UNITED STATES
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) July 18, 2013

ACELRX PHARMACEUTICALS, INC.

(Exact name of registrant as specified in charter)

DELAWARE	**001-35068**	**41-2193603**
(State of incorporation)	**(Commission File No.)**	**(IRS Employer Identification No.)**

351 Galveston Drive
Redwood City, CA 94063
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (650) 216-3500

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 (see General Instruction A.2. below):

☐ 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 Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under Exchange Act (17 CFR 240.13e-4(c))

Item 8.01 Other Events.

Public Offering

On July 18, 2013, AcelRx Pharmaceuticals, Inc. ("***AcelRx***," "***we***," "***our***" or "***us***") entered into an underwriting agreement (the "***Underwriting Agreement***") with Jefferies LLC and Piper Jaffray & Co., as representatives of the several underwriters named therein (collectively, the " ***Underwriters***"), relating to the issuance and sale of 3,800,000 shares of our common stock, par value $0.001 per share. The price to the public in this offering is $11.65 per share and the Underwriters have agreed to purchase the shares from us pursuant to the Underwriting Agreement at a price of $10.951 per share. The net proceeds to us from this offering are expected to be approximately $41.6 million, after deducting the underwriting discounts and commissions and other estimated offering expenses payable by us. The closing of the offering is expected to take place on or about July 23, 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 570,000 shares of our common stock, which option has been exercised in full.

The Underwriting Agreement contains customary representations, warranties and agreements by us, customary conditions to closing, indemnification obligations of AcelRx and the Underwriters, including for liabilities under the Securities Act of 1933, as amended (the " ***Act***"), 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 the Company's effective registration statement on Form S-3 and an accompanying prospectus (Registration Statement No. 333-183237) (the "***Registration Statement***") previously filed with the Securities and Exchange Commission (the " ***SEC***") and a preliminary and final prospectus supplement thereunder, and pursuant to a related registration statement on Form S-3 (No. 333-190003) previously filed with the SEC pursuant to Rule 462(b) of the Act. The Underwriting Agreement is filed as Exhibit 1.1 to this report, and the description of the material terms of the Underwriting Agreement is qualified in its entirety by reference to such exhibit. A copy of the opinion of Cooley LLP relating to the legality of the issuance and sale of the shares in the offering is attached as Exhibit 5.1 hereto.

Updated Company Disclosure

AcelRx is filing information for the purpose of supplementing and updating certain risks and uncertainties that could materially adversely affect its business, financial condition or results of operations from the description included under the heading "Item 1A. Risk Factors" in its Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, filed with the SEC on May 8, 2013. AcelRx is also updating certain aspects of the description of its business from that described under the heading, "Item 1. Business" in the Company's Annual Report on Form 10-K for the year ended December 31, 2012, filed with the SEC on March 12, 2013. The updated Company disclosures are filed herewith as Exhibit 99.1 and are incorporated herein by reference.

Forward-Looking Statements

This report contains "forward-looking" statements, including, without limitation, all statements related to the completion, timing and size of the public offering. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include, without limitation, risks and uncertainties related to market conditions and the satisfaction of customary closing conditions related to the public offering. There can be no assurance that AcelRx will be able to complete the proposed public offering on the anticipated terms, or at all. AcelRx will need to raise additional capital to fund its operations and may be unable to raise capital when needed, which would force AcelRx to delay, reduce or eliminate its product development programs or commercialization efforts. Additional risks and uncertainties relating to AcelRx and its business can be found in the updated risk factors filed herewith as Exhibit 99.1. AcelRx expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statements are based.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
1.1	Purchase Agreement, dated July 18, 2013, by and between AcelRx Pharmaceuticals, Inc. and Jefferies LLC and Piper Jaffray & Co.
5.1	Opinion of Cooley LLP.
23.1	Consent of Cooley LLP (included in Exhibit 5.1).
99.1	Updated Company Disclosure.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: July 19, 2013

ACELRX PHARMACEUTICALS, INC.

By: /s/ James H. Welch
Name: James H. Welch
Title: Chief Financial Officer

EXHIBIT INDEX

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Exhibit 1.1

EXECUTION COPY

3,800,000 Shares[1]

ACELRX PHARMACEUTICALS, INC.

Common Stock

PURCHASE AGREEMENT

July 18, 2013

JEFFERIES LLC
PIPER JAFFRAY & CO.
As Representatives of the several Underwriters
named in Schedule I hereto

c/o Jefferies LLC
520 Madison Avenue
New York, New York 10022

c/o Piper Jaffray & Co.
800 Nicollet Mall
Minneapolis, MN 55402

Ladies and Gentlemen:

AcelRx Pharmaceuticals, Inc., a Delaware corporation (the ***"Company"***), proposes to sell to the several Underwriters named in Schedule I hereto (the ***"Underwriters"***) an aggregate of authorized but unissued 3,800,000 shares (the ***"Firm Shares"***) of Common Stock, $0.001 par value per share (the ***"Common Stock"***), of the Company. The Company has also granted to the several Underwriters an option to purchase up to 570,000 additional shares of Common Stock on the terms and for the purposes set forth in Section 3 hereof (the ***"Option Shares"***). The Firm Shares and any Option Shares purchased pursuant to this Purchase Agreement are herein collectively called the ***"Securities."***

The Company hereby confirms its agreement with respect to the sale of the Securities to the several Underwriters, for whom you are acting as representatives (the ***"Representatives"***).

1. ***Registration Statement and Prospectus***. The Company has prepared and filed with the Securities and Exchange Commission (the ***"Commission"***) a shelf registration statement on Form S-3, File No. 333-183237, including a base prospectus (the ***"Base Prospectus"***) to be used in connection with the public offering and sale of the Securities. Such registration statement, as

[1] Plus an option granted by the Company to the Underwriters to purchase up to 570,000 additional shares.

amended, including the financial statements, exhibits and schedules thereto, in the form in which it became effective under the Securities Act of 1933, as amended (the ***"Act"***), and the rules and regulations promulgated thereunder (the ***"Rules and Regulations"***), including all documents incorporated or deemed to be incorporated by reference therein and any information deemed to be a part thereof at the time of effectiveness pursuant to Rule 430B under the Act, is called the ***"Original Registration Statement."*** Any registration statement filed by the Company pursuant to Rule 462(b) under the Act in connection with the offer and sale of the Securities is called the ***"Rule 462(b) Registration Statement,"*** and from and after the date and time of filing of any such Rule 462(b) Registration Statement the term ***"Registration Statement"*** shall include the Original Registration Statement and the Rule 462(b) Registration Statement. The preliminary prospectus supplement dated July 17, 2013, describing the Securities and the offering thereof (the ***"Preliminary Prospectus Supplement"***), together with the Base Prospectus, is called the ***"Preliminary Prospectus,"*** and the Preliminary Prospectus and any other prospectus supplement to the Base Prospectus in preliminary form that describes the Securities and the offering thereof and is used prior to the filing of the Prospectus (as defined below), together with the Base Prospectus, is called a ***"preliminary prospectus."*** As used herein, the term ***"Prospectus"*** shall mean the final prospectus supplement to the Base Prospectus that describes the Securities and the offering thereof (the ***"Final Prospectus Supplement"***), together with the Base Prospectus, in the form first used by the Underwriters to confirm sales of the Securities or in the form first made available to the Underwriters by the Company to meet requests of purchasers pursuant to Rule 173 under the Act. References herein to the Preliminary Prospectus, any preliminary prospectus and the Prospectus shall refer to both the prospectus supplement and the Base Prospectus components of such prospectus. As used herein, ***"Applicable Time"*** is 9:00 am (Eastern time) on July 18, 2013. As used herein, ***"free writing prospectus"*** has the meaning set forth in Rule 405 under the Act, and ***"Time of Sale Prospectus"*** means the Preliminary Prospectus, as amended or supplemented immediately prior to the Applicable Time, together with Issuer General Free Writing Prospectus(es) issued at or prior to the Applicable Time and set forth on Schedule II hereo. All references in this Agreement to the Registration Statement, the Preliminary Prospectus, any preliminary prospectus, the Base Prospectus and the Prospectus shall include the documents incorporated or deemed to be incorporated by reference therein. All references in this Agreement to financial statements and schedules and other information which are "contained," "described," "disclosed," "contemplated," "included," "set forth" or "stated" in, or "part of" the Registration Statement, the Preliminary Prospectus, the Base Prospectus, the Time of Sale Prospectus or the Prospectus, and all other references of like import, shall be deemed to mean and include all such financial statements and schedules and other information which is or is deemed to be incorporated by reference in the Registration Statement, the Preliminary Prospectus, the Base Prospectus, the Time of Sale Prospectus or the Prospectus, as the case may be. All references in this Agreement to amendments or supplements to the Registration Statement, the Preliminary Prospectus, the Base Prospectus, the Time of Sale Prospectus or the Prospectus shall be deemed to mean and include the filing of any document under the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder (collectively, the ***"Exchange Act"***) that is or is deemed to be incorporated by reference in the Registration Statement, the Preliminary Prospectus, the Base Prospectus, the Time of Sale Prospectus or the Prospectus, as the case may be.

2. ***Representations and Warranties of the Company***.

(a) The Company represents and warrants to, and agrees with, the several Underwriters as follows:

(i) The Registration Statement has become effective under the Act. At the time the Company's Annual Report on Form 10-K for the year ended December 31, 2012 (the ***"Annual Report"***) was filed with the Commission, or, if later, at the time the Registration Statement was originally filed with the Commission, the Company met the then-applicable requirements for use of Form S-3 under the Act. The conditions to the use of Form S-3 in connection with the offering and sales of the Securities as contemplated hereby, including General Instruction I.B.1 of Form S-3, have been satisfied. The documents incorporated by reference in the Registration Statement, the Time of Sale Prospectus and the Prospectus, at the time they were or hereafter are filed with the Commission, or became effective under the Exchange Act, as the case may be, complied and will comply in all material respects with the requirements of the Exchange Act.

(ii) No order preventing or suspending the use of any Preliminary Prospectus has been issued by the Commission and the Preliminary Prospectus included in the Time of Sale Disclosure Package (as defined below), at the time of filing thereof or the time of first use within the meaning of the Rules and Regulations, complied in all material respects with the requirements of the Act and the Rules and Regulations 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; except that the foregoing shall not apply to statements in or omissions from any Preliminary Prospectus in reliance upon, and in conformity with, written information furnished to the Company by you, or by any Underwriter through you, specifically for use in the preparation thereof, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 6(f).

(iii) As of the time any part of each of the Original Registration Statement and the 462(b) Registration Statement (or any post-effective amendment thereto) became effective and at all other subsequent times until expiration of the Prospectus Delivery Period (as defined below), upon the filing or first use within the meaning of the Rules and Regulations of the Prospectus (or any supplement to the Prospectus) and at all other subsequent times until expiration of the Prospectus Delivery Period and at the First Closing Date and Option Closing Date, (A) the Registration Statement and the Prospectus (in each case, as so amended and/or supplemented) conformed or will conform in all material respects to the requirements of the Act and the Rules and Regulations, (B) the Registration Statement (as so amended) did not or will not include 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, and (C) the Prospectus (as so supplemented) did not or will not include 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 light of the circumstances in which they are or were made, not misleading; except that each of the

foregoing shall not apply to statements in or omissions from any such document in reliance upon, and in conformity with, written information furnished to the Company by you, or by any Underwriter through you, specifically for use in the preparation thereof, it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 6(f). No stop order suspending the effectiveness of the Registration Statement has been issued, and no proceeding for that purpose has been initiated or communicated to the Company, or, to the Company's knowledge, threatened by the Commission.

(iv) Neither (A) the Time of Sale Prospectus and the information on Schedule III hereto, all considered together (collectively, the ***"Time of Sale Disclosure Package"***), nor (B) any individual Issuer Limited-Use Free Writing Prospectus, when considered together with the Time of Sale Disclosure Package, includes or included as of the Applicable Time any untrue statement of a material fact or omit or omitted as of the Applicable Time 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. The preceding sentence does not apply to statements in or omissions from any Time of Sale Disclosure Package or any Issuer Free Writing Prospectus, if any, based upon and in conformity with written information furnished to the Company by you or by any Underwriter through you specifically for use therein; it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 6(f). As used in this paragraph and elsewhere in this Agreement:

(1) ***"Issuer Free Writing Prospectus"*** means any "issuer free writing prospectus," as defined in Rule 433 under the Act, relating to the Securities in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g) under the Act.

(2) ***"Issuer General Free Writing Prospectus"*** means any Issuer Free Writing Prospectus that is intended for general distribution to prospective investors, as evidenced by its being specified in Schedule II to this Agreement.

(3) ***"Issuer Limited-Use Free Writing Prospectus"*** means any Issuer Free Writing Prospectus that is not an Issuer General Free Writing Prospectus.

(v) (A) Each Issuer Free Writing Prospectus, as of its issue date and at all subsequent times through the completion of the public offer and sale of the Securities or until any earlier date that the Company notified or notifies the Representatives as described in Section 4(a)(iii)(B), did not, does not and will not include any information that conflicted, conflicts or will conflict with the information contained in the Registration Statement, the Preliminary Prospectus or the Prospectus. The foregoing sentence does not apply to statements in or omissions from any Issuer Free Writing Prospectus based upon and in conformity with written information furnished to the Company by you or by any Underwriter through you specifically for use therein; it being understood and agreed that the only such information furnished by any Underwriter consists of the information described as such in Section 6(f).

(B) (1) At the time of filing the Registration Statement and (2) at the date hereof, the Company was not and is not an "ineligible issuer," as defined in Rule 405 under the Act, including the Company in the preceding three years not having been convicted of a felony or misdemeanor or having been made the subject of a judicial or administrative decree or order as described in Rule 405 under the Act (without taking account of any determination by the Commission pursuant to Rule 405 that it is not necessary that the Company be considered an ineligible issuer), nor an "excluded issuer" as defined in Rule 164 under the Act.

(C) Each Issuer Free Writing Prospectus satisfied, as of its issue date and at all subsequent times through the completion of the public offer and sale of the Securities, all other conditions to use thereof as set forth in Rules 164 and 433 under the Act.

(vi) The documents incorporated by reference in the Registration Statement, the Time of Sale 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, the Rules and Regulations or the Exchange Act, as applicable, and none of such documents contained any untrue statement of a material fact or omitted to state any material fact required to be stated therein or necessary to make the statements therein, in light of the circumstances under which they were made, not misleading.

(vii) The financial statements of the Company, together with the related notes, set forth in the Registration Statement, the Time of Sale Disclosure Package and Prospectus comply in all material respects with the requirements of the Act and fairly present, in all material respects, the financial condition of the Company as of the dates indicated and the results of operations and changes in cash flows for the periods therein specified in conformity with generally accepted accounting principles in the United States consistently applied throughout the periods involved (except in the case of unaudited financial statements, which are subject to normal year-end adjustments and do not contain certain footnotes as permitted by the applicable rules of the Commission); the supporting schedules included in the Registration Statement present fairly the information required to be stated therein; all non-GAAP financial measures (as such term is defined by the rules and regulations of the Commission), if any, included in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus comply with Regulation G under the Exchange Act and Item 10 of Regulation S-K under the Act, as applicable; and, except as disclosed in the Time of Sale Disclosure Package and the Prospectus, there are no material off-balance sheet arrangements (as defined in Regulation S-K under the Act, Item 303(a)(4)(ii)) or any other relationships with unconsolidated entities or other persons, that may have a material current or, to the knowledge of the Company, material future effect on the Company's financial condition, results of operations, liquidity, capital expenditures, capital resources or significant components of revenue or expenses. No other financial statements or schedules are required to be included in the Registration Statement, the Time

of Sale Disclosure Package or the Prospectus. Ernst & Young, which has expressed its opinion with respect to the financial statements and schedules included in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus, is (x) an independent public accounting firm within the meaning of the Act and the Rules and Regulations, (y) a registered public accounting firm (as defined in Section 2(a)(12) of the Sarbanes-Oxley Act of 2002 (the ***"Sarbanes-Oxley Act"***)) and (z) not in violation of the auditor independence requirements of the Sarbanes-Oxley Act.

(viii) The Company has been duly organized and is validly existing as a corporation in good standing under the laws of its jurisdiction of incorporation. The Company has full corporate power and authority to own its properties and conduct its business as currently being carried on and as described in the Registration Statement, the Time of Sale Disclosure Package and Prospectus, and is duly qualified to do business as a foreign corporation in good standing in each jurisdiction in which it owns or leases real property or in which the conduct of its business makes such qualification necessary and in which the failure to so qualify would have a material adverse effect upon the business, prospects, management, properties, operations, condition (financial or otherwise) or results of operations of the Company (***"Material Adverse Effect"***).

(ix) Except as contemplated in the Time of Sale Disclosure Package and in the Prospectus, subsequent to the respective dates as of which information is given in the Time of Sale Disclosure Package, the Company has not incurred any material liabilities or obligations, direct or contingent, or entered into any material transactions, or declared or paid any dividends or made any distribution of any kind with respect to its capital stock; and there has not been any change in the capital stock (other than a change in the number of outstanding shares of Common Stock due to the issuance of shares upon the exercise, vesting or conversion of outstanding options, restricted stock units, warrants, rights or convertible securities), or any material change in the short-term or long-term debt, or any issuance of options, restricted stock units, warrants, convertible securities or other rights to purchase the capital stock (except pursuant to equity compensation plans or arrangements described in the Time of Sale Disclosure Package and in the Prospectus) of the Company, or any material adverse change in the general affairs, condition (financial or otherwise), business, prospects, management, properties, operations or results of operations of the Company (***"Material Adverse Change"***) or any development which could reasonably be expected to result in any Material Adverse Change.

(x) Except as set forth in the Time of Sale Disclosure Package and in the Prospectus, there is not pending, or to the knowledge of the Company, threatened or contemplated, any action, suit or proceeding (a) to which the Company is a party or (b) which has as the subject thereof any officer or director of the Company, any employee benefit plan sponsored by the Company or any property or assets owned or leased by the Company before or by any court or Governmental Authority (as defined below), or any arbitrator, which, individually or in the aggregate, would reasonably be expected to result in any Material Adverse Change, or would materially and adversely affect the ability of the Company to perform its obligations under this Agreement or which are otherwise material in the context of the sale of the Securities (except that the foregoing representation as to any

non-employee outside director of the Company with respect to any pending action, suit or proceeding shall be to the knowledge of the Company). There are no current or, to the knowledge of the Company, pending, legal, governmental or regulatory actions, suits or proceedings (x) to which the Company is subject or (y) which has as the subject thereof any officer or director of the Company, any employee plan sponsored by the Company or any property or assets owned or leased by the Company, that are required to be described in the Registration Statement, Time of Sale Disclosure Package and Prospectus by the Act, the Rules and Regulations or the Exchange Act and that have not been so described (except that the foregoing representation as to any non-employee outside director of the Company shall be to the knowledge of the Company).

