on Schedule II(a) hereto.
- (b) The Company has complied and will comply with the requirements of Rule 433 under the Act applicable to any Issuer Free Writing Prospectus, including timely filing with the Commission or retention where required and legending; and
- (c) The Company agrees that if at any time following issuance of an Issuer Free Writing Prospectus any event occurred or occurs as a result of which such Issuer Free Writing Prospectus would conflict with the information in the Registration Statement, the Pricing

Prospectus or the Prospectus or would include an untrue statement of a material fact or omit to state any material fact necessary in order to make the statements therein, in the light of the circumstances then prevailing, not misleading, the Company will give prompt notice thereof to the Representatives, and, if requested by the Representatives, will prepare and furnish without charge to each Underwriter an Issuer Free Writing Prospectus or other document which will correct such conflict, statement or omission; provided, however, that this representation and warranty shall not apply to any statements or omissions in an Issuer Free Writing Prospectus made in reliance upon and in conformity with information furnished in writing to the Company by an Underwriter through the Representatives expressly for use therein.

7.

The Company covenants and agrees with the several Underwriters that the Company will pay or cause to be paid the following: (i) the fees, disbursements and expenses of the Company's counsel and accountants in connection with the registration of the Securities under the Act and all other expenses in connection with the preparation, printing, reproduction and filing of the Registration Statement, the Basic Prospectus, any Preliminary Prospectus, any Issuer Free Writing Prospectus and the Prospectus and amendments and supplements thereto and the mailing and delivering of copies thereof to the Underwriters and dealers; (ii) the cost of printing or producing any Agreement among Underwriters, this Agreement, any Blue Sky memoranda (subject to the limitations set forth below), closing documents (including any compilations thereof) and any other documents in connection with the offering, purchase, sale and delivery of the Securities; (iii) all expenses in connection with the qualification of the Securities for offering and sale under state securities laws as provided in Section 5(d) hereof, including the fees and disbursements of counsel for the Underwriters in connection with such qualification; (iv) the cost of preparing the Securities; (v) the fees and expenses of any transfer agent or registrar; (vi) any cost incurred in connection with the listing of the Securities on NASDAQ; and (vii) all other costs and expenses incident to the performance of its obligations hereunder which are not otherwise specifically provided for in this Section 7

(including any transfer taxes on the issuance and sale of the Securities to the Underwriters). It is understood, however, that, except as provided in this Section, and Sections 9 and 12 hereof, the Underwriters will pay all of their own costs and expenses, including the fees of their counsel (other than fees of such counsel plus reasonable disbursements incurred in connection with the preparation, printing and delivery of such Blue Sky memoranda, not to exceed \$7,500), transfer taxes on resale of any of the Securities by them, and any advertising expenses connected with any offers they may make.

8. The obligations of the Underwriters hereunder, as to the Securities to be delivered at each Time of Delivery, shall be subject, in their discretion, to the condition that all representations and warranties and other statements of the Company herein are, at and as of such Time of Delivery, true and correct, the condition that the Company shall have performed all of its obligations hereunder theretofore to be performed, and the following additional conditions:

(a) The Prospectus shall have been filed with the Commission pursuant to Rule 424(b) under the Act within the applicable time period prescribed for such filing by the rules and regulations under the Act and in accordance with Section 5(a) hereof; all material required to be filed by the Company pursuant to Rule 433(d) under the Act shall have been filed with the Commission within the applicable time period prescribed for such filings by Rule 433; no

20

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stop order suspending the effectiveness of the Registration Statement or any part thereof shall have been issued and no proceeding for that purpose shall have been initiated or threatened by the Commission and no notice of objection of the Commission to the use of the Registration Statement or any post-effective amendment thereto pursuant to Rule 401(g)(2) under the Act shall have been received; no stop order suspending or preventing the use of the Prospectus or any Issuer Free Writing Prospectus shall have been initiated or threatened by the Commission; and all requests for additional information on the part of the Commission shall have been complied with to your reasonable satisfaction;