(xi) There are no statutes, regulations, contracts or documents that are required to be described in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus or required to be filed as exhibits to the Registration Statement by the Act, the Rules and Regulations or the Exchange Act that have not been so described or filed.

(xii) This Agreement has been duly authorized, executed and delivered by the Company, and constitutes a valid, legal and binding obligation of the Company, enforceable in accordance with its terms, except as rights to indemnity hereunder may be limited by federal or state securities laws and except as such enforceability may be limited by bankruptcy, insolvency, reorganization or similar laws affecting the rights of creditors generally and subject to general principles of equity. The execution, delivery and performance of this Agreement and the consummation of the transactions herein contemplated will not (A) conflict with or result in a breach or violation of any of the terms or provisions of, or constitute a default under, or result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company is a party or by which the Company is bound or to which any of the property or assets of the Company is subject, (B) result in any violation of the provisions of the Company's charter or by-laws or (C) result in the violation of any law or statute or any judgment, order, rule, regulation or decree of any court or arbitrator or federal, state, local or foreign governmental agency or regulatory authority having jurisdiction over the Company or any of its properties or assets (each, a ***"Governmental Authority"***). No consent, approval, authorization or order of, or registration or filing with any Governmental Authority is required to be obtained or made by the Company for the execution, delivery and performance of this Agreement or for the consummation of the transactions contemplated hereby, including the issuance or sale of the Securities by the Company, except such as may be required under the Act, the rules of FINRA or state securities or blue sky laws; and the Company has full corporate power and authority to enter into this Agreement and to consummate the transactions contemplated hereby, including the authorization, issuance and sale of the Securities as contemplated by this Agreement.

(xiii) All of the issued and outstanding shares of capital stock of the Company, including the outstanding shares of Common Stock, are duly authorized and validly issued, fully paid and nonassessable, have been issued in compliance with all federal

and state and foreign securities laws, were not issued in violation of or subject to any preemptive rights or other rights to subscribe for or purchase securities that have not been waived or satisfied in writing (a copy of which has been delivered to counsel to the Representatives), and the holders thereof are not subject to personal liability by reason of being such holders; the Securities which may be sold hereunder by the Company have been duly authorized and, when issued, delivered and paid for in accordance with the terms of this Agreement, will have been validly issued and will be fully paid and nonassessable, and the holders thereof will not be subject to personal liability by reason of being such holders; and the capital stock of the Company, including the Common Stock, conforms to the description thereof in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus. Except as otherwise stated in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus, there are no preemptive rights or other rights to subscribe for or to purchase, or any restriction upon the voting or transfer of, any shares of Common Stock pursuant to the Company's charter, by-laws or any agreement or other instrument to which the Company is a party or by which the Company is bound. Except as disclosed in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus, neither the filing of the Registration Statement nor the offering or sale of the Securities as contemplated by this Agreement gives rise to any rights for or relating to the registration of any shares of Common Stock or other securities of the Company that have not been waived in writing (a copy of which has been delivered to counsel to the Representatives). Except as described in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus, there are no options, restricted stock units, warrants, agreements, contracts or other rights in existence to purchase or acquire from the Company any shares of the capital stock of the Company. The Company has an authorized and outstanding capitalization as set forth in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus under the caption "Capitalization." The Common Stock (including the Securities) conforms in all material respects to the description thereof contained in the Time of Sale Disclosure Package and the Prospectus. The description of the Company's stock option, stock bonus and other stock plans or arrangements, and the options, restricted stock units or other rights granted thereunder, set forth in the Time of Sale Disclosure Package and the Prospectus accurately and fairly presents the information required to be shown with respect to such plans, arrangements, options, restricted stock units and rights.

(xiv) The Company holds, and is operating in compliance in all material respects with, all franchises, grants, authorizations, licenses, permits, easements, consents, certificates and orders of any Governmental Authority or self-regulatory body required for the conduct of its business and, to the knowledge of the Company, all such franchises, grants, authorizations, licenses, permits, easements, consents, certifications and orders are valid and in full force and effect; and the Company has not received notice of any revocation or modification of any such franchise, grant, authorization, license, permit, easement, consent, certification or order or has reason to believe that any such franchise, grant, authorization, license, permit, easement, consent, certification or order will not be renewed in the ordinary course.

(xv) The Company has good and marketable title to all property (whether real or personal) described in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus as being owned by it, in each case free and clear of all material liens, claims, security interests, other encumbrances or defects except such as are described in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus. The property held under lease by the Company is held by it under valid, subsisting and enforceable leases with only such exceptions with respect to any particular lease as do not interfere in any material respect with the conduct of the business of the Company.

(xvi) Except as described in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus, the Company owns, possesses, or can acquire on reasonable terms, all Intellectual Property necessary for the conduct of the Company's business as now conducted or as described in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus to be conducted, except as such failure to own, possess, or acquire such rights would not result in a Material Adverse Effect. Furthermore, (A) to the knowledge of the Company, 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, threatened, action, suit, proceeding or claim by others challenging the Company's rights 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; (C) the Intellectual Property owned by the Company, and to the knowledge of the Company, the Intellectual Property licensed to the Company, has not been adjudged invalid or unenforceable, in whole or in part, and there is no pending or threatened 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; (D) there is no pending or, to the knowledge of the Company, threatened action, suit, proceeding or claim by others that the Company infringes, misappropriates or otherwise violates any Intellectual Property or other proprietary rights of others, the Company has not received any written notice of such claim and the Company is unaware of any other fact which would form a reasonable basis for any such claim; and (E) to the knowledge of the Company, no employee 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 such employee's employment with the Company or actions undertaken by the employee while employed with the Company, except as such violation would not result in a Material Adverse Effect. ***"Intellectual Property"*** shall mean all patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets, domain names, technology, know-how and other intellectual property.

(xvii) The Company is not in violation of its charter or by-laws, nor is the Company in material breach of or otherwise in default in any material respect of, and no event has occurred which, with notice or lapse of time or both, would constitute such a

default in the performance of any material obligation, agreement or condition contained in any bond, debenture, note, indenture, loan agreement or any other material contract, lease or other instrument to which it is subject or by which it may be bound, or to which any of the material property or assets of the Company is subject.

(xviii) The Company has duly and properly filed or caused to be filed with the U.S. Patent and Trademark Office (the ***"PTO"***) and applicable foreign and international patent authorities all patent applications owned by the Company (the ***"Company Patent Applications"***). To the knowledge of the Company, the Company has complied with the PTO's duty of candor and disclosure for the Company Patent Applications and has made no material misrepresentation in the Company Patent Applications. To the knowledge of the Company, except as disclosed in the Time of Sale Disclosure Package and the Prospectus, the Company Patent Applications disclose patentable subject matters, and the Company has not been notified of any inventorship challenges nor has any interference been declared or provoked nor is any material fact known by the Company that would preclude the issuance of patents with respect to the Company Patent Applications or would render such patents invalid or unenforceable, except in each case as would not individually or in the aggregate have a Material Adverse Effect. To the knowledge of the Company, except as disclosed in the Time of Sale Disclosure Package and the Prospectus, no third party possesses rights to the Company's Intellectual Property that, if exercised, could enable such party to develop products competitive to those the Company intends to develop as described in each of the Time of Sale Disclosure Package and the Prospectus

(xix) The Company has timely filed all federal, state, local and foreign income and franchise tax returns required to be filed, and are not in default in the payment of any taxes which were payable pursuant to said returns or any assessments with respect thereto, other than (A) those currently payable without penalty or interest, or (B) which the Company is contesting in good faith. There is no pending dispute with any taxing authority relating to any of such returns, and the Company has no knowledge of any proposed liability for any tax to be imposed upon the properties or assets of the Company for which there is not an adequate reserve reflected in the Company's financial statements included in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus.

(xx) The Company has not distributed and will not distribute any prospectus or other offering material in connection with the offering and sale of the Securities other than any Preliminary Prospectus, the Time of Sale Disclosure Package or the Prospectus or other materials permitted by the Act to be distributed by the Company; *provided, however,* that, except as set forth on Schedule II, the Company has not made and will not make any offer relating to the Securities that would constitute a free writing prospectus, except in accordance with the provisions of Section 4(a)(xviii) of this Agreement.

(xxi) The Company is subject to and in compliance in all material respects with the reporting requirements of Section 13 or Section 15(d) of the Exchange Act. The Common Stock is registered pursuant to Section 12(b) of the Exchange Act and is listed on

The NASDAQ Global Market. The Company has filed with The NASDAQ Stock Market a notification of the listing of the Securities on The NASDAQ Global Market. Except as previously disclosed to counsel for the Underwriters or as set forth in the Time of Sale Disclosure Package and the Prospectus, there are no affiliations with members of the FINRA among the Company's officers or directors or, to the knowledge of the Company, any five percent or greater stockholders of the Company that are affiliated with any of the Company's officers or directors.

(xxii) The Company, directly or indirectly, does not own capital stock or other equity or ownership or proprietary interest in any corporation, partnership, association, trust or other entity.

(xxiii) The Company maintains a system of internal accounting controls sufficient to provide reasonable assurances that (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles in the United States and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences. Except as disclosed in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus, the Company's internal control over financial reporting is effective and none of the Company, its board of directors and audit committee is aware of any "significant deficiencies" or "material weaknesses" (each as defined by the Public Company Accounting Oversight Board) in its internal control over financial reporting, or any fraud, whether or not material, that involves management or other employees of the Company who have a significant role in the Company's internal controls; and since the end of the latest audited fiscal year, there has been no change in the Company's internal control over financial reporting (whether or not remediated) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting. The Company's board of directors has, subject to the exceptions and cure periods specified in the applicable NASDAQ Marketplace Rules (***"Exchange Rules"***) and the Exchange Act, validly appointed an audit committee to oversee internal accounting controls whose composition satisfies the applicable requirements of the Exchange Rules and the Company's board of directors and/or the audit committee has adopted a charter that satisfies the requirements of the Exchange Rules.

(xxiv) Other than as contemplated by this Agreement, the Company has not incurred any liability for any finder's or broker's fee or agent's commission in connection with the execution and delivery of this Agreement or the consummation of the transactions contemplated hereby.

(xxv) The Company carries, or is covered by, insurance from insurers with appropriately rated claims paying abilities in such amounts and covering such risks as is adequate for the conduct of its business and the value of its properties and as is customary for companies engaged in similar businesses in similar industries; all policies of insurance

and any fidelity or surety bonds insuring the Company or its business, assets, employees, officers and directors are in full force and effect; the Company is in compliance with the terms of such policies and instruments in all material respects; there are no claims by the Company under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause; and the Company has no 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 have a Material Adverse Effect.

(xxvi) The Company is not and, after giving effect to the offering and sale of the Securities, will not be an "investment company," as such term is defined in the Investment Company Act of 1940, as amended.

(xxvii) The Company is in compliance in all material respects with all applicable provisions of the Sarbanes-Oxley Act and the rules and regulations of the Commission thereunder.

(xxviii) The Company has established and maintains disclosure controls and procedures (as defined in Rules 13a-14 and 15d-14 under the Exchange Act) and such controls and procedures are effective in ensuring that material information relating to the Company is made known to the principal executive officer and the principal financial officer. The Company has utilized such controls and procedures in preparing and evaluating the disclosures in the Registration Statement, in the Time of Sale Disclosure Package and in the Prospectus.

(xxix) Each of the Company, its officers, directors and current employees has not violated, and the Company's participation in the offering will not violate, and the Company has instituted and maintains policies and procedures designed to ensure continued compliance with, each of the following laws: (a) anti-bribery laws, including but not limited to, any applicable law, rule, or regulation of any locality, including but not limited to any law, rule, or regulation promulgated to implement the OECD Convention on Combating Bribery of Foreign Public Officials in International Business Transactions, signed December 17, 1997, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, or any other law, rule or regulation of similar purposes and scope, (b) anti-money laundering laws, including but not limited to, applicable federal, state, international, foreign or other laws, regulations or government guidance regarding anti-money laundering, including, without limitation, Title 18 US. Code section 1956 and 1957, the Patriot Act, the Bank Secrecy Act, and international anti-money laundering principles or procedures by an intergovernmental group or organization, such as the Financial Action Task Force on Money Laundering, of which the United States is a member and with which designation the United States representative to the group or organization continues to concur, all as amended, and any Executive order, directive, or regulation pursuant to the authority of any of the foregoing, or any orders or licenses issued thereunder or (c) laws and regulations imposing U.S. economic sanctions measures, including, but not limited to, the International Emergency Economic Powers Act, the Trading with the Enemy Act, the United Nations Participation Act and the Syria Accountability and Lebanese Sovereignty Act, all as

amended, and any Executive Order, directive, or regulation pursuant to the authority of any of the foregoing, including the regulations of the United States Treasury Department set forth under 31 CFR, Subtitle B, Chapter V, as amended, or any orders or licenses issued thereunder.

(xxx) Neither the Company nor, to the knowledge of the Company, any director, officer or employee of the Company, is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Department of the Treasury.

(xxxi) To the knowledge of the Company, no transaction has occurred between or among the Company, on the one hand, and any of the Company's officers, directors or 5% stockholders or any affiliate or affiliates of any such officer, director or 5% stockholders that is required to be described under the Rules and Regulations that is not so described in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus. The Company has not, directly or indirectly, extended or maintained credit, or arranged for the extension of credit, or renewed an extension of credit, in the form of a personal loan to or for any of its directors or executive officers in violation of applicable laws, including Section 402 of the Sarbanes-Oxley Act.

(xxxii) Except as disclosed in the Time of Disclosure Package and the Prospectus, the Company is not in violation of any statute, any rule, regulation, decision or order of any Governmental Authority or any court, domestic or foreign, relating to the use, disposal or release of hazardous or toxic substances or relating to the protection or restoration of the environment or human exposure to hazardous or toxic substances (collectively, ***"Environmental Laws"***), owns or operates any real property contaminated with any substance that is subject to any environmental laws, is liable for any off-site disposal or contamination pursuant to any environmental laws, or is subject to any claim relating to any environmental laws, which violation, contamination, liability or claim would individually or in the aggregate, have a Material Adverse Effect; and the Company is not aware of any pending investigation which could reasonably be expected to lead to such a claim.

(xxxiii) The Company (A) is in compliance, in all material respects, with any and all applicable foreign, federal, state and local laws, rules, regulations, treaties, statutes and codes promulgated by any and all governmental authorities (including pursuant to the Occupational Health and Safety Act) relating to the protection of human health and safety in the workplace (***"Occupational Laws"***); (B) has received all material permits, licenses or other approvals required of it under applicable Occupational Laws to conduct its business as currently conducted, except as would not reasonably be expected to result in a Material Adverse Effect; and (C) is in compliance, in all material respects, with all terms and conditions of such permit, license or approval. No action, proceeding, revocation proceeding, writ, injunction or claim is pending or, to the knowledge of the Company, threatened against the Company relating to Occupational Laws.

(xxxiv) (i) To the knowledge of the Company, no "prohibited transaction" as defined under Section 406 of ERISA or Section 4975 of the Code and not exempt under ERISA Section 408 and the regulations and published interpretations thereunder has occurred with respect to any Employee Benefit Plan. At no time has the Company or any ERISA Affiliate maintained, sponsored, participated in, contributed to or has or had any liability or obligation in respect of any Employee Benefit Plan subject to Part 3 of Subtitle B of Title I of ERISA, Title IV of ERISA, or Section 412 of the Code or any "multiemployer plan" as defined in Section 3(37) of ERISA or any multiple employer plan for which the Company or any ERISA Affiliate has incurred or could reasonably be expected to incur any liability under Section 4063 or 4064 of ERISA. No Employee Benefit Plan provides or promises, or at any time provided or promised, retiree health, retiree life insurance, or other retiree welfare benefits except as may be required by the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended, or similar state law. Each Employee Benefit Plan is and has been operated in material compliance with its terms and all applicable laws, including but not limited to ERISA and the Code and, to the knowledge of the Company, no event has occurred (including a "reportable event" as such term is defined in Section 4043 of ERISA) and no condition exists that would subject the Company or any ERISA Affiliate to any material tax, fine, lien, penalty or liability imposed by ERISA, the Code or other applicable law. Each Employee Benefit Plan intended to be qualified under Code Section 401(a) is so qualified and has a favorable determination or opinion letter from the IRS upon which it can rely, and any such determination or opinion letter remains in effect and has not been revoked; to the knowledge of the Company, nothing has occurred since the date of any such determination or opinion letter that is reasonably likely to adversely affect such qualification; (ii) with respect to each Foreign Benefit Plan, such Foreign Benefit Plan (A) if intended to qualify for special tax treatment, meets, in all material respects, the requirements for such treatment, and (B) if required to be funded, is funded to the extent required by applicable law, and with respect to all other Foreign Benefit Plans, adequate reserves therefore have been established on the accounting statements of the applicable Company; (iii) the Company does not have any obligations under any collective bargaining agreement with any union and no organization efforts are underway with respect to Company employees. As used in this Agreement, ***"Code"*** means the Internal Revenue Code of 1986, as amended; ***"Employee Benefit Plan"*** means any "employee benefit plan" within the meaning of Section 3(3) of ERISA, including, without limitation, all stock purchase, stock option, stock-based severance, employment, change-in-control, medical, disability, fringe benefit, bonus, incentive, deferred compensation, employee loan and all other employee benefit plans, agreements, programs, policies or other arrangements, whether or not subject to ERISA, under which (A) any current or former employee, director or independent contractor of the Company has any present or future right to benefits and which are contributed to, sponsored by or maintained by the Company or (B) the Company has any present or future obligation or liability; ***"ERISA"*** means the Employee Retirement Income Security Act of 1974, as amended; ***"ERISA Affiliate"*** means any member of the company's controlled group as defined in Code Section 414(b), (c), (m) or (o); and ***"Foreign Benefit Plan"*** means any Employee Benefit Plan established, maintained or contributed to outside of the United States of America or which covers any employee working or residing outside of the United States.

(xxxv) Except as disclosed in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus, the Company has not granted rights to develop, manufacture, produce, assemble, distribute, license, market or sell its product candidates to any other person and is not bound by any agreement that affects the exclusive right of the Company to develop, manufacture, produce, assemble, distribute, license, market or sell its products.

(xxxvi) No labor problem or dispute with the employees of the Company exists or is threatened or, to the knowledge of the Company, imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its principal suppliers, contractors or customers, that would reasonably be expected to have a Material Adverse Effect.

(xxxvii) Any third-party statistical and market-related data included in the Registration Statement, the Time of Sale Disclosure Package and the Prospectus are based on or derived from sources that the Company believes to be reliable and accurate in all material respects.