- (b) Davis Polk & Wardwell LLP, counsel for the Underwriters, shall have furnished to you such opinion or opinions, dated such Time of Delivery, with respect to such matters as you may reasonably request, and such counsel shall have received such papers and information as they may reasonably request to enable them to pass upon such matters;
- (c) Cooley LLP, outside counsel for the Company, shall have furnished to you their written opinion and negative assurance letters, each dated such Time of Delivery, in form and substance as attached hereto as Exhibit B.
- (d) Jones Day, outside counsel for the Company, shall have furnished to you their written opinion, dated such Time of Delivery, in the form and substance as attached hereto as Exhibit C.
- (e) Jason Ferrone, the Company's Vice President of Patents and Corporate Development, shall have furnished to you his written opinion, dated such Time of Delivery, in the form and substance as attached hereto as Exhibit D.
- (f) On the date of the Prospectus at a time prior to the execution of this Agreement, at 9:30 a.m., New York City time, on the effective date of any post-effective amendment to the Registration Statement filed subsequent to the date of this Agreement and prior to the last Time of Delivery and also at each Time of Delivery, Ernst & Young LLP shall have furnished to you a letter or letters, dated the respective dates of delivery thereof, in form and substance reasonably satisfactory to you containing statements and information of the type customarily included in accountants' "comfort letters" to underwriters with respect to the historical financial statements and certain financial information contained or incorporated by reference in the Pricing Disclosure Package and the Prospectus.
- (g) (i) Neither the Company nor any of its subsidiaries shall have sustained since the date of the latest audited financial statements included in the Pricing Disclosure Package any loss or interference with its business from fire, explosion, flood or other calamity, whether or not covered by insurance, or from any labor dispute or court or governmental action, order or decree, otherwise than as set forth or contemplated in the Pricing Disclosure Package, and (ii) since the respective dates as of which information is given in the Pricing Disclosure Package there shall not have been any change in the capital stock (except for changes made in the ordinary course of business consistent with past practice pursuant to the Company's equity incentive plans disclosed in Exchange Act Reports filed prior to the date of this Agreement, and changes pursuant to the exercise of options outstanding prior to the date of this Agreement) or long-term debt of the Company or any of its subsidiaries or any change, or any development involving a prospective change, in or affecting the general affairs, management, financial position, stockholders' equity, results of operations, business or prospects of the Company and its subsidiaries, taken as a whole, otherwise than as set forth or contemplated in the Pricing Disclosure Package, the effect of which, in any such

21

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case described in clause (i) or (ii), is in your judgment so material and adverse as to make it impracticable or inadvisable to proceed with the offering or the delivery of the Securities being issued at such Time of Delivery on the terms and in the manner contemplated in this Agreement and in the Prospectus;

- (h) On or after the Applicable Time (i) no downgrading shall have occurred in the rating accorded the Company's debt securities by any "nationally recognized statistical rating organization", as such term is defined in Section 3(a)(62) of the Exchange Act, and (ii) no such organization shall have publicly announced that it has under surveillance or review, with possible negative implications, its rating of any of the Company's debt securities;
- (i) On or after the Applicable Time there shall not have occurred any of the following: (i) a suspension or material limitation in trading in securities generally on the New York Stock Exchange; or on NASDAQ; (ii) a suspension or material limitation in trading in the Company's securities on NASDAQ; (iii) a general moratorium on commercial banking activities declared by either Federal, New York or California State authorities or a material disruption in commercial banking or securities settlement or clearance services in the United States; (iv) the outbreak or escalation of hostilities involving the United States or the declaration by the United States of a national emergency or war or (v) the occurrence of any other calamity or crisis or any change in financial, political or economic conditions in the United States or elsewhere, if the effect of any such event

specified in clause (iv) or (v) in your judgment makes it impracticable or inadvisable to proceed with the offering or the delivery of the Securities being issued at such Time of Delivery on the terms and in the manner contemplated in the Prospectus;