(xxxviii) There are no outstanding loans, advances (except normal advances for business expenses in the ordinary course of business) or guarantees or indebtedness, in each case made by or from the Company to or for the benefit of any of the officers or directors of the Company or any of the Company's stockholders, except as disclosed in the Time of Sale Disclosure Package and the Prospectus.

(xxxix) Except as disclosed in the Time of Sale Disclosure Package and the Prospectus, the Company (i) does not have any material lending or other relationship with any bank or lending affiliate of any Underwriter and (ii) does not intend to use any of the proceeds from the sale of the Securities hereunder to repay any outstanding debt owed to any affiliate of any Underwriter.

(xl) To the knowledge of the Company, and except as would not, individually or in the aggregate, have a Material Adverse Effect, the Company's manufacturing facilities and operations are in compliance with applicable regulations of the U.S. Food and Drug Administration (the ***"FDA"***), including current Good Manufacturing Practices.

(xli) To the knowledge of the Company, the descriptions of the results of the studies, tests and trials contained in the Time of Sale Disclosure Package and the Prospectus are accurate in all material respects; there are no other studies or tests, the results of which could reasonably be expected to discredit or call into question the results described in the Time of Sale Disclosure Package and the Prospectus; and except with respect to clinical trial holds that have been lifted with respect to completed clinical trials previously conducted by the Company, the Company has not received any notice or correspondence from the FDA or any other governmental agency requiring the termination or suspension of any pre-clinical or clinical trials conducted by, or on behalf of, the Company or in which the Company has participated.

(xlii) Except as would not, individually or in the aggregate, have a Material Adverse Effect, the Company is in compliance in all material respects with all applicable rules and regulations of the FDA, and all applicable U.S. and foreign laws, statutes, ordinances, rules or regulations.

(b) Any certificate signed by any officer of the Company and delivered to you or to counsel for the Underwriters shall be deemed a representation and warranty by the Company to each Underwriter as to the matters covered thereby.

3. ***Purchase, Sale and Delivery of Securities*** .

(a) On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company agrees to issue and sell 3,800,000 Firm Shares, and each Underwriter agrees, severally and not jointly, to purchase from the Company the number of Firm Shares set forth opposite the name of such Underwriter in Schedule I hereto. The purchase price for each Firm Share shall be $10.951 per share (the ***"Basic Purchase Price"***). The obligation of each Underwriter to the Company shall be to purchase from the Company that number of Firm Shares (to be adjusted by the Representatives to avoid fractional shares) which represents the same proportion of the number of Firm Shares to be sold by the Company pursuant to this Agreement as the number of Firm Shares set forth opposite the name of such Underwriter in Schedule I hereto represents to the total number of Firm Shares to be purchased by all Underwriters pursuant to this Agreement. In making this Agreement, each Underwriter is contracting severally and not jointly; except as provided in paragraph (c) of this Section 3 and in Section 8 hereof, the agreement of each Underwriter is to purchase only the respective number of Firm Shares specified in Schedule I.

The Firm Shares will be delivered by the Company to you for the accounts of the several Underwriters against payment of the purchase price therefor by wire transfer of same day funds payable to the order of the Company, at the offices of Morgan, Lewis & Bockius LLP, Two Palo Alto Square, Palo Alto, CA 94306, or such other location as may be mutually acceptable, at 9:00 a.m. Eastern time on the third (or if the Securities are priced, as contemplated by Rule 15c6-1(c) under the Exchange Act, after 4:30 p.m. Eastern time, the fourth) full business day following the date hereof, or at such other time and date as you and the Company determine pursuant to Rule 15c6-1(a) under the Exchange Act, such time and date of delivery being herein referred to as the ***"First Closing Date."*** If the Representatives so elect, delivery of the Firm Shares may be made by credit through full fast transfer to the accounts at The Depository Trust Company designated by the Representatives. Certificates representing the Firm Shares, in definitive form and in such denominations and registered in such names as you may request upon at least two business days' prior notice to the Company, or evidence of their issuance, will be made available for checking at a reasonable time preceding the First Closing Date at the offices of Morgan, Lewis & Bockius LLP, Two Palo Alto Square, Palo Alto, CA 94306, or such other location as may be mutually acceptable.

(b) On the basis of the representations, warranties and agreements herein contained, but subject to the terms and conditions herein set forth, the Company, with respect to the Option Shares, hereby grants to the several Underwriters an option to purchase all or any portion of the Option Shares at a price per share equal to the Basic Purchase Price, less an amount per share equal to any dividend or distribution declared by the Company and payable on the Firm Shares but not payable on Optional Shares. The option granted hereunder may be exercised in whole or in part, at any time and from time to time, within 30 days after the effective date of this Agreement upon notice (confirmed in writing) by the Representatives to the Company setting forth the aggregate number of Option Shares as to which the several Underwriters are exercising the option, the names and denominations in which the certificates for the Option Shares are to be registered and the date and time, as determined by you, when the Option Shares are to be delivered, each such time and date being herein referred to as the "Option Closing" and "Option Closing Date", respectively; provided, however, that each Option Closing Date shall not be earlier than the First Closing Date nor earlier than the second business day after the date on which the option shall have been exercised. If the option is exercised, the obligation of each Underwriter shall be to purchase from the Company up to an aggregate of 570,000 Option Shares. The number of Option Shares to be purchased by each Underwriter shall be the same percentage of the total number of Option Shares to be purchased by the several Underwriters as the number of Firm Shares to be purchased by such Underwriter is of the total number of Firm Shares to be purchased by the several Underwriters, as adjusted by the Representatives in such manner as the Representatives deem advisable to avoid fractional shares. No Option Shares shall be sold and delivered unless the Firm Shares previously have been, or simultaneously are, sold and delivered.

The Option Shares will be delivered by the Company to you for the accounts of the several Underwriters against payment of the purchase price therefor by wire transfer of same day funds payable to the order of the Company at the offices of Morgan, Lewis & Bockius LLP, Two Palo Alto Square, Palo Alto, CA 94306, or such other location as may be mutually acceptable at 10:00 a.m., Eastern time, on each Option Closing Date. If the Representatives so elect, delivery of the Option Shares may be made by credit through full fast transfer to the accounts at The Depository Trust Company designated by the Representatives. Certificates representing the Option Shares in definitive form and in such denominations and registered in such names as you have set forth in your notice of option exercise, or evidence of their issuance, will be made available for checking at a reasonable time preceding each Option Closing Date at the office of Morgan, Lewis & Bockius LLP, Two Palo Alto Square, Palo Alto, CA 94306, or such other location as may be mutually acceptable.

(c) It is understood that you, individually and not as Representatives of the several Underwriters, may (but shall not be obligated to) make payment to the Company on behalf of any Underwriter for the Securities to be purchased by such Underwriter. Any such payment by you shall not relieve any such Underwriter of any of its obligations hereunder. Nothing herein contained shall constitute any of the Underwriters an unincorporated association or partner with the Company.

4. ***Covenants***.

(a) The Company covenants and agrees with the several Underwriters as follows:

(i) If the Original Registration Statement has not already been declared effective by the Commission, the Company will use its best efforts to cause the Original Registration Statement and any post-effective amendments thereto to become effective as promptly as possible; the Company will notify you promptly of the time when the Original Registration Statement or any post-effective amendment to the Original Registration Statement has become effective or any supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Original Registration Statement or Prospectus or additional information; if the Company has elected to rely on Rule 430B of the Rules and Regulations, the Company will prepare and file a Prospectus containing the information omitted therefrom pursuant to Rule 430B of the Rules and Regulations with the Commission within the time period required by, and otherwise in accordance with the provisions of, Rules 424(b) and 430B of the Rules and Regulations; if the Company has elected to rely upon Rule 462(b) of the Rules and Regulations to increase the size of the offering registered under the Act and the Rule 462(b) Registration Statement has not yet been filed and become effective, the Company will prepare and file the Rule 462 Registration Statement with the Commission within the time period required by, and otherwise in accordance with the provisions of, Rule 462(b) and the Act; the Company will prepare and file with the Commission, promptly upon your request, any amendments or supplements to the Registration Statement or Prospectus that, based on the advice of counsel, may be necessary or advisable in connection with the distribution of the Securities by the Underwriters; and the Company will furnish the Representatives and counsel for the Underwriters a copy of any proposed amendment or supplement to the Registration Statement or Prospectus and will not file any amendment or supplement to the Registration Statement or Prospectus to which you shall reasonably object by notice to the Company after having been furnished a copy a reasonable time prior to the filing.

(ii) The Company will advise you, promptly after it shall receive notice or obtain knowledge thereof, of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, or any post-effective amendment thereto or preventing or suspending the use of any Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus or any Issuer Free Writing Prospectus, of the suspension of the qualification of the Securities for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and the Company will promptly use its best efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued. Additionally, the Company agrees that it shall comply with the provisions of Rules 424(b) and 430B, as applicable, under the Act and will use its reasonable efforts to confirm that any filings made by the Company under Rule 424(b), Rule 433 or Rule 462 were received in a timely manner by the Commission.

(iii) (A) Within the time during which a prospectus (assuming the absence of Rule 172) relating to the Securities is required to be delivered under the Act by

any Underwriter or dealer (the ***"Prospectus Delivery Period"***), the Company will use its best effort to comply with all requirements imposed upon it by the Act, as now and hereafter amended, and by the Rules and Regulations, as from time to time in force, so far as necessary to permit the continuance of sales of or dealings in the Securities as contemplated by the provisions hereof, the Time of Sale Disclosure Package and the Prospectus. If during such period any event occurs as a result of which the Prospectus (or if the Prospectus is not yet available to prospective purchasers, the Time of Sale Disclosure Package) would include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend the Registration Statement or supplement the Prospectus (or if the Prospectus is not yet available to prospective investors, the Time of Sale Disclosure Package) to comply with the Act, the Company will promptly notify you and will amend the Registration Statement or supplement the Prospectus (or, if the Prospectus is not yet available to prospective purchasers, the Time of Sale Disclosure Package) (at the expense of the Company) so as to correct such statement or omission or effect such compliance.

(B) If at any time following issuance of an Issuer Free Writing Prospectus and through the Prospectus Delivery Period, there occurred or occurs an event or development as a result of which such Issuer Free Writing Prospectus conflicted or would conflict, during such time, with the information contained in the Registration Statement, the Preliminary Prospectus or the Prospectus relating to the Securities or included or, during such time, would include an untrue statement of a material fact or omitted or would omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances prevailing at that subsequent time, not misleading, the Company has promptly notified or promptly will notify the Representatives and has promptly amended or will promptly amend or supplement, at its own expense, such Issuer Free Writing Prospectus to eliminate or correct such conflict, untrue statement or omission.

(iv) The Company shall take or cause to be taken all necessary action to qualify the Securities for sale under the securities laws of such jurisdictions as you reasonably designate and to continue such qualifications in effect so long as required for the distribution of the Securities, except that the Company shall not be required in connection therewith to qualify as a foreign corporation or to execute a general consent to service of process in any state.

(v) The Company will furnish, at its own expense, to the Underwriters and counsel for the Underwriters copies of the Registration Statement (one of which will be signed and will include all consents and exhibits filed therewith), and to the Underwriters and any dealer each Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus, any Issuer Free Writing Prospectus and all amendments and supplements to such documents, in each case as soon as available and in such quantities as you may from time to time reasonably request.

(vi) During a period of five years commencing with the date hereof, the Company will furnish to the Representatives, as the Representatives may from time to

time reasonably request in writing, copies of all periodic and special reports furnished to the stockholders of the Company generally, and all public information, documents and reports filed with the Commission, FINRA or any securities exchange (other than any such information, documents and reports that are filed with the Commission electronically via EDGAR or any successor system).

(vii) The Company will make generally available to its security holders as soon as practicable, but in no event later than 15 months after the end of the Company's current fiscal quarter, an earnings statement (which need not be audited) covering a 12-month period beginning after the effective date of the Original Registration Statement (or if later the Rule 462(b) Registration Statement) that shall satisfy the provisions of Section 11(a) of the Act and Rule 158 of the Rules and Regulations.

(viii) The Company, whether or not the transactions contemplated hereunder are consummated or this Agreement is prevented from becoming effective under the provisions of Section 9(a) hereof or is terminated, will pay or cause to be paid (A) all expenses (including transfer taxes allocated to the respective transferees) incurred in connection with the delivery to the Underwriters of the Securities, (B) all expenses and fees (including, without limitation, fees and expenses of the Company's accountants and counsel but, except as otherwise provided below, not including fees of the Underwriters' counsel) in connection with the preparation, printing, filing, delivery, and shipping of the Registration Statement (including all amendments, schedules, and exhibits thereto), the Securities, each Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus, any Issuer Free Writing Prospectus and any amendment thereof or supplement thereto, and the printing, delivery, and shipping of this Agreement and other underwriting documents, including Blue Sky Memoranda (covering the states and other applicable jurisdictions); (C) all filing fees and reasonable fees and disbursements of the Underwriters' counsel incurred in connection with the qualification of the Securities for offering and sale by the Underwriters or by dealers under the securities or blue sky laws of the states and other jurisdictions which you shall designate, (D) the fees and expenses of any transfer agent or registrar, (E) the filing fees and fees and disbursements of Underwriters' counsel incident to any required review and approval by FINRA of the terms of the sale of the Securities, which shall not exceed $20,000 in the aggregate, (F) listing fees, if any, (G) the cost and expenses of the Company relating to investor presentations or any "road show" undertaken in connection with marketing of the Securities, and (I) all other costs and expenses of the Company incident to the performance of its obligations hereunder that are not otherwise specifically provided for herein, *provided that* the Underwriters shall pay for the expenses incurred by the Company in connection with the offering contemplated hereunder in the amount of $354,160, and in the event the Underwriters exercise the option, either in full or in part, to purchase the Option Shares, an additional $53,124. If the sale of the Firm Shares provided for herein is not consummated by reason of action by the Company pursuant to Section 9(a)(i) hereof which prevents this Agreement from becoming effective, if this Agreement is terminated by the Representatives pursuant to Section 9 hereof prior to the First Closing or if the sale of the Firm Shares provided for herein is not consummated by reason of any failure, refusal or inability on the part of the Company to perform any agreement on its or their part to be performed, or because any other condition of the Underwriters' obligations hereunder required to be fulfilled by the Company prior to

the First Closing is not fulfilled, the Company will reimburse the several Underwriters for all out-of-pocket disbursements (including but not limited to fees and disbursements of counsel, printing expenses, travel expenses, postage, facsimile and telephone charges) incurred by the Underwriters in connection with their investigation, preparing to market and marketing the Securities or in contemplation of performing their obligations hereunder. Except as provided in this Section 4(a)(viii) and in Section 6 hereof, the Underwriters will pay all of their own costs and expenses, including, but not limited to, the fees and disbursements of Underwriters' counsel, stock transfer taxes, if any, on resale of any of the Securities by them, and any advertising expenses of the Underwriters in connection with any offers they may make.

(ix) The Company will apply the net proceeds from the sale of the Securities to be sold by it hereunder for the purposes set forth in the Time of Sale Disclosure Package and in the Prospectus.

(x) The Company will not, without the prior written consent of Jefferies LLC and Piper Jaffray & Co., from the date of execution of this Agreement and continuing to and including the date 90 days after the date of the Prospectus (the ***"Lock-Up Period"***), (A) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, any shares of Stock or any securities convertible into or exercisable or exchangeable for Common Stock or (B) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the Common Stock, whether any such transaction described in clause (A) or (B) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise, except (i) to the Underwriters pursuant to this Agreement; (ii) to one or more counterparties in connection with the consummation of any strategic partnership, joint venture, collaboration or other strategic transaction, or the acquisition or license of any business products or technology, provided that the total number of shares of Common Stock, including shares underlying convertible or exercisable securities, which may be issued pursuant to this subclause (ii) may not exceed an aggregate of 2,080,366 shares of Common Stock of the Company (as adjusted for stock splits, stock dividends, reclassification and the like after the date hereof), (iii) pursuant to the exercise, vesting or conversion of any options, restricted stock units, warrants, rights or convertible securities outstanding on the date hereof or (iv) pursuant to any equity compensation plans or arrangements described in the Time of Sale Disclosure Package and the Prospectus. For the avoidance of doubt, this Section 4(a)(x) shall not apply to the filing by the Company of any registration statement under the Act (including any amendments or supplements to existing registration statements or the prospectuses included therein) (x) on Form S-8 in respect of any equity compensation plans or arrangements maintained or assumed by the Company or (y) that the Company is contractually obligated to file pursuant to the terms of that certain Securities Purchase Agreement, dated as of May 29, 2012, by and between the Company and the other parties thereto, and nothing in this Section 4(a)(x) shall otherwise

be deemed to prohibit or limit the Company's ability to effect any such registrations or filings. In addition, notwithstanding anything to the contrary contained in this Section 4(a)(x), the Company shall be permitted to keep in effect the At Market Issuance Sales Agreement, dated August 31, 2012, by and between the Company and MLV & Co. LLC (the "MLV Agreement") and the prospectus supplement to the Base Prospectus related thereto, *provided* that pursuant to the terms of this Section 4(a)(x), no sales of Common Stock under the Sales Agreement may be made during the Lock-Up Period. If (1) during the last 17 days of the Lock-Up Period, (a) the Company issues an earnings release, (b) the Company publicly announces material news or (c) a material event relating to the Company occurs; or (2) prior to the expiration of the Lock-Up Period, the Company announces that it will release earnings results during the 16-day period beginning on the last day of the Lock-Up Period, then the restrictions in this Agreement, unless otherwise waived by Jefferies LLC and Piper Jaffray & Co. in writing, shall continue to apply until the expiration of the date that is 18 calendar days after the date on which (a) the Company issues the earnings release, (b) the Company publicly announces material news or (c) a material event relating to the Company occurs; *provided*, *however*, that such extension shall not apply if (i) the Company's securities are "actively traded securities" (as defined in Regulation M of the Exchange Act), (ii) the Company meets the applicable requirements of paragraph (a)(1) of Rule 139 under the Act in the manner contemplated by NASD Conduct Rule 2711(f)(4), and (iii) the provisions of NASD Conduct Rule 2711(f)(4) are not applicable to any research reports relating to the Company published or distributed by any of the Underwriters during the 15 days before or after the last day of the Lock-Up Period (before giving effect to such extension). The Company will provide the Representatives with prior notice of any such announcement (but not the substance of such announcement) that gives rise to the extension of the Lock-Up Period.