- (j) The Company shall have complied with the provisions of Section 5(e) hereof with respect to the furnishing of prospectuses on the New York Business Day next succeeding the date of this Agreement;
  - (k) The Securities shall have been duly listed, subject to notice of issuance, for listing on NASDAQ;
  - (l) The Company shall have obtained and delivered to the Underwriters executed copies of a lock-up agreement in the form attached hereto as Exhibit A from each of the parties listed on Schedule I thereto; and
  - (m) The Company shall have furnished or caused to be furnished to you at such Time of Delivery certificates of officers of the Company (in their capacity as officers of the Company) satisfactory to you as to the accuracy of the representations and warranties of the Company herein at and as of such Time of Delivery, as to the performance by the Company of all of its obligations hereunder to be performed at or prior to such Time of Delivery, as to the matters set forth in subsections (a) and (g) of this Section and as to such other matters as you may reasonably request.
9. (a) The Company will indemnify and hold harmless each Underwriter against any losses, claims, damages or liabilities, joint or several, to which such Underwriter may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, the Basic Prospectus, any Preliminary Prospectus, the Pricing Disclosure Package or the Prospectus, or any amendment or supplement thereto, any Issuer Free Writing Prospectus or any "issuer information" filed or required to be filed pursuant to Rule 433(d) under the Act, or arise out of

22

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or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, and will reimburse each Underwriter for any legal or other expenses reasonably incurred by such Underwriter in connection with investigating or defending any such action or claim as such expenses are incurred; provided, however, that the Company shall not be liable in any such case to the extent that any such loss, claim, damage or liability arises out of or is based upon an untrue statement or alleged untrue statement or omission or alleged omission made in the Registration Statement, the Basic Prospectus, any Preliminary Prospectus, the Pricing Disclosure Package or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, in reliance upon and in conformity with written information furnished to the Company by any Underwriter through the Representatives expressly for use therein.

- (b) Each Underwriter will indemnify and hold harmless the Company against any losses, claims, damages or liabilities to which the Company may become subject, under the Act or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon an untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, the Basic Prospectus, any Preliminary Prospectus, the Pricing Disclosure Package or the Prospectus, or any amendment or supplement thereto, or any Issuer Free Writing Prospectus, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in each case to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in the Registration Statement, the Basic Prospectus, any Preliminary Prospectus, the Pricing Disclosure Package or the Prospectus or any such amendment or supplement thereto, or any Issuer Free Writing Prospectus, in reliance upon and in conformity with written information furnished to the Company by such Underwriter through the Representatives expressly for use therein; and will reimburse the Company for any legal or other expenses reasonably incurred by the Company in connection with investigating or defending any such action or claim as such expenses are incurred.
- (c) Promptly after receipt by an indemnified party under subsection (a) or (b) above of notice of the commencement of any action, such indemnified party shall, if a claim in respect thereof is to be made against the indemnifying party under such subsection, notify the indemnifying party in writing of the commencement thereof (an "Indemnity Notice"); but the omission so to notify the indemnifying party shall not relieve it from any liability which it may have to any indemnified party otherwise than under such subsection except to the extent such omission shall have actually materially prejudiced the indemnifying party. In case any such action shall be brought against any indemnified party and it shall have provided the indemnifying party an Indemnity Notice, the indemnifying party shall be entitled to participate therein and, to the extent that it shall wish, jointly with any other indemnifying party similarly notified, to assume the defense thereof, with counsel reasonably satisfactory to such indemnified party (who shall not, except with the consent of the indemnified party, be counsel to the indemnifying party), and, after notice from the indemnifying party to such indemnified party of its election so to assume the defense thereof, the indemnifying party shall not be liable to such indemnified party under such subsection for any legal expenses of other counsel or any other expenses, in each case subsequently incurred by such indemnified party, in connection with the defense thereof other than reasonable costs of investigation. No indemnifying party shall be liable for (or be required to make any contribution with respect to)

23

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any settlement of any action or claim effected without its written consent (which consent shall not be unreasonably withheld), but if settled with the consent of the indemnifying party or if there be a final judgment of the plaintiff in any such action, the indemnifying party agrees to indemnify and hold harmless any indemnified party from and against any loss or liability by reason of such settlement or judgment (including making any required contribution pursuant to this Section 9). No indemnifying party shall, without the written consent of the indemnified party, effect the settlement or compromise of, or consent to the entry of any judgment with respect to, any pending or threatened action or claim in respect of which indemnification or contribution may be sought hereunder (whether or not the indemnified party is an actual or potential party to such action or claim) unless such settlement, compromise or judgment (i) includes an unconditional release of the indemnified party from all liability arising out of such action or claim and (ii) does not include a statement as to, or an admission of, fault, culpability or a failure to act, by or on behalf of any indemnified party.