(xi) The Company has caused to be delivered to you prior to the date of this Agreement a letter, in the form of Exhibit A hereto (the ***"Lock-Up Agreement"***), from each of the Company's directors and officers and certain stockholders of the Company, which such directors, officer and stockholders are listed on Exhibit B hereto. The Company will enforce the terms of each Lock-Up Agreement, which such obligation will be satisfied solely by issuing stop-transfer instructions to the transfer agent for the Common Stock with respect to any transaction or contemplated transaction that would constitute a breach of or default under the applicable Lock-Up Agreement.

(xii) The Company has not taken and will not take, directly or indirectly, any action designed to or which might reasonably be expected to cause or result in, or which has constituted, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Securities, and has not effected any sales of Common Stock which are required to be disclosed in response to Item 701 of Regulation S-K under the Act which have not been so disclosed in the Registration Statement.

(xiii) The Company will not incur any liability for any finder's or broker's fee or agent's commission in connection with the execution and delivery of this Agreement or the consummation of the transactions contemplated hereby.

(xiv) During the Prospectus Delivery Period, the Company will file on a timely basis with the Commission such periodic and special reports as required by the Rules and Regulations and the Exchange Act.

(xv) During the one-year period from the date of this Agreement, the Company will maintain such controls and other procedures, including without limitation those required by Sections 302 and 906 of the Sarbanes-Oxley Act and the applicable regulations thereunder, that are designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Commission's rules and forms, including without limitation, controls and procedures designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive officer and its principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure, to ensure that material information relating to Company is made known to them by others within those entities.

(xvi) During the one-year period from the date of this Agreement, the Company will comply in all material respects with all applicable provisions of the Sarbanes-Oxley Act.

(xvii) The Company represents and agrees that, unless it obtains the prior written consent of Jefferies LLC, and each Underwriter severally represents and agrees that, unless it obtains the prior written consent of the Company and Jefferies LLC, it has not made and will not make any offer relating to the Securities that would constitute an "issuer free writing prospectus," as defined in Rule 433 under the Act, or that would otherwise constitute a free writing prospectus required to be filed with the Commission; provided that the prior written consent of the parties hereto shall be deemed to have been given in respect of the free writing prospectuses included in Schedule II. Any such free writing prospectus consented to by the Company and Jefferies LLC is hereinafter referred to as a ***"Permitted Free Writing Prospectus."*** The Company represents that it has treated or agrees that it will treat each Permitted Free Writing Prospectus as an "issuer free writing prospectus," as defined in Rule 433, and has complied and will comply with the requirements of Rules 164 and 433 applicable to any Permitted Free Writing Prospectus, including timely Commission filing where required, legending and record keeping. The Company represents that it has satisfied and agrees that it will satisfy the conditions in Rule 433 to avoid a requirement to file with the Commission any electronic road show.

5. ***Conditions of Underwriters' Obligations***. The obligations of the several Underwriters hereunder are subject to the accuracy, as of the date hereof and at each of the First Closing Date and the Option Closing Date (as if made at such Closing Date), of and compliance with all representations, warranties and agreements of the Company contained herein, to the performance by the Company and to the following additional conditions:

(a) The Registration Statement shall have become effective not later than 5:00 p.m., Eastern time, on the date of this Agreement, or such later time and date as you, as Representatives of the several Underwriters, shall approve and all filings required by Rules 424, 430B and 433 of the Rules and Regulations shall have been timely made (without reliance on Rule 424(b)(8) or Rule 164(b)); no stop order suspending the effectiveness of the Registration Statement or any part thereof or any amendment thereof, nor suspending or preventing the use of the Time of Sale Disclosure Package, the Prospectus or any Issuer Free Writing Prospectus shall have been issued; no proceedings for the issuance of such an order shall have been initiated or threatened; and any request of the Commission for additional information (to be included in the Registration Statement, the Time of Sale Disclosure Package, the Prospectus, any Issuer Free Writing Prospectus or otherwise) shall have been complied with to your satisfaction.

(b) The Representatives shall not have advised the Company that (i) the Registration Statement or any amendment thereof or supplement thereto contains an untrue statement of a material fact which, based on the advice of counsel, is material or omits to state a material fact which, based on the advice of counsel, is required to be stated therein or necessary to make the statements therein not misleading, or (ii) the Time of Sale Disclosure Package or the Prospectus, or any amendment thereof or supplement thereto, or any Issuer Free Writing Prospectus contains an untrue statement of fact which, based on the advice of counsel, is material, or omits to state a fact which, based on the advice of counsel, is material and is required to be stated therein, or necessary to make the statements therein, in light of the circumstances under which they are made, not misleading.

(c) Except as contemplated in the Time of Sale Disclosure Package and in the Prospectus, subsequent to the respective dates as of which information is given in the Time of Sale Disclosure Package and the Prospectus, the Company shall have not incurred any material liabilities or obligations, direct or contingent, or entered into any material transactions, or declared or paid any dividends or made any distribution of any kind with respect to its capital stock. There shall not have been any change in the capital stock (other than a change in the number of outstanding shares of Common Stock due to the issuance of shares upon the exercise, vesting or conversion of outstanding options, restricted stock units, warrants, rights or convertible securities), or any material change in the short-term or long-term debt of the Company, or any issuance of options, restricted stock units, warrants, convertible securities or other rights to purchase the capital stock of the Company except pursuant to equity compensation plans or arrangements described in the Time of Sale Disclosure Package and in the Prospectus, or any Material Adverse Change or any development that would result in a Material Adverse Change (whether or not arising in the ordinary course of business), that, in your judgment, makes it impractical or inadvisable to offer or deliver the Securities on the terms and in the manner contemplated in the Time of Sale Disclosure Package and in the Prospectus.

(d) On or after the Time of Sale (i) if applicable, no downgrading shall have occurred in the rating accorded the Company's debt securities or preferred stock by any "nationally recognized statistical organization," as that term is defined by the Commission for purposes of Rule 436(g)(2) under the 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 or preferred stock.

(e) On each Closing Date, there shall have been furnished to you, as Representatives of the several Underwriters, the opinion and negative assurance letter of Cooley LLP, corporate counsel for the Company, each dated such Closing Date and addressed to you in substantially the forms attached hereto as Exhibit B.

(f) On each Closing Date, there shall have been furnished to you, as Representatives of the several Underwriters, the opinion of Cooley LLP, intellectual property counsel for the Company, dated such Closing Date and addressed to you in substantially the form attached hereto as Exhibit C.

(g) On each Closing Date, there shall have been furnished to you, as Representatives of the several Underwriters, the opinion of Cooley LLP, regulatory counsel for the Company, dated such Closing Date and addressed to you in substantially the form attached hereto as Exhibit D.

(h) On each Closing Date, there shall have been furnished to you, as Representatives of the several Underwriters, such opinion or opinions from Morgan, Lewis & Bockius LLP, counsel for the several Underwriters, dated such Closing Date and addressed to you, with respect to the formation of the Company, the validity of the Securities, the Registration Statement, the Time of Sale Disclosure Package or the Prospectus and other related matters as you reasonably may request, and such counsel shall have received such papers and information as they request to enable them to pass upon such matters.

(i) On the date hereof and on each Closing Date you, as Representatives of the several Underwriters, shall have received a letter from Ernst & Young LLP, dated such date and addressed to you, confirming that it is an independent registered public accounting firm within the meaning of the Act and are in compliance with the applicable requirements relating to the qualifications of accountants under Rule 2-01 of Regulation S-X of the Commission, and stating, as of the date of such letter (or, with respect to matters involving changes or developments since the respective dates as of which specified financial information is given in the Time of Sale Disclosure Package, as of a date not prior to the date hereof or more than five days prior to the date of such letter), the conclusions and findings of said firm with respect to the financial information and other matters covered by its letter delivered to you concurrently with the execution of this Agreement, and the effect of the letter so to be delivered on such Closing Date shall be to confirm the conclusions and findings set forth in such prior letter.

(j) On each Closing Date, there shall have been furnished to you, as Representatives of the Underwriters, a certificate, dated such Closing Date and addressed to you, signed by the chief executive officer and by the chief financial officer of the Company, to the effect that:

(i) The representations and warranties of the Company in this Agreement are true and correct, in all material respects, as if made at and as of such Closing Date, and the Company has complied with all the agreements and satisfied all the conditions on its part to be performed or satisfied under this Agreement at or prior to such Closing Date;

(ii) No stop order or other order suspending the effectiveness of the Registration Statement or any part thereof or any amendment thereof or the qualification of the Securities for offering or sale, nor suspending or preventing the use of the Time of Sale Disclosure Package, the Prospectus or any Issuer Free Writing Prospectus, has been issued, and no proceeding for that purpose has been instituted or, to the best of their knowledge, is contemplated by the Commission or any state or regulatory body; and

(iii) The signers of said certificate have carefully examined the Registration Statement, the Time of Sale Disclosure Package and the Prospectus, and any amendments thereof or supplements thereto, and (A) each part of the Registration Statement and the Prospectus, and any amendments thereof or supplements thereto contain, and contained when such part of the Registration Statement, or any amendment thereof, became effective, all statements and information required to be included therein, the Registration Statement, or any amendment thereof, does not contain and did not contain when such part of the Registration Statement, or any amendment thereof, became effective, any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading, and the Prospectus, as amended or supplemented, does not include and did not include as of its date or the time of first use within the meaning of the Rules and Regulations, any untrue statement of material fact or omit to state and did not omit to state as of its date or the time of first use within the meaning of the rules and Regulations a material fact necessary to make the statements therein, in light of the circumstances under which they were made, not misleading, (B) neither (1) the Time of Sale Disclosure Package nor (2) any individual Issuer Limited-Use Free Writing Prospectus, when considered together with the Time of Sale Disclosure Package, include, nor included as of the Applicable Time any untrue statement of a material fact or omits, or omitted as of the Applicable Time, 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, (C) since the Applicable Time there has occurred no event required to be set forth in an amended or supplemented prospectus which has not been so set forth, (D) subsequent to the respective dates as of which information is given in the Time of Sale Disclosure Package and in the Prospectus, the Company has not incurred any material liabilities or obligations, direct or contingent, or entered into any material transactions, not in the ordinary course of business, or declared or paid any dividends or made any distribution of any kind with respect to its capital stock, and except as disclosed in the Time of Sale Disclosure Package and in the Prospectus, there has not been any change in the capital stock (other than a change in the number of outstanding shares of Common Stock due to the issuance of shares upon the exercise, vesting or conversion of outstanding options, restricted stock units, warrants, rights or convertible securities), or any material change in the short-term or long-term debt, or any issuance of options, restricted stock units, warrants, convertible securities or other rights to purchase the capital stock, except pursuant to equity compensation plans or arrangements described in the Time of Sale Disclosure Package and in the Prospectus, of the Company, or any other Material Adverse Change or any development which could reasonably be expected to result in any Material Adverse

Change (whether or not arising in the ordinary course of business), and (E) except as stated in the Time of Sale Disclosure Package and in the Prospectus, there is not pending, or, to the knowledge of the Company, threatened or contemplated, any action, suit or proceeding to which the Company is a party before or by any court, Governmental Agency or any arbitrator, which could reasonably be expected to result in any Material Adverse Change.

(k) The Underwriters shall have received all of the Lock-Up Agreements referenced in Section 4.

(l) The Company shall have furnished to you and counsel for the Underwriters such additional documents, certificates and evidence as you or they may have reasonably requested.

(m) FINRA shall have raised no objection to the fairness and reasonableness of the underwriting terms and arrangements.

(n) The Company shall have filed with The NASDAQ Stock Market a notification of the listing of the Securities on The NASDAQ Global Market and The NASDAQ Stock Market shall have raised no objection to such listing.

All such opinions, certificates, letters and other documents mentioned above and elsewhere in this Agreement will be in compliance with the provisions hereof only if they are satisfactory in form and substance to you and counsel for the Underwriters. The Company will furnish you with such conformed copies of such opinions, certificates, letters and other documents as you shall reasonably request.

6. ***Indemnification and Contribution***.

(a) The Company agrees to indemnify and hold harmless each Underwriter, its affiliates, directors and officers and each person, if any, who controls such Underwriter within the meaning of Section 15 of the Act or Section 20 of the Exchange Act, from and against any losses, claims, damages or liabilities, joint or several, to which such Underwriter may become subject, under the Act or otherwise (including in settlement of any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, if such settlement is effected with the written consent of the Company), 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 and any other information deemed to be a part of the Registration Statement at the time of effectiveness and at any subsequent time pursuant to the Rules and Regulations, if applicable, any Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus, or any amendment or supplement thereto, any Issuer Free Writing Prospectus or in any materials or information provided to investors by, or with the written approval of, the Company in connection with the marketing of the offering of the Common Stock (***"Marketing Materials"***), including any road show or investor presentations made to investors by the Company (whether in person or electronically), 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, in light of (other than in the case of the Registration Statement) the circumstances under which they are made, not misleading, and will reimburse each

Underwriter for any legal or other expenses reasonably incurred by it in connection with preparing, investigating or defending against such loss, claim, damage, liability or action as such expenses are incurred; *provided, however,* that the Company will not be liable in any such case to the extent that any such loss, claim, damage, liability or action arises out of or is based upon an untrue statement or alleged untrue statement or omission or alleged omission made in the Registration Statement, any Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus, or any such amendment or supplement, any Issuer Free Writing Prospectus or in any Marketing Materials, in reliance upon and in conformity with written information furnished to the Company by you, or by any Underwriter through you, specifically for use in the preparation thereof; it being understood and agreed that the only information furnished by an Underwriter consists of the information described as such in Section 6(f).

(b) Each Underwriter will, severally and not jointly, indemnify and hold harmless the Company, its affiliates, directors and officers and each person, if any, who controls the Company within the meaning of Section 15 of the Act and Section 20 of the Exchange Act, from and against any losses, claims, damages or liabilities to which the Company may become subject, under the Act or otherwise (including in settlement of any litigation, or any investigation or proceeding by any governmental agency or body, commenced or threatened, if such settlement is effected with the written consent of such Underwriter), 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, any Preliminary Prospectus, the Time of Sale Disclosure Package, 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, in light of (other than in the case of the Registration Statement) the circumstances under which they are made, 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, any Preliminary Prospectus, the Time of Sale Disclosure Package, the Prospectus, or any such amendment or supplement, or any Issuer Free Writing Prospectus in reliance upon and in conformity with written information furnished to the Company by you, or by such Underwriter through you, specifically for use in the preparation thereof (it being understood and agreed that the only information furnished by an Underwriter consists of the information described as such in Section 6 (f), and will reimburse the Company for any legal or other expenses reasonably incurred by the Company in connection with investigating or defending against any such loss, claim, damage, liability or action as such expenses are incurred.

(c) Promptly after receipt by an indemnified party under subsection (a), (b) or (c) 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; but the omission so to notify the indemnifying party shall not relieve the indemnifying party from any liability that it may have to any indemnified party except to the extent such indemnifying party has been materially prejudiced by such failure (through the forfeiture of substantive rights or defenses). In case any such action shall be brought against any indemnified party, and it shall notify the indemnifying party of the commencement thereof, the indemnifying party shall be entitled to participate in, and, to the extent that it shall wish, jointly with any other indemnifying party similarly notified, to assume the defense

thereof, with counsel satisfactory to such indemnified party, and after notice from the indemnifying party to such indemnified party of the indemnifying party's election so to assume the defense thereof, the indemnifying party shall not be liable to such indemnified party under such subsection for any legal or other expenses subsequently incurred by such indemnified party in connection with the defense thereof other than reasonable costs of investigation; provided, however, that if, in the sole judgment of the Representatives, it is advisable for the Underwriters to be represented as a group by separate counsel, the Representatives shall have the right to employ a single counsel (in addition to local counsel) to represent the Representatives and all Underwriters who may be subject to liability arising from any claim in respect of which indemnity may be sought by the Underwriters under subsection (a) or (b) of this Section 6, in which event the reasonable fees and expenses of such separate counsel shall be borne by the indemnifying party or parties and reimbursed to the Underwriters as incurred. An indemnifying party shall not be obligated under any settlement agreement relating to any action under this Section 6 to which it has not agreed in writing. In addition, no indemnifying party shall, without the prior written consent of the indemnified party (which consent shall not be unreasonably withheld or delayed, effect any settlement of any pending or threatened proceeding unless such settlement includes an unconditional release of such indemnified party for all liability on claims that are the subject matter of such proceeding and does not include a statement as to, or an admission of, fault, culpability or a failure to act by or on behalf of an indemnified party.

(d) If the indemnification provided for in this Section 6 is unavailable or insufficient to hold harmless an indemnified party under subsection (a) or (b) above, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of the losses, claims, damages or liabilities referred to in subsection (a) or (b) above, (i) 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 or (ii) if the allocation provided by clause (i) above is not permitted by applicable law, in such proportion as is appropriate to reflect not only the relative benefits referred to in clause (i) above 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 that resulted in such losses, claims, damages or liabilities, 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 or the Underwriters and the parties' relevant intent, knowledge, access to information and opportunity to correct or prevent such untrue statement or omission. The Company and the Underwriters agree that it would not be just and equitable if contributions pursuant to this subsection (d) were to be 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 in the first sentence of this subsection (d). The amount paid by an indemnified party as a result of the losses, claims, damages or liabilities referred to in the first sentence of this subsection (d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with preparing, investigating or defending against

any action or claim which is the subject of this subsection (d). Notwithstanding the provisions of this subsection (d), in no event shall an Underwriter be required to contribute any amount in excess of the amount by which the total underwriting discounts and commissions received by such Underwriter with respect to the offering of the Securities exceeds the amount of any damages that 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 (e) to contribute are several in proportion to their respective underwriting obligations and not joint.

(e) The obligations of the Company under this Section 6 shall be in addition to any liability which the Company may otherwise have and shall extend, upon the same terms and conditions, to each person, if any, who controls any Underwriter within the meaning of the Act; and the obligations of the Underwriters under this Section 6 shall be in addition to any liability that the respective Underwriters may otherwise have and shall extend, upon the same terms and conditions, to each director of the Company (including any person who, with his consent, is named in the Registration Statement as about to become a director of the Company), to each officer of the Company who has signed the Registration Statement and to each person, if any, who controls the Company within the meaning of the Act.

(f) The Underwriters severally confirm and the Company acknowledges that the statements with respect to the public offering of the Securities by the Underwriters regarding the names and corresponding share amounts set forth in the table of underwriters and paragraphs 5, 15, 16, 17, 18 and 20 under the caption "Underwriting" in the Time of Sale Disclosure Package and in the Prospectus, are correct and constitute the only information concerning such Underwriters furnished in writing to the Company by or on behalf of the Underwriters specifically for inclusion in the Registration Statement, any preliminary prospectus, the Time of Sale Disclosure Package, the Prospectus or any Issuer Free Writing Prospectus.