- (d) If the indemnification provided for in this Section 9 is unavailable to or insufficient to hold harmless an indemnified party under subsection (a) or (b) above in respect of any losses, claims, damages or liabilities (or actions in respect thereof) referred to therein, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (or actions in

respect thereof) in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Securities. If, however, the allocation provided by the immediately preceding sentence is not permitted by applicable law or if the indemnified party failed to give the notice required under subsection (c) above then each indemnifying party shall contribute to such amount paid or payable by such indemnified party in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and the Underwriters on the other in connection with the statements or omissions which resulted in such losses, claims, damages or liabilities (or actions in respect thereof), as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand and the Underwriters on the other shall be deemed to be in the same proportion as the total net proceeds from the offering (before deducting expenses) received by the Company bear to the total underwriting discounts and commissions received by the Underwriters, in each case as set forth in the table on the cover page of the Prospectus. The relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Underwriters agree that it would not be just and equitable if contribution pursuant to this subsection (d) were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this subsection (d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages or liabilities (or actions in respect thereof) referred to above in this subsection (d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this subsection (d), no Underwriter shall be required to contribute any amount in excess of the amount by which the total price at which the

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Securities underwritten by it and distributed to investors were offered to investors exceeds the amount of any damages which such Underwriter has otherwise been required to pay by reason of such untrue or alleged untrue statement or omission or alleged omission. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations in this subsection (d) to contribute are several in proportion to their respective underwriting obligations and not joint.

- (e) The obligations of the Company under this Section 9 shall be in addition to any liability which the Company may otherwise have and shall extend, upon the same terms and conditions, to any affiliate of each Underwriter and each person, if any, who controls any Underwriter within the meaning of the Act; and the obligations of the Underwriters under this Section 9 shall be in addition to any liability which the respective Underwriters may otherwise have and shall extend, upon the same terms and conditions, to each officer and director of the Company and to each person, if any, who controls the Company within the meaning of the Act.
10. (a) If any Underwriter shall default in its obligation to purchase the Securities which it has agreed to purchase hereunder at a Time of Delivery, you may in your discretion arrange for you or another party or other parties to purchase such Securities on the terms contained herein at the applicable Time of Delivery. If within thirty-six hours after such default by any Underwriter you do not arrange for the purchase of such Securities, then the Company shall be entitled to a further period of thirty-six hours within which to procure another party or other parties satisfactory to you to purchase such Securities on such terms. In the event that, within the respective prescribed periods, you notify the Company that you have so arranged for the purchase of such Securities, or the Company notifies you that it has so arranged for the purchase of such Securities, you or the Company shall have the right to postpone such Time of Delivery for a period of not more than seven days, in order to effect whatever changes may thereby be made necessary in the Registration Statement or the Prospectus, or in any other documents or arrangements, and the Company agrees to file promptly any amendments or supplements to the Registration Statement or the Prospectus which in your opinion may thereby be made necessary. The term "Underwriter" as used in this Agreement shall include any person substituted under this Section with like effect as if such person had originally been a party to this Agreement with respect to such Securities.
- (b) If, after giving effect to any arrangements for the purchase of the Securities of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above, the aggregate number of such Securities which remains unpurchased does not exceed one-eleventh of the aggregate number of all the Securities to be purchased at such Time of Delivery, then the Company shall have the right to require each non-defaulting Underwriter to purchase the number of Securities which such Underwriter agreed to purchase hereunder at such Time of Delivery and, in addition, to require each non-defaulting Underwriter to purchase its pro rata share (based on the number of Securities which such Underwriter agreed to purchase hereunder) of the Securities of such defaulting Underwriter or Underwriters for which such arrangements have not been made; but nothing herein shall relieve a defaulting Underwriter from liability for its default.
  - (c) If, after giving effect to any arrangements for the purchase of the Securities of a defaulting Underwriter or Underwriters by you and the Company as provided in subsection (a) above,