7. ***Representations and Agreements to Survive Delivery***. All representations, warranties, and agreements of the Company herein or in certificates delivered pursuant hereto, and the agreements of the several Underwriters and the Company contained in Section 6 hereof, shall remain operative and in full force and effect regardless of any investigation made by or on behalf of any Underwriter or any controlling person thereof, or the Company or any of its officers, directors, or controlling persons thereof, and shall survive delivery of, and payment for, the Securities to and by the Underwriters hereunder.

8. ***Substitution of Underwriters***.

(a) If any Underwriter or Underwriters shall fail to take up and pay for the amount of Firm Shares agreed by such Underwriter or Underwriters to be purchased hereunder, upon tender of such Firm Shares in accordance with the terms hereof, and the amount of Firm Shares not purchased does not aggregate more than 10% of the total amount of Firm Shares set forth in Schedule I hereto, the remaining Underwriters shall be obligated to take up and pay for (in proportion to their respective underwriting obligations hereunder as set forth in Schedule I hereto except as may otherwise be determined by you) the Firm Shares that the withdrawing or defaulting Underwriters agreed but failed to purchase.

(b) If any Underwriter or Underwriters shall fail to take up and pay for the amount of Firm Shares agreed by such Underwriter or Underwriters to be purchased hereunder, upon tender of such Firm Shares in accordance with the terms hereof, and the amount of Firm Shares not purchased aggregates more than 10% of the total amount of Firm Shares set forth in Schedule I hereto, and arrangements satisfactory to you for the purchase of such Firm Shares by other persons are not made within 36 hours thereafter, this Agreement shall terminate. In the event of any such termination the Company shall not be under any liability to any Underwriter (except to the extent provided in Section 6 hereof) nor shall any Underwriter (other than an Underwriter who shall have failed, otherwise than for some reason permitted under this Agreement, to purchase the amount of Firm Shares agreed by such Underwriter to be purchased hereunder) be under any liability to the Company (except to the extent provided in Section 6 hereof).

If Firm Shares to which a default relates are to be purchased by the non-defaulting Underwriters or by any other party or parties, the Representatives shall have the right to postpone the First Closing Date for not more than seven business days in order that the necessary changes in the Registration Statement, in the Time of Sale Disclosure Package, in the Prospectus or in any other documents, as well as any other arrangements, may be effected. As used herein, the term "Underwriter" includes any person substituted for an Underwriter under this Section 8.

9. ***Termination***.

(a) You, as Representatives of the several Underwriters, shall have the right to terminate this Agreement by giving notice as hereinafter specified at any time at or prior to the First Closing Date, and the option referred to in Section 3(b), if exercised, may be cancelled at any time prior to the Option Closing Date, if (i) the Company shall have failed, refused or been unable, at or prior to such Closing Date, to perform any agreement on its part to be performed hereunder, (ii) any other condition of the Underwriters' obligations hereunder is not fulfilled, (iii) trading on The NASDAQ Stock Market, New York Stock Exchange or the American Stock Exchange shall have been wholly suspended, (iv) minimum or maximum prices for trading shall have been fixed, or maximum ranges for prices for securities shall have been required, on The NASDAQ Stock Market, New York Stock Exchange or the American Stock Exchange, by such Exchange or by order of the Commission or any other Governmental Authority, (v) a banking moratorium shall have been declared by federal or state authorities, or (vi) there shall have occurred any outbreak or escalation of hostilities or any change in financial markets or any calamity or crisis that, in your judgment, is material and adverse and makes it impractical or inadvisable to proceed with the completion of the sale of and payment for the Securities. Any such termination shall be without liability of any party to any other party except that the provisions of Section 4(a)(viii) and Section 6 hereof shall at all times be effective.

(b) If you elect to terminate this Agreement as provided in this Section, the Company shall be notified promptly by you by telephone, confirmed by letter.

10. ***Default by the Company***. If the Company shall fail at the First Closing Date to sell and deliver the number of Securities which it is obligated to sell hereunder, then this Agreement shall terminate without any liability on the part of any Underwriter or, except as provided in Section 4(a)(viii) and Section 6 hereof, any non-defaulting party.

No action taken pursuant to this Section shall relieve the Company so defaulting from liability, if any, in respect of such default.

11. ***Notices***. Except as otherwise provided herein, all communications hereunder shall be in writing and, if to the Underwriters, shall be mailed or delivered to the Representatives, c/o Jefferies LLC, 520 Madison Avenue New York, New York 10022, Attention: General Counsel, or sent via facsimile at 646-619-4437 and c/o Piper Jaffray & Co., 800 Nicollet Mall, Minneapolis, MN 55402, Attention: General Counsel and Capital Markets, or sent via facsimile at 612-303-1068; if to the Company, shall be mailed or delivered to it at AcelRx Pharmaceuticals, Inc., 351 Galveston Drive, Redwood City, CA 94063 Attention: Chief Financial Officer, with a copy (which shall not constitute notice hereunder) to Cooley LLP, 3175 Hanover Street, Palo Alto, California 94304-1130, Attention: Mark Weeks. Any party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose.

12. ***Persons Entitled to Benefit of Agreement***. This Agreement shall inure to the benefit of and be binding upon the parties hereto and their respective successors and assigns and the controlling persons, officers and directors referred to in Section 6. Nothing in this Agreement is intended or shall be construed to give to any other person, firm or corporation any legal or equitable remedy or claim under or in respect of this Agreement or any provision herein contained. The term "successors and assigns" as herein used shall not include any purchaser, as such purchaser, of any of the Securities from any of the several Underwriters.

13. ***Absence of Fiduciary Relationship***. The Company acknowledges and agrees that: (a) the Representatives have been retained solely to act as an underwriter in connection with the sale of the Securities and that no fiduciary, advisory or agency relationship between the Company and the Representatives has been created in respect of any of the transactions contemplated by this Agreement, irrespective of whether the Representatives have advised or are advising the Company on other matters; (b) the price and other terms of the Securities set forth in this Agreement were established by the Company following discussions and arms-length negotiations with the Representatives and the Company is capable of evaluating and understanding and understands and accepts the terms, risks and conditions of the transactions contemplated by this Agreement; (c) it has been advised that the Representatives and their affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and that the Representatives have no obligation to disclose such interest and transactions to the Company by virtue of any fiduciary, advisory or agency relationship; (d) it has been advised that the Representatives are acting, in respect of the transactions contemplated by this Agreement, solely for the benefit of the Representatives and the other Underwriters, and not on behalf of the Company; (e) it, he or she waives to the fullest extent permitted by law, any claims it may have against the Representatives for breach of fiduciary duty or alleged breach of fiduciary duty in respect of any of the transactions contemplated by this Agreement and agrees that the Representatives shall have no liability (whether direct or indirect) to the Company in respect of such a fiduciary duty claim on behalf of or in right of the Company, including stockholders, employees or creditors of the Company.

14. ***Governing Law***. This Agreement shall be governed by and construed in accordance with the laws of the State of New York.

15. ***Counterparts***. This Agreement may be executed in one or more counterparts and, if executed in more than one counterpart, the executed counterparts shall each be deemed to be an original and all such counterparts shall together constitute one and the same instrument.

16. ***General Provisions***. This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. This Agreement may not be amended or modified unless in writing by all of the parties hereto, and no condition herein (express or implied) may be waived unless waived in writing by each party whom the condition is meant to benefit. The Section headings herein are for the convenience of the parties only and shall not affect the construction or interpretation of this Agreement.

[Signature Page Follows]

Please sign and return to the Company the enclosed duplicates of this letter whereupon this letter will become a binding agreement between the Company and the several Underwriters in accordance with its terms.

Very truly yours,

AcelRx Pharmaceuticals, Inc.

By /s/ Richard King
Name: Richard King
Title: Chief Executive Officer

Confirmed as of the date first above mentioned, on behalf of themselves and the other several Underwriters named in Schedule I hereto.

JEFFERIES LLC

By /s/ Michael Brinkman
Name: Michael Brinkman
Title: Managing Director

PIPER JAFFRAY & CO.

By /s/ David W. Stadinski
Name: David W. Stadinski
Title: Managing Director

SCHEDULE I

Underwriter	Number of Firm Shares (1)
Jefferies LLC	1,900,000
Piper Jaffray & Co.	1,520,000
Guggenheim Securities, LLC	380,000
Total	3,800,000

(1) The Underwriters may purchase up to an additional 570,000 Option Shares, to the extent the option described in Section 3(b) of the Agreement is exercised, in the proportions and in the manner described in the Agreement.

SCHEDULE II

Issuer General Free Writing Prospectuses

None.

SCHEDULE III

Pricing Information

Issuer:	AcelRx Pharmaceuticals, Inc. (NASDAQ "ACRX")
Maximum Number of Firm Shares:	3,800,000
Price Per Share:	$11.65
Maximum Number of Option Shares:	570,000
Underwriting Discount:	$0.699 per Share
Estimated Net Proceeds Before Expenses (assuming no exercise of option to purchase additional shares):	$41.61 Million
Amount of Expense Reimbursement by the Underwriters:	$354,160
Additional Amount of Expense Reimbursement by the Underwriters (assuming exercise of option to purchase additional shares):	$53,124

EXHIBIT A

Form of Lockup Agreement

Jefferies LLC
As representative of the underwriters named in
Schedule 1 to the Purchase Agreement
referred to below
c/o 520 Madison Avenue
New York, New York 10022

Dear Madam or Sir:

As an inducement to the underwriters (the *"Underwriters")* to execute a purchase agreement (the *"Purchase Agreement")* providing for the public offering (the *"Offering")* of common stock, par value $0.001 per share, (the *"Common Stock"),* of AcelRx Pharmaceuticals, Inc., a Delaware company, and any successor (by merger or otherwise) thereto (the *"Company"),* the undersigned hereby agrees that without, in each case, the prior written consent of Jefferies & Company, Inc. *("Jefferies"),* during the period commencing on the date of this Lock-Up Agreement and continuing to and including the 60th day after the date of the Purchase Agreement (the *"Lock-Up Period"),* the undersigned will not (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into, exercisable or exchangeable for or that represent the right to receive Common Stock (including without limitation, Common Stock which may be deemed to be beneficially owned by the undersigned in accordance with the rules and regulations of the Securities and Exchange Commission and securities which may be issued upon exercise of a stock option or warrant) whether now owned or hereafter acquired, including the undersigned's securities, if any, registered under an effective registration statement on Form S-3 filed by the Company on June 21, 2012 (the *"Securities")* or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the undersigned's Securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of Common Stock or such other securities, in cash or otherwise. The foregoing restriction is expressly agreed to preclude the undersigned from engaging in any hedging or other transaction which is designed to or which reasonably could be expected to lead to or result in a sale or disposition of the undersigned's Securities even if such Securities would be disposed of by someone other than the undersigned. Such prohibited hedging or other transactions would include without limitation any short sale or any purchase, sale or grant of any right (including without limitation any put or call option) with respect to any of the undersigned's Securities or with respect to any security that includes, relates to, or derives any significant part of its value from such Securities.

Notwithstanding the foregoing, if (1) during the last 17 days of the Lock-Up Period the Company issues an earnings release or material news or a material event relating to the Company

occurs; or (2) prior to the expiration of the Lock-Up Period, the Company announces that it will release earnings results during the 16-day period beginning on the last day of the Lock-Up Period, the restrictions imposed in this Lock-Up Agreement shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, unless Jefferies waives, in writing, such extension; *provided, however,* that such extension shall not apply if (i) the Company's securities are "actively traded securities" (as defined in Regulation M of the Securities Exchange Act of 1934, as amended (the *"Exchange Act")),* (ii) the Company meets the applicable requirements of paragraph (a)(1) of Rule 139 under the Securities Act of 1933, as amended, in the manner contemplated by NASD Conduct Rule 2711(0(4), and (iii) the provisions of NASD Conduct Rule 2711(0(4) are not applicable to any research reports relating to the Company published or distributed by any of the Underwriters during the 15 days before or after the last day of the Lockup Period (before giving effect to such extension).

The undersigned hereby acknowledges that the Company will be requested to agree in the Purchase Agreement to provide written notice to the undersigned of any event that would result in an extension of the Lock-Up Period pursuant to the previous paragraph and agrees that any such notice properly delivered will be deemed to have been given to, and received by, the undersigned. The undersigned further agrees that, prior to engaging in any transaction or taking any other action that is subject to the terms of this Agreement during the period from the date of this Agreement to and including the 34th day following the expiration of the initial Lock-Up Period, it will give notice thereof to the Company and will not consummate such transaction or take any such action unless it has received written confirmation from the Company that the Lock-Up Period (as may have been extended pursuant to the previous paragraph) has expired.

In addition, the undersigned agrees that, without the prior written consent of Jefferies, it will not, during the Lock-Up Period, make any demand for or exercise any right with respect to, the registration of any Common Stock or any security convertible into or exercisable or exchangeable for Common Stock, other than the exercise of the undersigned's rights with respect to the registration of the undersigned's securities, if any, pursuant to that certain Securities Purchase Agreement, dated as of May 29, 2012, by and between the Company and the other parties thereto (the " *Existing SPA*").

The undersigned further agrees that, prior to engaging in any transaction or taking any other action that is subject to the terms of this Lock-Up Agreement during the period from the date of this Lock-Up Agreement to the expiration of the Lock-Up Period, it will give notice thereof to the Company and will not consummate such transaction or take any such action unless it has received written confirmation from the Company that the Lock-Up Period has expired.

Notwithstanding the foregoing, the undersigned may transfer the undersigned's Securities (i) as a *bona fide* gift or gifts, (ii) by will or intestate succession; (iii) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned; (iv) if the undersigned is a limited liability company, to a member or an affiliate of such limited liability company, (v) if the undersigned is a partnership, to a partner or an affiliate of the partnership; *provided,* in each case, that (x) such transfer shall not involve a disposition for value, *(y)* the transferee agrees in writing with the Underwriters to be bound by the terms of this Lock-Up Agreement and (z) no filing by any party under Section 16(a) of the Exchange Act shall be

required or shall be made voluntarily in connection with such transfer (other than a filing of a Form 5 made after the expiration of the Lock-Up Period). For purposes of this Lock-Up Agreement, (i) "immediate family" shall mean any relationship by blood, marriage or adoption, not more remote than first cousin and (ii) "affiliate" of the undersigned shall mean any business entity that directly, or indirectly through one or more intermediaries, controls, or is controlled by, or is under common control with, the undersigned. The term "control" in this paragraph means beneficial ownership of more than fifty percent (50%) of the issued and outstanding equity interest or share capital of an entity.

In addition, the foregoing restrictions shall not apply to (i) the exercise or settlement of any equity awards pursuant to the Company's equity incentive plans or the exercise of warrants issued by the Company; provided that such restrictions shall apply to any of the undersigned's Securities issued upon such exercise; (ii) any transfers of the undersigned's Securities to the Company (a) in full or partial payment of exercise or purchase prices and taxes or tax withholding obligations required to be paid or satisfied upon the settlement, vesting or exercise of any equity award or warrant granted or issued by the Company or (b) in exercise of the Company's right to repurchase or reacquire the undersigned's Securities pursuant to agreements that permit the Company to repurchase or reacquire the undersigned's Securities upon termination of services to the Company; (iii) any transfers of the undersigned's Securities pursuant to a sale or an offer to purchase 100% of the outstanding Common Stock of the Company, whether pursuant to a merger, tender offer or otherwise, to a third party or group of third parties; or (iv) the establishment of any contract, instruction or plan (a *"Plan")* that satisfies all of the requirements of Rule 10b5-1 under the Exchange Act; *provided* that no sales of the undersigned's Securities shall be made pursuant to such a Plan prior to the expiration of the Lock-Up Period (as such may be extended pursuant to the provisions hereof), and such a Plan may only be established if no public announcement of the establishment or existence thereof and no filing with the Securities and Exchange Commission or other regulatory authority in respect thereof or transactions thereunder or contemplated thereby, by the undersigned, the Company or any other person, shall be required, and no such announcement or filing is made voluntarily, by the undersigned, the Company or any other person, prior to the expiration of the Lock-Up Period (as such may be extended pursuant to the provisions hereof).

In furtherance of the foregoing, the Company and its transfer agent and registrar are hereby authorized to decline to make any transfer of shares of Common Stock if such transfer would constitute a violation or breach of this Lock-Up Agreement.

The undersigned hereby agrees that, to the extent that the terms of this Lock-Up Agreement conflict with or are in any way inconsistent with any registration rights agreement to which the undersigned and the Company may be a party, other than the Existing SPA, this Lock-Up Agreement supersedes such registration rights agreement. It is expressly understood that this Lock-Up Agreement shall not in any way affect the undersigned's rights with respect to the registration of the undersigned's securities, if any, under the Existing SPA.

The undersigned hereby represents and warrants that the undersigned has full power and authority to enter into this Lock-Up Agreement. All authority herein conferred or agreed to be conferred and any obligations of the undersigned shall be binding upon the successors, assigns, heirs or personal representatives of the undersigned.

The undersigned understands that the undersigned shall be released from all obligations under this Lock-Up Agreement if (i) the Company notifies the Underwriters that it does not intend to proceed with the Offering, (ii) the Purchase Agreement does not become effective, or if the Purchase Agreement (other than the provisions thereof which survive termination) shall terminate or be terminated prior to payment for and delivery of the Common Stock to be sold thereunder, or (iii) the Offering is not completed by September 30, 2013.

The undersigned understands that the Underwriters are entering into the Purchase Agreement and proceeding with the Offering in reliance upon this Lock-Up Agreement.

This Lock-Up Agreement shall be governed by, and construed in accordance with, the laws of the State of New York.

EXHIBIT B

List of Stockholders subject to Lockup Agreement:

Anil (Badri) Dasu
James W. Welch
Lawrence G. Hamel
Pamela P. Palmer
Richard A. King
Stephen J. Hoffman
Mark G. Edwards
Mark A. Wan
Adrian Adams
Guy P. Nohra
Howard B. Rosen
ACP IV, L.P.
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.
Three Arch Associates III, L.P.
Three Arch Associates IV, L.P.
Three Arch Partners III, L.P.
Three Arch Partners IV, L.P.

Exhibit 5.1

Cooley LLP

July 18, 2013

AcelRx Pharmaceuticals, Inc.
351 Galveston Drive
Redwood City, CA 94063

Ladies and Gentlemen:

You have requested our opinion with respect to certain matters in connection with the sale by AcelRx Pharmaceuticals, Inc. (the "***Company***"), of up to 4,370,000 shares of the Company's common stock, par value $0.001 per share (the "***Shares***") (including up to 570,000 shares that may be sold pursuant to the exercise of an over-allotment option), pursuant to the Registration Statement on Form S-3 (File No. 333-183237), originally filed with the Securities and Exchange Commission (the "***Commission***") under the Securities Act of 1933, as amended (the "***Act***"), on August 10, 2012 and declared effective by the Commission on August 31, 2012 (the "***Initial Registration Statement***"), as supplemented by subsequent filings, including the Registration Statement on Form S-3 filed with the Commission pursuant to Rule 462(b) of the Act (File No. 333-190003) (together with the Initial Registration Statement, the "***Registration Statements***"), and the related Prospectus and Prospectus Supplement to be filed with the Commission pursuant to Rule 424 under the Act. All of the Shares are to be sold by the Company as described in the Registration Statements and the related Prospectus and Prospectus Supplement.