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the aggregate number of such Securities which remains unpurchased exceeds one-eleventh of the aggregate number of all the Securities to be purchased at such Time of Delivery, or if the Company shall not exercise the right described in subsection (b) above to require non-defaulting Underwriters to purchase Securities of a defaulting Underwriter or Underwriters, then this Agreement (or, with respect to a Subsequent Time of Delivery, the obligation of the Underwriters to purchase and of the Company to sell the Optional Securities) shall thereupon terminate, without liability on the part of any non-defaulting Underwriter or the Company, except for the expenses to be borne by the Company and the Underwriters as provided in Section 7 hereof and the indemnity and contribution agreements in Section 9 hereof; but nothing herein shall relieve a defaulting Underwriter from liability for its default.

11. The respective indemnities, agreements, representations, warranties and other statements of the Company and the several Underwriters, as set forth in this Agreement or made by or on behalf of them, respectively, pursuant to this Agreement, shall remain in full force and effect, regardless of any investigation (or any statement as to the results thereof) made by or on behalf of any Underwriter or any controlling person of any Underwriter, or the Company, or any officer or director or controlling person of the Company, and shall survive delivery of and payment for the Securities.

12. If this Agreement shall be terminated pursuant to Section 10 hereof, the Company shall not then be under any liability to any Underwriter except as provided in Sections 7 and 9 hereof; but, if for any other reason, the Securities are not delivered by or on behalf of the Company as provided herein (a) prior to the First Time of Delivery, the Company will reimburse the Underwriters through you for all expenses approved in writing by you, including fees and disbursements of counsel, reasonably incurred by the Underwriters in making preparations for the purchase, sale and delivery of the Securities, and (b) after the First Time of Delivery, the Company will reimburse the Underwriters through you for all expenses approved in writing by you, including fees and disbursements of counsel, reasonably incurred by the Underwriters solely in making preparations for the purchase, sale and delivery of the Optional Securities relating to the applicable Subsequent Time of Delivery, but in each case the Company shall then be under no further liability to any Underwriter except as provided in Sections 7 and 9 hereof.

13. In all dealings hereunder, you shall act on behalf of each of the Underwriters, and the parties hereto shall be entitled to act and rely upon any statement, request, notice or agreement on behalf of any Underwriter made or given by you jointly.

All statements, requests, notices and agreements hereunder shall be in writing, and if to the Underwriters shall be delivered or sent by mail, telex or facsimile transmission to you as the Representatives in care of Goldman, Sachs & Co., 200 West Street, New York, New York 10282, Attention: Registration Department and J.P. Morgan Securities LLC, 383 Madison Avenue, New York, New York 10179, Attention: Equity Syndicate Desk; and if to the Company shall be delivered or sent by mail, telex or facsimile transmission to the address of the Company set forth in the Prospectus, Attention: Chief Operating Officer (with a copy via facsimile transmission to General Counsel at (760) 268-4922); *provided, however*, that any notice to an Underwriter pursuant to Section 9(c) hereof shall be delivered or sent by mail, telex or facsimile transmission to such Underwriter at its address set forth in its Underwriters' Questionnaire, or telex constituting such Questionnaire, which address will be

26

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supplied to the Company by you upon request. Any such statements, requests, notices or agreements shall take effect upon receipt thereof.

In accordance with the requirements of the USA Patriot Act (Title III of Pub. L. 107-56 (signed into law October 26, 2001)), the Underwriters are required to obtain, verify and record information that identifies their respective clients, including the Company, which information may include the name and address of their respective clients, as well as other information that will allow the Underwriters to properly identify their respective clients.

14. This Agreement shall be binding upon, and inure solely to the benefit of, the Underwriters, the Company and, to the extent provided in Sections 9 and 11 hereof, the officers and directors of the Company and each person who controls the Company or any Underwriter, and their respective heirs, executors, administrators, successors and assigns, and no other person shall acquire or have any right under or by virtue of this Agreement. No purchaser of any of the Securities from any Underwriter shall be deemed a successor or assign by reason merely of such purchase.