In connection with this opinion, we have examined and relied upon the Registration Statements and the related Prospectus and Prospectus Supplement, the Company's Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, as currently in effect, and the originals or copies certified to our satisfaction of such other documents, records, certificates, memoranda and other instruments as we deem necessary or appropriate to enable us to render the opinion expressed below. We have assumed the genuineness and authenticity of all documents submitted to us as originals, the conformity to originals of all documents submitted to us as copies thereof and the due execution and delivery of all documents where due execution and delivery are a prerequisite to the effectiveness thereof.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when sold and issued in accordance with the Registration Statements and the related Prospectus and Prospectus Supplement, will be validly issued, fully paid and non-assessable.

We consent to the reference to our firm under the caption "Legal Matters" in the Prospectus and Prospectus Supplement included in the Registration Statements and to the filing of this opinion as an exhibit to a Current Report of the Company on Form 8-K.

Sincerely,

Cooley LLP

By: /s/ Mark B. Weeks
Mark B. Weeks

Forward-Looking Statements

This Current Report on Form 8-K, or Form 8-K, contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by that section. In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Form 8-K, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- the success, cost and timing of our product development activities;
- our ability to obtain and maintain regulatory approval of Zalviso and other product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations, including funding necessary for the planned commercialization and manufacturing of Zalviso in the United States and advancement of clinical trials for other product candidates;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our use of the proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- our ability to obtain and maintain intellectual property protection for our product candidates.

In addition, you should refer to "Risk Factors" in this Form 8-K for a discussion of these and other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Form 8-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Also, forward-looking statements represent our estimates and assumptions only as of the date of this Form 8-K. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

BUSINESS OVERVIEW

We are a development stage specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. Our lead product candidate, Zalviso, formerly known as the Sufentanil NanoTab PCA System, or ARX-01, is designed to improve the management of moderate-to-severe acute pain in patients in the hospital setting. Although widely used, the current standard of care for patients with moderate-to-severe post-operative pain in the hospital, intravenous patient-controlled analgesia, or IV PCA, has been shown to cause harm and inconvenience to patients following surgery because of the side effects of commonly used IV PCA opioids, the invasive IV needle route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps.

Zalviso

Zalviso is an investigational pre-programmed, non-invasive, handheld system that allows hospitalized patients with moderate-to-severe acute pain to self-dose with sublingual sufentanil NanoTabs to manage their pain. Zalviso is designed to address the limitations of IV PCA by offering:

- **A high therapeutic index opioid:** Zalviso uses the high therapeutic index opioid sufentanil; it offers hospitalized patients with moderate-to-severe acute pain the potential for effective patient-controlled analgesia with a low incidence of drug-related side effects.
- **A non-invasive route of delivery:** The sublingual route of delivery used by Zalviso provides rapid onset of analgesia, therefore eliminating the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections in IV PCA treated patients. In addition, because patients are not tethered to IV tubing and a pump for pain relief, Zalviso allows for ease of patient mobility.
- **A simple, pre-programmed PCA solution:** Zalviso is a pre-programmed PCA system designed to eliminate the risk of pump programming errors.

Our Phase 3 clinical program for Zalviso consists of three trials; two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA morphine. Each of the three Phase 3 trials achieved its primary endpoint, and we believe the trial data support the submission of a New Drug Application, or NDA, which we anticipate will occur in the third quarter of 2013. A summary of the Phase 3 trials and results is as follows:

Active comparator trial (IAP 309)

In November 2012, we reported top-line data demonstrating that Zalviso met its primary endpoint of non-inferiority in a Phase 3 open-label active comparator

trial designed to compare the efficacy and safety of Zalviso (15 mcg/dose, 20 minute lock-out) to IV PCA with morphine (1mg/dose, 6 minute lock-out) for the treatment of moderate-to-severe acute post-operative pain immediately following major abdominal or orthopedic surgery.

Top-line primary endpoint results of this Phase 3 clinical trial demonstrate that:

- Zalviso was non-inferior ($p<0.001$) to IV PCA morphine for the primary endpoint of Patient Global Assessment of method of pain control, or PGA, comparison over the 48-hour trial period as determined by the combined percentage of patients with PGA ratings of "good" or "excellent" (78.5% vs. 65.6%, respectively).
- A secondary comparison of the primary endpoint, specifically a statistical analysis of superiority, demonstrated that Zalviso was statistically superior to IV PCA morphine for the PGA endpoint ($p=0.007$). Statistically superior and non-inferior PGA for Zalviso compared to IV PCA morphine was also seen at the 24 hour and 72 hour time points.

The trial also demonstrated that Zalviso produced a significantly faster onset of pain relief and reduction in pain intensity compared to IV PCA morphine that separated at 45 minutes and achieved statistical significance at 1, 2 and 4 hours ($p<0.01$). Furthermore, there were statistically fewer patients in the Zalviso group that experienced oxygen desaturation to a level less than 95% compared to the IV PCA morphine group ($p=0.028$).

Throughout the course of the trial, 7.3% of patients treated with Zalviso dropped out of the trial prematurely due to lack of efficacy compared to 8.9% of patients treated with IV PCA morphine. Additionally, 7.3% of the patients treated with Zalviso dropped out of the trial due to an adverse event compared to 10.0% of the IV PCA morphine patients. We observed 13 patients who experienced serious adverse events, or SAEs, in the trial, of whom three patients experienced serious adverse events assessed as possibly or probably related to the trial drug, with one related to Zalviso and two related to IV PCA morphine.

Double-blind, placebo-controlled, abdominal surgery trial (IAP 310)

In March 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 178 adult patients at 13 U.S. sites.

The primary endpoint evaluated pain intensity over the 48-hour trial period compared to baseline, or Summed Pain Intensity Difference (SPID-48), in patients following major open abdominal surgery. SPID-48 is the endpoint requested by FDA to demonstrate effectiveness of a pain control medicine. Patients receiving Zalviso demonstrated a significantly greater SPID-48 (pain reduction) compared to placebo treated patients during the trial period (105.6 and 55.6, respectively; $p=0.001$). Additionally, secondary endpoint data showed that 24 hours and 72 hours after first dose, SPID was significantly greater in Zalviso-treated patients than in the placebo-treated patients ($p<0.001$ and $p=0.004$ respectively).

Eighty, or 70.2%, of the Zalviso-treated patients completed the 48-hour trial period, compared to 30, or 51.7%, of placebo-treated patients. Reasons for drop-out in Zalviso-treated and placebo-treated groups were adverse events (5.3% and 6.9%, respectively), lack of efficacy (16.7% and 31.0%, respectively) and other (7.9% and 10.3%, respectively).

Treatment-emergent adverse events occurred in 64.0% of Zalviso-treated patients and 67.2% of placebo-treated patients. Adverse events with an occurrence greater than 5% in either the Zalviso group or the placebo group were nausea (30.7% and 41.4%, respectively), fever (14.9% and 8.6%, respectively), vomiting (8.8% and 6.9%, respectively), itching (8.8% and 0.0%, respectively), oxygen saturation decrease (6.1% and 1.7%, respectively), and hypertension (2.6% and 5.2%, respectively). Itching, a frequently observed side effect of opioids, was the only adverse event that was significantly different between the groups ($p=0.017$). All reported cases of itching in the trial were mild in nature.

Only one patient, in the Zalviso group, experienced a serious adverse event, which was determined to be unrelated to the trial drug by the investigator.

Double-blind, placebo-controlled, orthopedic surgery trial (IAP 311)

In May 2013, we reported top-line data results demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 426 adult patients at 34 U.S. sites.

The primary endpoint evaluated pain intensity over the 48-hour trial period compared to baseline, or SPID-48, in patients following major orthopedic surgery. Patients receiving Zalviso demonstrated a significantly greater SPID-48 (pain reduction) compared to placebo -treated patients during the trial period (+76.1 vs -11.5, $p<0.001$). Secondary endpoint data demonstrated that SPID at 24 hours and 72 hours was also significantly greater in the Zalviso-treated patients than in the placebo-treated patients ($p<0.001$ in each case).

Two hundred fifteen, or (68.3%), Zalviso-treated patients completed the 48-hour trial period, compared to 43 (41.3%) placebo-treated patients. Primary reasons for drop-out in the Zalviso- and placebo-treated groups were adverse events (7.0% and 6.7%, respectively) and lack of efficacy (14.3% and 48.1%, respectively).

Treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between Zalviso and placebo treated patients, despite the shorter duration of exposure in the placebo-treated patients caused by early termination due to inadequate analgesia. Adverse events of nausea (occurring in 52.7% of sufentanil-treated patients vs 33.7% of placebo-treated patients), vomiting (12.7% vs 5.8%, respectively), dizziness (6% vs 1%, respectively) and itching (6% vs 0%, respectively) were the only adverse effects that were statistically significantly greater for Zalviso-treated patients as compared to placebo-treated patients. Nausea, vomiting and itching are common in treatment of post-operative patients, and are managed with anti-emetic and anti-histamine treatment. Effective management of these symptoms is demonstrated by the low drop-out rate due to nausea (1.6% of Zalviso-treated patients vs 2.9% of placebo-treated patients), vomiting (0.6% vs 0%, respectively) and itching (0.3% vs 0%, respectively) in this trial. Two patients (one each in the Zalviso group and placebo group) experienced an SAE considered possibly or probably related to the trial drug by the investigator.

ARX-04

We are also developing a Sufentanil Single-Dose NanoTab, or ARX-04, for the treatment of moderate-to-severe acute pain on the battlefield, in the emergency room or in ambulatory care facilities. In April 2013, we reported top-line data showing that the primary endpoint was achieved in a placebo-controlled, dose-finding, Phase 2 clinical trial of ARX-04 for acute pain. This trial randomized 101 patients following bunionectomy surgery in a 2:2:1 ratio to 30 mcg sufentanil, 20 mcg sufentanil or placebo treatment arms. Ninety-one percent of patients entering the trial completed the 12-hour trial period.

Results demonstrated that patients receiving 30 mcg sufentanil NanoTab doses, administered by a healthcare professional, no more frequently than once per hour, had significantly greater pain reduction as measured by Summed Pain Intensity Difference to baseline during the 12-hour trial period (SPID-12) than placebo-treated patients ($p=0.003$). Adverse events reported in the trial were generally mild-to-moderate in nature, with two serious adverse events of post-surgical infection reported, both of which were determined by the investigator to be unrelated to trial drug. Two patients dropped out of the trial due to adverse events, one patient's discontinuation considered unrelated to trial drug, and the other considered probably related to trial drug, both in the 30 mcg-treated group.

Research and development of ARX-04, including the Phase 2 trial and pre-Phase 3 development, is funded by a $5.6 million grant from the U.S. Army Medical Research and Materiel Command, or USAMRMC. Future development of ARX-04 is contingent on identification of additional resources.

ARX-02 and ARX-03

In addition to Zalviso and ARX-04, our product candidate pipeline consists of two other sufentanil-based product candidates. The Sufentanil NanoTab BTP Management System, or ARX-02, is a pain management system for the potential treatment of cancer patients who suffer from breakthrough pain, or BTP. The Sufentanil/Triazolam NanoTab, or ARX-03, is a single, fixed-dose product designed to provide mild sedation, anxiety reduction and pain relief for patients undergoing painful procedures in a physician's office. We have successfully completed Phase 2 clinical trials for ARX-02 and ARX-03. Future development of ARX-02 and ARX-03 is contingent on identification of corporate partnership resources.

Our Strategy

Our strategy is to develop and commercialize a portfolio of sufentanil NanoTab-based products in specialty markets. We have designed and are developing product candidates that have clearly defined clinical development programs, target large commercial market opportunities, and require modestly-sized commercial organizations in the United States. We selectively utilize third party contractors in order to maximize the capital efficiency of our development and planned commercialization efforts. We plan to enter into partnerships to market our product candidates outside the United States.

Our lead product candidate, Zalviso, has been evaluated in three positive Phase 3 clinical trials. We intend to submit an NDA to the FDA in the third quarter of 2013 and, if approved, to commercialize Zalviso ourselves in the United States, and commercialize it outside the United States with a partner. Our strategy for Zalviso is to develop a hospital-directed sales force and/or collaborate with third parties to promote Zalviso to healthcare professionals and third-party payors in the United States. We have completed Phase 2 development of ARX-04, and plan to explore regulatory approaches for Phase 3 development of this candidate, subject to establishment of funding for that program. Further development of ARX-02 or ARX-03 will likely depend on the identification of a partner to support this effort.

Intellectual Property

We have developed significant know-how regarding our manufacturing process and protect our technology through trade secrets and patents. We seek patent protection in the United States and internationally for our product candidates.

As of July 1, 2013, we were the owner of record of six issued U.S. patents, five of which provide coverage for composition of matter and methods of using NanoTabs for oral transmucosal delivery of sufentanil, and one of which provides coverage of key features of the Zalviso device. Of these six patents, five expire in 2027 and one expires in 2030. We are also the owner of record of three issued European patents. Issued European patents EP 2114383 and EP 1873593, each expire in 2027 and include national validation in ten countries and seven countries, respectively. A third issued European patent EP 2367537 expires in 2029 and includes national validation in ten countries. Further, we own one issued Mexican patent and one issued New Zealand patent, each of which expires in 2029, one issued Chinese patent, which expires in 2028, and one issued Japanese patent, which expires in 2027. We are pursuing 15 U.S. non-provisional patent applications, and 53 foreign national applications, including six European Regional Phase applications directed to our product candidates. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

We continue to seek and expand our patent protection for both compositions of matter and delivery devices, as well as methods of treatment related to our product candidates. In particular, we are pursuing additional patent protection for our Zalviso, ARX-02, ARX-03 and ARX-04 NanoTabs and formulations, our Zalviso PCA device, the combination of drugs and our Zalviso PCA device, our ARX-02, ARX-03 and ARX-04 single dose applicator, or SDA, as well as to methods of treatment using such drug and device compositions.

We have filed for additional patent coverage in the United States, Europe as well as many other foreign jurisdictions, including Japan, China, India, Canada and Korea. If issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, we expect that these patents will expire between 2027 and 2030, excluding any additional term for patent term adjustments or patent term extensions in the United States. The patent laws of foreign countries differ from those in United States, and the degree of protection afforded by foreign patents may be different from the protection offered by U.S. patents.

Further, we seek trademark protection in the United States and internationally where available and when appropriate. We have registered our ACELRX mark in Class 5, “Pharmaceutical preparations for treating pain; pharmaceutical preparations for treating anxiety,” and Class 10, “Drug delivery systems; medical device, namely, a mechanical and electronic device used to administer medications, perform timed medication delivery, and to provide secure access to and delivery of medications,” in the United States.

Our ACELRX mark is also registered in the European Community, Canada, and India. We have also registered our NANOTAB mark in the United States, Hong Kong, and Singapore and our ACCELERATE. INNOVATE. ALLEVIATE. tagline in the United States. We have additionally applied for registration of our ZALVISO mark in the United States on an intent-to-use basis and that application has been allowed.

RISK FACTORS

We have identified the following additional risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. Investors should carefully consider the risks described below before making an investment decision. Our business faces significant risks, and the risks described below may not be the only risks we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. If any of these risks occur, our business, results of operations or financial condition could suffer, the market price of our common stock could decline and you could lose all or part of your investment in our common stock.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a development stage company with limited operating history. To date, we have focused primarily on developing our lead product candidate, Zalviso. We have three additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, the Sufentanil/Triazolam NanoTab, or ARX-03, and Sufentanil Single-Dose Acute Pain NanoTab, or ARX-04. We have incurred significant net losses in each year since our inception in July 2005 and as of March 31, 2013 we had an accumulated deficit of $134.8 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. We expect to continue to incur substantial expenses as we prepare for the potential commercialization of Zalviso and continue our research and development activities for our product candidates. To date, none of our product candidates have been commercialized, and if our product candidates are not successfully developed or commercialized, or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail. Even if we successfully obtain regulatory approval to market our product candidates in the United States, our revenues are also dependent upon the size of the markets outside of the United States, as well as our ability to obtain market approval and achieve commercial success. As a result of the foregoing, we expect to continue to incur significant and increasing operating losses and negative cash flows for the foreseeable future.

We have never generated any product or commercial revenue and may never be profitable.

Our ability to generate revenue from commercial sales and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize our product candidates. Other than the revenue received from the U.S. Army Medical Research and Materiel Command, or USAMRMC, for research and development reimbursement under the terms of the grant for ARX-04 we received from the USAMRMC, we do not anticipate generating revenues from sales of our product candidates for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- obtaining and maintaining regulatory approval for Zalviso;
- launching and commercializing Zalviso, including building or contracting out, a hospital-directed sales force in the U.S. and collaborating with third parties internationally, which will require additional funding; and
- completing the clinical development of, obtaining regulatory approval for, and launching and commercializing ARX-02, ARX-03 and ARX-04, which will require additional funding or corporate partnership resources.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are delayed in obtaining approval of, or launching, Zalviso, or are required by the United States Food and Drug Administration, or FDA, to perform trials in addition to those that we have completed.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of our products, we may not become profitable and may need to obtain additional funding to continue operations.

We have a limited operating history that may make it difficult to predict our future performance or evaluate our business and prospects.

We were incorporated in 2005. Since inception, our operations have been primarily limited to organizing and staffing our company, developing our technology and undertaking preclinical studies and clinical trials for our product candidates. We have not yet obtained regulatory approval for any of our product candidates. Consequently, any predictions you make about our future success or viability or evaluation of our business and prospects may not be accurate.

We will require substantial additional capital and may be unable to raise capital, which would force us to delay, reduce or eliminate our product development programs and could cause us to cease operations.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect to incur significant expenditures in connection with our ongoing activities, particularly preparation for the potential commercialization of Zalviso and future advancement of our other product candidates. As of March 31, 2013, we had working capital of $35.4 million.