15. Time shall be of the essence of this Agreement.

16. The Company acknowledges and agrees that (i) the purchase and sale of the Securities pursuant to this Agreement is an arm's-length commercial transaction between the Company, on the one hand, and the several Underwriters, on the other, (ii) in connection therewith and with the process leading to such transaction each Underwriter is acting solely as a principal and not the agent or fiduciary of the Company, (iii) no Underwriter has assumed an advisory or fiduciary responsibility in favor of the Company with respect to the offering contemplated hereby or the process leading thereto (irrespective of whether such Underwriter has advised or is currently advising the Company on other matters) or any other obligation to the Company except the obligations expressly set forth in this Agreement and (iv) the Company has consulted its own legal and financial advisors to the extent it deemed appropriate. The Company agrees that it will not claim that the Underwriters, or any of them, has rendered advisory services of any nature or respect, or owes a fiduciary or similar duty to the Company, in connection with such transaction or the process leading thereto.

17. This Agreement supersedes all prior agreements and understandings (whether written or oral) between the Company and the Underwriters, or any of them, with respect to the subject matter hereof.

18. **THIS AGREEMENT AND ANY MATTERS RELATED TO THIS TRANSACTION SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO PRINCIPLES OF CONFLICT OF LAWS THAT WOULD RESULT IN THE APPLICATION OF ANY LAW OTHER THAN THE LAWS OF THE STATE OF NEW YORK. The Company agrees that any suit or proceeding arising in respect of this agreement or our engagement will be tried exclusively in the U.S. District Court for the Southern District of New York or, if that court does not have subject matter jurisdiction, in any state court located in The City and County of New York and the Company agrees to submit to the jurisdiction of, and to venue in, such courts.**

19. The Company and each of the Underwriters hereby irrevocably waives, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to this Agreement or the transactions contemplated hereby.

27

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20. This Agreement may be executed by any one or more of the parties hereto in any number of counterparts, each of which shall be deemed to be an original, but all such respective counterparts shall together constitute one and the same instrument.

21. Notwithstanding anything herein to the contrary, the Company (and the Company's employees, representatives, and other agents) are authorized to disclose to any and all persons, the tax treatment and tax structure of the potential transaction and all materials of any kind (including tax opinions and other tax analyses) provided to the Company relating to that treatment and structure, without the Underwriters' imposing any limitation of any kind. However, any information relating to the tax treatment and tax structure shall remain confidential (and the foregoing sentence shall not apply) to the extent necessary to enable any person to comply with securities laws. For this purpose, "tax treatment" means US federal and state income tax treatment, and "tax structure" is limited to any facts that may be relevant to that treatment.



If the foregoing is in accordance with your understanding, please sign and return to us a counterpart hereof, and upon the acceptance hereof by you, on behalf of each of the Underwriters, this letter and such acceptance hereof shall constitute a binding agreement between each of the Underwriters and the Company. It is understood that your acceptance of this letter on behalf of each of the Underwriters is pursuant to the authority set forth in a form of Agreement among Underwriters, the form of which shall be submitted to the Company for examination upon request, but without warranty on your part as to the authority of the signers thereof.

[Signature Page Follows]

28

Very truly yours,

**Isis Pharmaceuticals, Inc.**

By: /s/ Stanley T. Crooke, M.D., Ph.D.  
Name: Stanley T. Crooke, M.D., Ph.D.  
Title: Chief Executive Officer

[Signature Page to Underwriting Agreement]

Accepted as of the date hereof:

**Goldman, Sachs & Co.**

By: /s/ Adam T. Greene  
Name: Adam T. Greene  
Title: Vice President

**J.P. Morgan Securities LLC**

By: /s/ Khaled Habayeb  
Name: Khaled Habayeb  
Title: Executive Director

On behalf of each of the Underwriters

[Signature Page to Underwriting Agreement]

SCHEDULE I

<u>Underwriter</u>	<u>Number of Firm Securities to be Purchased</u>
Goldman, Sachs & Co.	3,060,000
J.P. Morgan Securities LLC	3,060,000
Stifel, Nicolaus & Company, Incorporated	1,080,000
BMO Capital Markets Corp.	720,000
Cowen and Company, LLC	720,000
Needham & Company, LLC	360,000
Total	<u>9,000,000</u>

A-1

SCHEDULE II

- (a) Approved Supplemental Disclosure Documents:
  - (i) Investor road show slide presentation
- (b) Pricing Disclosure Package
  - (i) Approved Supplemental Disclosure Documents

(ii) The price to public of the Securities

(c) Additional Documents Incorporated by Reference: None

A-2

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**Exhibit A**

**Form of Lock-Up Agreement**

A-3

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**Exhibit B**

**Form of Cooley Opinion**

B-4

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**Form of Cooley Negative Assurance Letter**

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**Exhibit C**

**Form of Jones Day Opinion**

C-1

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**Exhibit D**

**Form of Internal IP Opinion**

D-1

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## OPINION OF PATRICK R. O'NEIL

May 8, 2013

Isis Pharmaceuticals, Inc.  
2855 Gazelle Court  
Carlsbad, CA 92010

Ladies and Gentlemen:

I have acted as counsel to Isis Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), with respect to certain matters in connection with the offering by the Company of up to 10,350,000 shares of the Company's common stock, par value \$0.001 (the "**Shares**"), including up to 1,350,000 shares of common stock that may be sold upon the exercise of a 30-day option granted by the Company, in each case pursuant to a Registration Statement on Form S-3 (No. 333-188407) (the "**Registration Statement**"), filed with the Securities and Exchange Commission (the "**Commission**") under the Securities Act of 1933, as amended (the "**Act**"), the prospectus included within the Registration Statement (the "**Base Prospectus**"), and the prospectus supplement dated May 8, 2013 relating to the Shares, filed with the Commission pursuant to Rule 424(b) of the Rules and Regulations of the Act (the "**Prospectus Supplement**"). (The Base Prospectus and Prospectus Supplement are collectively referred to as the "**Prospectus**.") All of the Shares are to be sold by the Company as described in the Registration Statement and Prospectus.

In connection with this opinion, I have examined and relied upon the Registration Statement, the Prospectus, the Company's Certificate of Incorporation and Bylaws, as currently in effect, and the originals or copies certified to my satisfaction of such records, documents, certificates, opinions, memoranda and other instruments as in my judgment are necessary or appropriate to enable me to render the opinion expressed below. As to certain factual matters, I have relied upon certificates of officers of the Company and have not independently sought to verify such matters.

In rendering this opinion, I have assumed the genuineness and authenticity of all signatures on original documents; the authenticity of all documents submitted to me as originals; the conformity to originals of all documents submitted to me as copies; the accuracy, completeness and authenticity of certificates of public officials; and the due authorization, execution and delivery of all documents where authorization, execution and delivery are prerequisites to the effectiveness of such documents.

My opinion herein is expressed solely with respect to the federal laws of the United States and the Delaware General Corporation Law. My opinion is based on these laws as in effect on the date hereof. I express no opinion as to whether the laws of any jurisdiction are applicable to the subject matter hereof. I am not rendering any opinion as to compliance with any federal or state law, rule or regulation relating to securities, or to the sale or issuance thereof.

On the basis of the foregoing and in reliance thereon, and subject to the qualifications herein stated, I am of the opinion that, the Shares when sold in accordance with the Registration Statement and the Prospectus, will be validly issued, and the Shares fully paid and nonassessable.

I hereby consent to the reference to me under the caption "Legal Matters" in the Prospectus included in the Registration Statement and to the filing of this opinion as an exhibit to a current report of the Company on Form 8-K. In giving this consent, I do not admit that I am in the category of persons whose consent is required under Section 7 of the Act.

Very truly yours,

/s/ Patrick R. O'Neil

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Patrick R. O'Neil  
Senior Vice President, Legal and  
General Counsel

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## ISIS PHARMACEUTICALS ANNOUNCES PROPOSED PUBLIC OFFERING OF COMMON STOCK

CARLSBAD, Calif., May 7, 2013 — Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it intends to offer for sale 9 million shares of its common stock in an underwritten public offering. In connection with this offering, Isis intends to grant the underwriters an option to purchase an additional 1.35 million shares of its common stock. All shares in the offering are being offered by Isis. The offering is subject to market conditions, and there can be no assurance as to whether or when the offering may be completed, or as to the actual size or terms of the offering.