We believe that the anticipated net proceeds from our proposed public offering announced on July 18, 2013, together with our current cash, cash equivalents and investment balances will be sufficient to fund our current operations at least through the end of 2014. We may be able to extend this time period to the extent that we can access additional capital through equity offerings, including our Sales Agreement with MLV. However, we will need to raise additional funds following this offering to support our future operations, and such funding may not be available to us on acceptable terms, or at all. Additionally, changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. For example, we believe that the net proceeds from our proposed public offering announced on July 18, 2013, together with our existing cash resources, based on our current estimates, are adequate to fund potential regulatory approval of Zalviso both in the United States and Europe, and to continue preparation for the potential commercial launch of Zalviso in the United States. However, our planned regulatory filings and commercialization efforts may encounter technical or other difficulties that could increase our development costs more than we expected. Even if we are able to submit an NDA, the FDA could require us to complete further studies, which would require additional capital before we receive our regulatory approval, if at all. In any event, we will require substantial additional capital to obtain regulatory approval for, and to commercialize, our product candidates, including Zalviso. To raise capital, we may seek to sell additional equity or debt securities, obtain a credit facility or enter into product development, license or distribution agreements with third parties or divest one or more of our product candidates. Any product development, licensing, distribution or sale agreements that we enter into may require us to relinquish valuable rights. We may not be able to obtain sufficient additional funding or enter into a strategic transaction in a timely manner. If adequate funds are not available, we would be required to reduce our workforce, delay, reduce the scope of or eliminate one or more of our research and development programs in advance of the date on which we exhaust our cash resources to ensure that we have sufficient capital to meet our obligations and continue on a path designed to preserve stockholder value.

Securing additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of our product candidates;
- seek corporate partners for Zalviso on terms that might be less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, including under our Sales Agreement with MLV, which would result in dilution to our stockholders or impose restrictive covenants that may adversely impact our business. The sale of additional equity or convertible debt securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected and we may not be able to meet our debt service obligations.

We might be unable to service our existing debt due to a lack of cash flow and might be subject to default.

In June 2011, we entered into a loan and security agreement with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, under which we borrowed $20.0 million in two tranches of $10.0 million each, represented by secured convertible term promissory notes. The interest rate is 8.50%, with the initial 12 months of the facility requiring interest only payments. The notes issued pursuant to the loan and security agreement mature on December 1, 2014. According to the terms of the Hercules agreement, beginning on July 1, 2012, we began repaying Hercules principal, with equal monthly payments of $742,000, consisting of both principal and interest payments, until the maturity date of the loan in December, 2014. As of March 31, 2013, our outstanding debt balance related to the Hercules agreement was $14.2 million. We granted Hercules a first priority security interest in substantially all of our assets, with the exception of our intellectual property, where the security interest is limited to proceeds of intellectual property.

If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, or if we breach the agreement or become insolvent, Hercules could elect to declare all amounts outstanding, together with accrued and unpaid interest and penalty, to be immediately due and payable. Additional capital may not be available on terms acceptable to us, or at all. Even if we were able to repay the full amount in cash, any such repayment could leave us with little or no working capital for our business. If we are unable to repay those amounts, Hercules will have a first claim on our assets pledged under the loan agreement. If Hercules should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the loan agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of Zalviso, which may not receive regulatory approval or be successfully commercialized.

We have not marketed, distributed or sold any products. The success of our business depends primarily upon our ability to develop and commercialize Zalviso for the management of moderate-to-severe acute pain in patients in the hospital setting. Our Phase 3 program consisted of three Phase 3 clinical trials. We have reported positive top-line data from each of these trials and intend to submit an NDA for Zalviso to the FDA in the third quarter of 2013. There is no guarantee that the NDA will be completed on schedule or at all, or if completed and submitted, will be successfully filed or approved by the FDA. Even if we are able to submit an NDA, the FDA could require us to complete further studies, which could delay or preclude any approval of the NDA and would require us to obtain significant additional funding.

Our proposed tradename of Zalviso has not received final approval from FDA, which must approve all drug tradenames to avoid medication errors and misbranding. Any brand recognition or goodwill that we establish with the name Zalviso prior to approval may be worthless if the FDA rejects this tradename.

Any delay or change in the current schedule of our planned NDA filing for Zalviso may negatively impact our stock price and harm our business operations. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing Zalviso, generating revenues and achieving profitability. If any of these events occur, we may be forced to delay or abandon our development efforts for Zalviso, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Positive clinical results obtained to date for our product candidates may be disputed in FDA review, do not guarantee regulatory approval and may not be obtained from future clinical trials.

We have reported positive top-line data from each of our three Zalviso Phase 3 clinical trials. However, even if we believe that the data from required Phase 3 clinical trials is positive, the FDA could analyze our data using alternative strategies and determine that the data from our trials was negative or inconclusive. Negative or inconclusive results of a Phase 3 clinical trial could cause the FDA to require us to repeat the trial or conduct additional clinical trials prior to obtaining approval for commercialization, and there is no guarantee that additional trials would achieve positive results. Any such determination by the FDA would delay the timing of our commercialization plan for Zalviso and adversely affect our business operations.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

We have experienced and may in the future experience delays in clinical trials of our product candidates. While we have completed our planned trials for Zalviso and the Phase 2 clinical trial for ARX-04, and have no additional trials currently planned, potential future clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. Our clinical trials for any of our product candidates could be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required institutional review board approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the device components of our product candidates;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment or being delayed in entering data to allow for clinical trial database closure;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If any future clinical trials are delayed for any of the above reasons, our development costs may increase, our approval process could be delayed and our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events, or AEs, caused by our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. In our Phase 3 active comparator clinical trial (IAP 309), 7.9% of Zalviso treated patients dropped out of the trial prematurely due to an AE, and we observed one serious adverse event, or SAE, that was assessed as possibly or probably related to Zalviso. In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP 310), adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. In addition, one patient in the trial, who was in the sufentanil group, experienced an SAE, which was determined to be unrelated to the trial drug. In our Phase 3, double-blind, placebo-controlled, orthopedic surgery trial (IAP 311), treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between sufentanil and placebo treated patients. Two patients (one each in the sufentanil group and placebo group) experienced a serious adverse event considered possibly or probably related to the trial drug by the investigator.

Phase 2 clinical trials conducted by us with our Zalviso, ARX-02, ARX-03 and ARX-04 product candidates have generated some AEs, but no SAEs, related to the trial drug.

Further, if our products cause serious or unexpected side effects after receiving market approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified Risk Evaluation and Mitigation Strategy, or REMS;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

Additional time may be required to obtain regulatory approval for Zalviso because it is a drug/device combination.

Zalviso is a drug/device combination product candidate with both drug and device components submitted in the investigational new drug, or IND, application. Based on our discussions with the FDA, we believe that Zalviso is viewed as a combination product by the FDA, and both drug and device components will be required for review as part of an NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as Zalviso. As a result, we have in the past and may in the future experience delays in the development and commercialization of Zalviso due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device combination product approval under an NDA.

After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize any of our product candidates, and we cannot, therefore, predict the timing of any future revenue.

We cannot commercialize any of our product candidates, including Zalviso, until the appropriate regulatory authorities, such as the FDA or the European Medicines Agency, or EMA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for Zalviso. Additional delays may result if Zalviso is taken before an FDA Advisory Committee which may recommend restrictions on approval or recommend non-approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

The process for obtaining approval of an NDA is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources.

If the FDA determines that the clinical trials submitted for a product candidate, including Zalviso, in support of an NDA were not conducted in full compliance with the applicable protocols for these trials, as well as with applicable regulations and standards, or if the FDA does not agree with our interpretation of the results of such trials, the FDA may reject the data from such trials. Such rejection would negatively impact our ability to obtain marketing authorization for a product candidate and would have a material adverse effect on our business and financial condition.

In addition, an NDA may not be approved, or approval may be delayed, as a result of changes in FDA policies for drug approval during the review period. For example, although many products have been approved by the FDA in recent years under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, objections have been raised to the FDA's interpretation of Section 505(b)(2). If challenges to the FDA's interpretation of Section 505(b)(2) are successful, the FDA may be required to change its interpretation, which could delay or prevent the approval of such an NDA. Any significant delay in the review or approval of an NDA that we submit would have a material adverse effect on our business and financial condition.

Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.
The FDA and other foreign regulatory agencies, such as the EMA, can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- the manufacturing processes or facilities we have selected may not meet the applicable requirements; and
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Part of the regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The regulatory agency may delay, limit or deny marketing approval of our product candidates as a result of such inspections.

Any delay in, or failure to receive or maintain, approval for any of our product candidates could prevent us from generating meaningful revenues or achieving profitability.

Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors may disagree with our trial design and our interpretations of data from preclinical trials and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. The FDA exercises significant discretion over the regulation of combination products, including the discretion to require separate marketing applications for the drug and device components in a combination product. To date, our product candidates are being regulated as drug products under the NDA process administered by the FDA. The FDA could in the future require additional regulation of our product candidates under the medical device provisions of the FDCA. Our systems are designed to comply with Quality Systems Regulation, or QSR, which sets forth the FDA's current good manufacturing practice, or GMP, requirements for medical devices, and other applicable government regulations and corresponding foreign standards for drug GMPs. If we fail to comply with these regulations, it could have a material adverse effect on our business and financial condition.

Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing trials. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, we intend to seek approval of Zalviso for the management of moderate-to-severe acute pain in patients in the hospital setting; however, our clinical trial data was generated exclusively from the post-operative segment of this population, and FDA may restrict any approval to post-operative patients only, which would limit our commercial opportunity.

Even if we obtain regulatory approval for Zalviso and our other product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.
Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval trials or post-market surveillance. For example, the labeling ultimately approved for Zalviso and our other product candidates will likely include restrictions on use due to the opioid nature of sufentanil. Zalviso and our other product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we, or a regulatory agency, discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to

that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our product candidate, a regulatory agency may:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenues.

Even if we obtain FDA approval for Zalviso or any of our product candidates in the United States, we may never obtain approval for or commercialize our products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. In October 2012, we received notice from the EMA that Zalviso was eligible for centralized European review. Outside of Europe, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical trials or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of our products will be harmed.

Zalviso and our other product candidates will require Risk Evaluation and Mitigation Strategies.

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and require the adoption of REMS. Our product candidates will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. While we have received information from the FDA regarding certain aspects of the required REMS for Zalviso, we cannot predict the specific REMS to be required as part of any FDA approval of Zalviso. Depending on the extent of the REMS requirements, our costs to commercialize Zalviso may be substantial. ARX-02, ARX-03 and ARX-04, if approved, will also require REMS programs that may significantly increase our costs to commercialize these product candidates. Furthermore, risks of sufentanil that are not adequately addressed through proposed REMS for our product candidates may also prevent or delay their approval for commercialization.

Risks Related to Our Reliance on Third Parties

We rely on third party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates.

Reliance on third party manufacturers entails many risks including:

- the inability to meet our product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;

- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production.

We rely on limited sources of supply for the drug component of our product candidates and any disruption in the chain of supply may cause delay in developing and commercializing our product candidates.

Currently, we use two established suppliers of sufentanil citrate for our NanoTabs. For each product candidate, only one of the two suppliers will be qualified as a vendor with the FDA. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. The alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional trials if a new sufentanil supplier is relied upon for commercial production. In addition, the Drug Enforcement Administration, or the DEA, may reduce, delay or refuse our quota for sufentanil, which would disrupt our supply of sufentanil citrate and cause delay in the development and commercialization of our product candidates.

Manufacture of Sufentanil NanoTabs requires specialized equipment and expertise.

Ethanol, which is used in the manufacturing process for our Sufentanil NanoTabs, is flammable, and sufentanil is a highly potent, Schedule II compound. These factors necessitate the use of specialized equipment and facilities for manufacture of sufentanil NanoTabs. There are a limited number of facilities that can accommodate our manufacturing process and we need to use dedicated equipment throughout development and commercial manufacturing to avoid the possibility of cross-contamination. If our equipment breaks down or needs to be repaired or replaced, it may cause significant disruption in clinical or commercial supply, which could result in delay in the process of obtaining approval for or sale of our products. Furthermore, we are using one manufacturer to produce our sufentanil NanoTabs and have not identified a back-up commercial facility to date. Any problems with our existing facility or equipment may delay or impair our ability to complete our clinical trials or commercialize our product candidates and increase our cost.

Manufacturing issues may arise that could delay or increase costs related to product and regulatory approval and commercialization.

As we scale up manufacturing of our product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to obtain regulatory approval for commercial marketing. In the past we have identified impurities in our product candidates. In the future we may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our products.

Historically, we have manufactured the majority of our NanoTab supplies at Patheon in Toronto, Canada. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon's production facility in Cincinnati, Ohio, where we have built out a suite within their existing buildings that will serve as a manufacturing facility for clinical and commercial supplies of NanoTabs. The new facility has been qualified; however, we have not yet produced commercial supplies out of this facility and we may encounter difficulties in production at the new facility, which may adversely affect our clinical and commercial plans. In addition, regulatory agencies may require that a bioequivalence trial be conducted, which is designed to ensure that the Phase 3 drug lots made at Patheon, Toronto are equivalent to one of the registration drug lots made at Patheon, Cincinnati. There is risk that this bioequivalence trial could fail the FDA's bioequivalence requirements which would adversely affect our clinical and commercial plans. Any such additional trials or other FDA requirements would delay the timing of our commercialization plans for Zalviso and adversely affect our business operations.

The Zalviso PCA device components may not be fully functional or commercially viable.

The Zalviso device we have used in our Phase 3 clinical trials and plan to use commercially has more features than the device used in Phase 2, including additional software. We have conducted multiple Design Validation, Software Verification and Validation, Reprocessing and Human Factors studies, which have informed the design of the Zalviso device and we plan to conduct additional Human Factors studies prior to submitting the planned NDA for Zalviso. However, we cannot predict if the Phase 3 device will be fully functional or ready for commercial use. If we need to modify the Phase 3 device, we may incur higher costs and experience delay in regulatory approval and commercialization of Zalviso. Furthermore, if the changes to the device are substantial, we may need to conduct further clinical trials in order to have the commercial device approved by the FDA.

We have limited experience manufacturing the Zalviso device on a clinical scale, no experience on a commercial scale and do not own or operate a manufacturing facility.

We have manufactured Zalviso devices and supplies on a small scale, including those needed for our Phase 3 clinical trials. We will continue to rely on contract manufacturers, component fabricators and third party service providers to produce the necessary Zalviso devices for the commercial marketplace. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the Zalviso device to third parties and intend to continue to do so. These purchases and components were made and will continue to be made utilizing short term purchase agreements and we may not be able to enter into long-term agreements for commercial supply of Zalviso devices with third party manufacturers, or may be unable to do so on acceptable terms. We may encounter unanticipated problems in the scale-up and automation process that will result in delays in the manufacturing of Zalviso cartridge, dispenser or controller.

We may not be able to establish additional sources of supply for device manufacture. Such suppliers are subject to FDA regulations requiring that materials be produced under current Good Manufacturing Practices, or cGMPs, or Quality System Regulations, or QSR, and subject to ongoing inspections by regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in delays and interruptions to our product candidate supply while we seek to secure another supplier that meets all regulatory requirements.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including the possible breach of the manufacturing agreements by the third parties because of factors beyond our control; and the possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on their own business priorities.

We rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We utilized CROs for the conduct of our Phase 3 clinical trials of Zalviso and for the Phase 2 clinical trial of ARX-04. We rely on CROs, as well as clinical trial sites, to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our clinical programs for Zalviso and our other product candidates, as well as the execution of nonclinical trials. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA may determine that our Phase 3 clinical trials do not comply with cGCPs. Accordingly, if our CROs or clinical trial sites fail to comply with these regulations, we may be required to repeat the Phase 3 clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may allow our potential competitors to access our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize Zalviso, or our other product candidates. As a result, our financial results and the commercial prospects for Zalviso and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Pre-Phase 3 development of ARX-04 is dependent on funding from our government grant with the USAMRMC.

In May 2011, we received a grant from the USAMRMC, effective June 1, 2011, in which the USAMRMC granted $5.6 million to us in order to support the development of ARX-04. Under the terms of the grant, the USAMRMC will reimburse us for development, manufacturing and clinical costs necessary to prepare for and complete the Phase 2 dose-finding trial for the treatment of moderate-to-severe acute pain as well as Phase 3 readiness activities. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research.

Pre-Phase 3 development of ARX-04 is dependent on the continued performance by the USAMRMC of its responsibilities under this agreement, including adequate continued funding of USAMRMC programs. We have no control over the resources and funding that USAMRMC may devote to this or future agreements, which may be subject to annual renewal and which generally may be terminated by USAMRMC at any time. USAMRMC may fail to perform their responsibilities under the agreement, which may result in the termination of the agreement. In addition, we may fail to perform our responsibilities under the agreement, which may also lead to the termination of this agreement. Our government agreement is subject to audits, which may occur several years after the period to which the audit relates. If an audit identifies significant unallowable costs, we could incur a material charge to our earnings or reduction in our cash position. As a result, we may be unsuccessful in entering, or ineligible to enter, into future government agreements.

There can be no assurances that this agreement will continue or that we will be able to enter into new contracts with USAMRMC or obtain funding from other sources to continue to support development of ARX-04 beyond the Phase 2 clinical trial and preparation for Phase 3 activities. The process of obtaining USAMRMC contracts is lengthy and uncertain and we will have to compete with other companies for each contract. Further, changes in government budgets and agendas may result in a decreased and de-prioritized emphasis on supporting research and development programs, including ARX-04.

Risks Related to Commercialization of Our Product Candidates

The commercial success of Zalviso and our other product candidates will depend upon the acceptance of these products by the medical community, including physicians, nurses, patients, and pharmacy and therapeutics committees.

The degree of market acceptance of any of our product candidates will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;

- the prevalence and severity of any AEs or SAEs;
- overcoming the perception of sufentanil as a potentially unsafe drug due to its high potency;
- limitations or warnings contained in the FDA-approved label for Zalviso;
- availability of alternative treatments;
- existing capital investment by hospitals in IV PCA technology;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage or reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third party coverage.

If Zalviso is approved, but does not achieve an adequate level of acceptance by physicians, nurses, patients and pharmacy and therapeutics committees, or P&T Committees, we may not generate sufficient revenue from Zalviso and we may not become or remain profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

We currently do not have an organization for the sales, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We intend to enter into strategic partnerships with third parties to commercialize our product candidates outside of the United States. We will also consider the option to enter into strategic partnerships for our product candidates in the United States.

To date, we have not entered into any strategic partnerships for any of our product candidates. We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document.

We may not be able to negotiate strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships. Our strategy for Zalviso is to develop a hospital-directed sales force and/or collaborate with third parties to promote the product to healthcare professionals and third-party payors in the United States. Our future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If we obtain approval to commercialize our products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates, including Zalviso, is approved for commercialization, we intend to enter into agreements with third parties to market our product candidates outside the United States. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;

- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

If we, or potential partners, are unable to compete effectively, our product candidates may not reach their commercial potential.