Goldman, Sachs & Co. and J. P. Morgan Securities LLC are acting as joint book-running managers in the offering. Stifel is acting as lead manager. BMO Capital Markets, Cowen and Company, LLC and Needham & Company are acting as co-managers.

The securities described above are being offered by Isis pursuant to a shelf registration statement previously filed with the Securities and Exchange Commission (the "SEC"), which became effective on May 7, 2013. A preliminary prospectus supplement related to the offering will be filed with the SEC and will be available on the SEC's website located at <http://www.sec.gov>. Copies of the preliminary prospectus supplement and the accompanying prospectus relating to these securities may be obtained, when available, from Goldman, Sachs & Co. (Attn: Prospectus Department, 200 West Street, New York, New York 10282, Fax: 212-902-9316 or Email at [prospectus-ny@ny.email.gs.com](mailto:prospectus-ny@ny.email.gs.com) or by calling 1-866-471-2526) or J.P. Morgan Securities LLC (c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717 or by calling 866-803-9204). Electronic copies of the prospectus supplements may be obtained by visiting EDGAR on the SEC's website at <http://www.sec.gov/>

This press release shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or other jurisdiction.

### ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, in the United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. Isis' patents provide strong and extensive protection for its drugs and technology.

### ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis' financing plans, including statements related to Isis' offering of common stock. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject

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to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. 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 are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2012 and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

Isis Pharmaceuticals® is a registered trademark of Isis Pharmaceuticals, Inc. KYNAMRO™ is a trademark of Genzyme Corporation.

### 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

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## ISIS PHARMACEUTICALS PRICES PUBLIC OFFERING OF COMMON STOCK

CARLSBAD, Calif., May 8, 2013 — Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the pricing of an underwritten public offering of 9,000,000 shares of its common stock, offered at a price to the public of \$19.00 per share. The gross proceeds to Isis from this offering are expected to be \$171.0 million, before deducting the underwriting discount and other estimated offering expenses payable by Isis. The offering is expected to close on or about May 14, 2013, subject to customary closing conditions. In addition, Isis has granted the underwriters a 30-day option to purchase at the public offering price up to an aggregate of 1,350,000 additional shares of its common stock. Isis anticipates using the net proceeds from the offering to increase its drug development activities, develop select drugs in its pipeline to later stages of development prior to partnering, and for general corporate and working capital purposes.

Goldman, Sachs & Co. and J. P. Morgan Securities LLC are acting as joint book-running managers in the offering. Stifel is acting as lead manager. BMO Capital Markets, Cowen and Company, LLC and Needham & Company are acting as co-managers.

The securities described above are being offered by Isis pursuant to a shelf registration statement previously filed with the Securities and Exchange Commission (the "SEC"), which became effective on May 7, 2013. A final prospectus supplement related to the offering will be filed with the SEC and will be available on the SEC's website located at <http://www.sec.gov>. Copies of the final prospectus supplement and the accompanying prospectus relating to these securities may be obtained, when available, from Goldman, Sachs & Co. (Attn: Prospectus Department, 200 West Street, New York, New York 10282, Fax: 212-902-9316 or Email at [prospectus-ny@ny.email.gs.com](mailto:prospectus-ny@ny.email.gs.com) or by calling 1-866-471-2526) or J.P. Morgan Securities LLC (c/o Broadridge Financial Solutions, 1155 Long Island Avenue, Edgewood, NY 11717 or by calling 866-803-9204). Electronic copies of the prospectus supplements may be obtained by visiting EDGAR on the SEC's website at <http://www.sec.gov/>.

This press release shall not constitute an offer to sell or the solicitation of an offer to buy these securities, nor shall there be any sale of these securities in any state or jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of any such state or other jurisdiction.

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### ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT

This press release includes forward-looking statements regarding Isis' financing plans, including statements related to Isis' offering of common stock and intended use of the proceeds of the offering.

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Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential of KYNAMRO, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. 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 are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2012 and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

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