The market for our product candidates is characterized by intense competition and rapid technological advances. If our product candidates obtain FDA approval, they will compete with a number of existing and future pharmaceuticals and drug delivery devices developed, manufactured and marketed by others. We or our potential partners will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations.

We believe that Zalviso would compete with a number of opioid-based treatment options that are currently available. The hospital market for opioids for moderate-to-severe acute pain is large and competitive. The primary competition for Zalviso is the IV PCA pump, which is widely used in the moderate-to-severe acute pain in the hospital setting. Leading manufacturers of IV PCA pumps include Hospira Inc., CareFusion Corporation, Baxter International Inc., Curlin Medical, Inc. and Smiths Medical. The most common opioids used to treat moderate-to-severe acute pain are morphine, hydromorphone and fentanyl, all of which are available as generics. Also available on the market is the Avancen Medication on Demand, or MOD, Oral PCA Device developed by Avancen MOD Corporation.

Additional potential competitors for Zalviso include products in development, including the fentanyl iontophoretic transdermal system, IONSYS, originally developed by ALZA Corporation and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson subsidiaries, and currently under development by Incline Therapeutics, Inc., which was acquired by The Medicines Company. Also in development is MoxDuo, an orally administered, fixed ratio combination of morphine and oxycodone being developed by QRx Pharma, an Australian company. This drug is also in development as an IV product.

Our potential competitors for ARX-02 include products approved in the United States for cancer breakthrough pain, including: ACTIQ and FENTORA, currently manufactured by Teva Pharmaceuticals; Onsolis, currently manufactured by BioDelivery Sciences International, Inc.; Abstral, currently manufactured by ProStrakan Group plc; Lazanda, currently manufactured by Archimedes Pharma Limited, as well as products approved in Europe, including: Instanyl, currently manufactured by Nycomed International Management GmbH. The active ingredient in all approved products for cancer breakthrough pain is fentanyl. Additional potential competitors for ARX-02 include products in late stage development for cancer breakthrough pain, such as: Fentanyl TAIFUN, currently manufactured by Akela Pharma, Inc.; and SL Spray, currently manufactured by Insys Therapeutics, Inc.

We are not aware of any approved or development stage non-IV sedative/analgesic products that would present competition to ARX-03. In the future, there may be products developed or approved for this market which could directly compete with ARX-03.

Competitors for ARX-04 within the military environment include intramuscular morphine injections which are marketed by a variety of generic manufacturers. Within the civilian environment, there are a wide variety of approved injectable and oral opioid products to treat moderate-to-severe acute pain, including IV opioids such as morphine, fentanyl, hydromorphone and meperidine or oral opioids such as oxycodone and hydrocodone.

It is possible that any of these competitors could develop or improve technologies or products that would render our product candidates obsolete or non-competitive, which could adversely affect our revenue potential. Key competitive factors affecting the commercial success of our product candidates are likely to be efficacy, safety profile, reliability, convenience of dosing, price and reimbursement.

Many of our potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of drug candidates, obtaining FDA and other regulatory approval of products and the commercialization of those products. Accordingly, our competitors may be more successful than we are in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs or drug delivery systems may be more effective, have fewer adverse effects, be less expensive to develop and manufacture, or be more effectively marketed and sold than any product candidate we may commercialize. This may render our product candidates obsolete or non-competitive before we can recover our losses. We anticipate that we will face intense and increasing competition as new drugs enter the market and additional technologies become available. These entities may also establish collaborative or licensing relationships with our competitors, which may adversely affect our competitive position. Finally, the development of different methods for the treatment of mild-to-moderate acute pain or breakthrough pain could render Zalviso and ARX-02, respectively, non-competitive or obsolete. These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

Hospital formulary approval and reimbursement may not be available for Zalviso and our other product candidates, which could make it difficult for us to sell our products profitably.

Obtaining formulary approval can be an expensive and time-consuming process. We cannot be certain if and when we will obtain formulary approval to allow us to sell our products into our target markets. Failure to obtain timely formulary approval will limit our commercial success.

Furthermore, market acceptance and sales of Zalviso, or any of our other product candidates, will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, hospitals and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for Zalviso, or any of our other product candidates. Also, reimbursement amounts may reduce the demand for, or the price of, our products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize Zalviso, or any of our other product candidates.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell our products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for our products, following approval. The availability of numerous generic pain medications may also substantially reduce the likelihood of reimbursement for Zalviso or any of our other product candidates. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with any sale of Zalviso and any of our other product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

Risks Related to Our Business Operations and Industry

Failure to comply with the Drug Enforcement Administration regulations, or the cost of compliance with these regulations, may adversely affect our business.

Our sufentanil-based products are subject to extensive regulation by the DEA, due to their status as scheduled drugs. Sufentanil is a Schedule II opioid, considered to present the highest risk of abuse. The manufacture, shipment, storage, sale and use of controlled substances are subject to a high degree of regulation, including security, record-keeping and reporting obligations enforced by the DEA. This high degree of regulation can result in significant costs in order to comply with the required regulations, which may have an adverse effect on the development and commercialization of our product candidates.

The DEA limits the availability and production of all Schedule II substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers have applied annually for a quota on our behalf. In future years, we may need greater amounts of sufentanil to continue development of our product candidates, and we will need significantly greater amounts of sufentanil to implement our commercialization plans for any of our products that may be approved by the FDA, including Zalviso if approved by the FDA. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for sufentanil or a failure to increase it over time to meet anticipated increases in demand could delay or stop the clinical development or commercial sale of Zalviso or any of our other product candidates. This could have a material adverse effect on our business, results of operations, financial condition and prospects.

We have not yet produced commercial supplies and we may encounter difficulties in production, which may adversely affect our clinical and commercial plans.

A substantial portion of our clinical trial manufacturing to date has been completed at Patheon in Toronto, Canada. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon's production facility in Cincinnati, Ohio, where we have built out a suite within their existing buildings that will serve as a manufacturing facility for clinical and commercial supplies of NanoTabs. The new facility has been qualified; however, we have not yet produced commercial supplies at this facility and we may encounter difficulties in production at the new facility, which may adversely affect our clinical and commercial plans.

In January 2013, we entered into a Manufacturing Services Agreement, or the Services Agreement, with Patheon under which Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to Zalviso for potential sales in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. There is no guarantee that Patheon's services will be satisfactory or that they will continue to meet the strict regulatory guidelines of the FDA or other regulatory agencies. In addition, in January 2013, we entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement, with Patheon, relating to the manufacture of Sufentanil NanoTabs. Under the terms of the Capital Agreement, we have planned certain future modifications to Patheon's Cincinnati facility. If equipment manufacture or modifications do not meet expected deadlines, the timing for our planned NDA submission for Zalviso may be delayed.

If Patheon cannot provide us with an adequate supply of NanoTabs, we may be required to pursue alternative sources of manufacturing capacity. Switching or adding commercial manufacturing capability can involve substantial cost and require extensive management time and focus, as well as additional regulatory filings. In addition, there is a natural transition period when a new manufacturing facility commences work. As a result, delays may occur, which can materially impact our ability to meet our desired commercial timelines, thereby increasing our costs and reducing our ability to generate revenue.

The facilities of any of our future manufacturers of sufentanil-containing NanoTabs must be approved by the FDA after we submit our planned NDA and before approval of Zalviso and our other product candidates for commercial distribution. We do not fully control the manufacturing process of sufentanil NanoTabs and are completely dependent on these third party manufacturing partners for compliance with the FDA's requirements for manufacture. In addition, although our third party manufacturers are well established commercial manufacturers, we are dependent on their continued adherence to cGMP manufacturing and acceptable changes to their process. If our manufacturers do not meet the FDA's strict regulatory requirements, they will not be able to secure FDA approval for their manufacturing facilities. If the FDA does not approve these facilities for the commercial manufacture of sufentanil NanoTabs, we will need to find alternative suppliers, which would result in significant delays in obtaining FDA approval for Zalviso. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

Business interruptions could delay us in the process of developing our products and could disrupt our sales.

Our headquarters is located in the San Francisco Bay Area, near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We are also vulnerable to other types of natural disasters and other events that

could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of March 31, 2013, we had 25 full-time employees. As our company matures, we expect to expand our employee base to increase our managerial, scientific and engineering, operational, sales, marketing, financial and other resources and to hire more consultants and contractors, particularly in preparation for the commercial launch of Zalviso if our NDA submission is approved by the FDA. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize Zalviso and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to

liability. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Risks Related to Our Intellectual Property

If we cannot defend our issued patents from third party claims or if our pending patent applications fail to issue, our business could be adversely affected.

To protect our proprietary technology, we rely on patents as well as other intellectual property protections including trade secrets, nondisclosure agreements, and confidentiality provisions. As of July 1, 2013, we were the owner of record of one issued European patent (EP 2114383), including national validation in ten countries, which expires in 2027, one issued European patent (EP 2367537), including national validation in ten countries, which expires in 2029, one issued European patent (EP 1873593), including national validation in seven countries, which expires in 2027, one Mexican patent, which expires in 2029, one Japanese patent, which expires in 2027, one New Zealand patent, which expires in 2029, one Chinese patent, which expires in 2028, five issued U.S. patents which expire in 2027, and one issued U.S. patent which expires in 2030. In addition, we are pursuing 15 U.S. non-provisional patent applications, and 53 foreign national applications, including six European Regional Phase applications directed to our product candidates. One of our issued U.S. patents, Patent Number 8,357,114, covers key features of our Zalviso (ARX-01) PCA device, but we have not yet obtained any issued patents that provide protection for key features of our ARX-02, ARX-03 and ARX-04 SDAs independent of the drug composition used in them. We have received a Notice of Allowance for two of our pending U.S. applications that include claims covering key features of our ARX-02, ARX-03 and ARX-04 SDA device. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

Our commercial success will depend in part on successfully defending our current sufentanil formulation patents against third party challenges and expanding our existing formulation patent portfolio to provide additional layers of patent protection, as well as extending patent protection to our proprietary delivery devices. There can be no assurance that we will be successful in defending our existing and future patents against third party challenges, or that our pending patent applications will result in issued patents.

The patent positions of pharmaceutical companies, including us, can be highly uncertain and involve complex and evolving legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. Legal developments may preclude or limit the scope of available patent protection.

There is also no assurance that any patents issued to us will not become the subject of adversarial proceedings such as opposition, inter partes review, post-grant review, reissue, re-examination or other post-issuance proceedings, will provide us with competitive advantages, will not be challenged by any third parties, or that the patents of others will not prevent the commercialization of products incorporating our technology. Furthermore, there can be no guarantee that others will not independently develop similar products, duplicate any of our products, or design around our patents.

Litigation involving patents, patent applications and other proprietary rights is expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing our product candidates to market and interfere with our business.

Our commercial success depends in part on not infringing patents and proprietary rights of third parties. Although we are not currently aware of litigation or other proceedings or third party claims of intellectual property infringement related to our product candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights.

As we enter our target markets, it is possible that competitors or other third parties will claim that our products and/or processes infringe their intellectual property rights. These third parties may have obtained and may in the future

obtain patents covering products or processes that are similar to, or may include compositions or methods that encompass our technology, allowing them to claim that the use of our technologies infringes these patents.

In a patent infringement claim against us, we may assert, as a defense, that we do not infringe the relevant patent claims, that the patent is invalid or both. The strength of our defenses will depend on the patents asserted, the interpretation of these patents, and our ability to invalidate the asserted patents. However, we could be unsuccessful in advancing non-infringement and/or invalidity arguments in our defense. In the United States, issued patents enjoy a presumption of validity, and the party challenging the validity of a patent claim must present clear and convincing evidence of invalidity, which is a high burden of proof. Conversely, the patent owner need only prove infringement by a preponderance of the evidence, which is a lower burden of proof.

If we were found by a court to have infringed a valid patent claim, we could be prevented from using the patented technology or be required to pay the owner of the patent for the right to license the patented technology. If we decide to pursue a license to one or more of these patents, we may not be able to obtain a license on commercially reasonable terms, if at all, or the license we obtain may require us to pay substantial royalties or grant cross licenses to our patent rights. For example, if the relevant patent is owned by a competitor, that competitor may choose not to license patent rights to us. If we decide to develop alternative technology, we may not be able to do so in a timely or cost-effective manner, if at all.

In addition, because patent applications can take years to issue and are often afforded confidentiality for some period of time there may currently be pending applications, unknown to us, that later result in issued patents that could cover one or more of our products.

It is possible that we may in the future receive, particularly as a public company, communications from competitors and other companies alleging that we may be infringing their patents, trade secrets or other intellectual property rights, offering licenses to such intellectual property or threatening litigation. In addition to patent infringement claims, third parties may assert copyright, trademark or other proprietary rights against us. We may need to expend considerable resources to counter such claims and may not be able to successful in our defense. Our business may suffer if a finding of infringement is established.

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent Office has developed new and untested regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, that became effective March 16, 2013. It is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in the patents that may be issued from the applications we currently or may in the future own or license from third parties. Further, if any patents license we obtain is deemed invalid and/or unenforceable, it could impact our ability to commercialize or partner our technology.

Competitors or third parties may infringe our patents. We may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or that the third party's technology does not in fact infringe upon our patents. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of

being invalidated or interpreted narrowly and could put our related pending patent applications at risk of not issuing. Litigation may fail and, even if successful, may result in substantial costs and be a distraction to our management. We may not be able to prevent misappropriation of our proprietary rights, particularly in countries outside the United States where patent rights may be more difficult to enforce. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential or sensitive information could be compromised by disclosure in the event of litigation. In addition, during the course of litigation there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we were the first to make the inventions covered by each of our pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents issued to us or our collaborators will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; or
- the patents of others will not have an adverse effect on our business.

If we do not adequately protect our proprietary rights, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could materially harm our business, negatively affect our position in the marketplace, limit our ability to commercialize our product candidates and delay or render impossible our achievement of profitability.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications will be due to be paid to the United States Patent and Trademark Office and various foreign governmental patent agencies in several stages over the lifetime of the patents and/or applications.

We have systems in place, including use of third party vendors, to manage payment of periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees. The United States Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. There are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents

against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and the enforcement of intellectual property.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

We have registered our ACELRX mark in the United States, Canada, the European Union and India. We have also registered our NANOTAB mark in the United States, Hong Kong and Singapore, and our ACCELERATE. INNOVATE. ALLEVIATE. tagline in the United States. We have additionally applied for registration of our ZALVISO mark in the United States on an intent-to-use basis and that application has been allowed. Although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. It is also possible that we have not yet registered all of our trademarks in all of our potential markets, and that there are names or symbols other than "ACELRX" that may be protectable marks for which we have not sought registration, and failure to secure those registrations could adversely affect our business. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile.

Since our initial public offering, or IPO, in February 2011, the trading price of our common stock has experienced significant volatility and is likely to be volatile in the future. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- any delay in submitting an NDA for Zalviso or any of our other product candidates and any adverse development or perceived adverse development with respect to the FDA's filing or review of that NDA;
- adverse results or delays in future clinical trials;
- inability to obtain additional funding, including funding necessary for the planned commercialization and manufacturing of Zalviso in the United States and advancement of clinical trials for other product candidates;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our products;
- inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;

- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, the stock market in general, and The NASDAQ Global Market, or NASDAQ, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Until recently our common stock has thinly traded and in the future, may continue to be thinly traded, and our stockholders may be unable to sell at or near asking prices or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.

Until recently, we had a low volume of daily trades in our common stock on NASDAQ. For example, the average daily trading volume in our common stock on NASDAQ during the first quarter of 2013 was approximately 275,000 shares per day. A more active market for our stock has only recently developed and may not be sustained. Our stockholders may be unable to sell their common stock at or near their asking prices or at all, which may result in substantial losses to our stockholders.

The market for our common stock may be characterized by significant price volatility when compared to seasoned issuers, and we expect that our share price will be more volatile than a seasoned issuer for the indefinite future. As noted above, our common stock may be sporadically and/or thinly traded. As a consequence of this lack of liquidity, the trading of relatively small quantities of shares by our stockholders may disproportionately influence the price of those shares in either direction. The price for our shares could, for example, decline significantly in the event that a large number of our common stock are sold on the market without commensurate demand, as compared to a seasoned issuer that could better absorb those sales without adverse impact on its share price.

Our principal stockholders and management own a significant percentage of our stock and are able to exert significant control over matters subject to stockholder approval.

Our executive officers and directors, together with the stockholders with whom our executive officers and directors are affiliated or associated, beneficially own a significant percentage of our voting stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders are able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, are able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We incur significant increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and NASDAQ, have imposed various requirements on public companies. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

As a public company, we are subject to the requirements of Section 404 of the Sarbanes-Oxley Act. If we are unable to comply with Section 404 in a timely manner, it may affect the reliability of our internal control over financial reporting. Assessing our staffing and training procedures to improve our internal control over financial reporting is an ongoing process.

We have been and will continue to be involved in a substantial effort to implement appropriate processes, document the system of internal control over key processes, assess their design, remediate any deficiencies identified and test

their operation. We cannot be certain at this time whether our measures to improve internal controls will be successful, that we will be able to successfully complete the procedures, certification and attestation requirements of Section 404 or that we or our independent registered public accounting firm will not identify material weaknesses in our internal control over financial reporting. If we fail to comply with the requirements of Section 404, it may affect the reliability of our internal control over financial reporting and negatively impact the quality of disclosure to our stockholders. If we or our independent registered public accounting firm identify and report a material weakness, it could adversely affect our stock price.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall. Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. As of March 31, 2013, we had 37,237,319 shares of common stock outstanding, all of which is eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements of Rule 144 under the Securities Act. Sales of stock by our stockholders could have a material adverse effect on the trading price of our common stock.

Our executive officers and directors and their affiliated funds have agreed that, subject to certain exceptions, during the period ending September 16, 2013, they will not offer, pledge, sell or otherwise transfer or dispose of shares of our common stock or any securities convertible into or exchangeable for our common stock, without the prior written consent of Jefferies LLC, who may release any of the securities subject to these lock-up agreements at any time without notice.

In addition, certain holders of our securities are entitled to certain rights with respect to the registration of their shares of common stock under the Securities Act, subject to the 60 day lock up described above with respect to executive officers and directors and their affiliated funds. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, including pursuant to our Sales Agreement with MLV, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to the 2011 Incentive Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under our 2011

Incentive Plan will automatically increase each year by 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under our 2011 Incentive Plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

We are at risk of securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. The completion of our recent offering in July 2013, together with our public offering in December 2012, our initial public offering, private placements and other transactions that have occurred, may trigger such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our loan and security agreement with Hercules. Regardless of the restrictions in our loan and security agreement with Hercules or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;

- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.