

ACELRX PHARMACEUTICALS INC

Form 10-K

March 12, 2013

[Table of Contents](#)

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

WASHINGTON, DC 20549

**FORM 10-K**

þ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT  
OF 1934

For the fiscal year ended December 31, 2012

or

.. TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE  
ACT OF 1934

For the transition period from to

Commission File Number: 001-35068

**ACELRX PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**41-2193603**  
(IRS Employer  
Identification No.)

**351 Galveston Drive**

**Redwood City, CA 94063**

**(650) 216-3500**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Securities registered pursuant to Section 12(b) of the Act:**

| <b>Title of Each Class</b>      | <b>Name of Each Exchange on Which Registered</b> |
|---------------------------------|--|
| Common Stock, \$0.001 par value | The NASDAQ Stock Market LLC                      |

**Securities registered pursuant to Section 12(g) of the Act:**

**None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§-232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§-229.405) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Large accelerated filer ☐ Accelerated filer ☐  
Non-accelerated filer ☐ (Do not check if a smaller reporting company) Smaller reporting company ☐  
Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2) Yes ☐ No ☒

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 29, 2012 (the last business day of the registrant's most recently completed second fiscal quarter), based upon the last sale price reported on the NASDAQ Global Market on that date, was approximately \$22,421,000. The calculation excludes 15,726,270 shares of the registrant's common stock held by current executive officers, directors and stockholders that the registrant has concluded are affiliates of the registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of January 31, 2013, the number of outstanding shares of the registrant's common stock was 37,059,802.

### DOCUMENTS INCORPORATED BY REFERENCE

None.

**Table of Contents**

**ACELRX PHARMACEUTICALS, INC.**

**2012 ANNUAL REPORT ON FORM 10-K**

**TABLE OF CONTENTS**

|   | <b>Page</b> |
|---|-------------|
| <b>PART I</b>   |             |
| <u>Item 1. Business</u>   | 4           |
| <u>Item 1A. Risk Factors</u>  | 31          |
| <u>Item 1B. Unresolved Staff Comments</u>   | 56          |
| <u>Item 2. Properties</u>   | 56          |
| <u>Item 3. Legal Proceedings</u>  | 57          |
| <u>Item 4. Mine Safety Disclosures</u>  | 57          |
| <b>PART II</b>  |             |
| <u>Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u> | 58          |
| <u>Item 6. Selected Financial Data</u>  | 60          |
| <u>Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>                        | 61          |
| <u>Item 7A. Quantitative and Qualitative Disclosures About Market Risk</u>  | 73          |
| <u>Item 8. Financial Statements and Supplementary Data</u>  | 74          |
| <u>Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure</u>                         | 75          |
| <u>Item 9A. Controls and Procedures</u>   | 75          |
| <u>Item 9B. Other Information</u>   | 76          |
| <b>PART III</b>   |             |
| <u>Item 10. Directors, Executive Officers and Corporate Governance</u>  | 77          |
| <u>Item 11. Executive Compensation</u>  | 81          |
| <u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>              | 91          |
| <u>Item 13. Certain Relationships and Related Transactions, and Director Independence</u>                                   | 93          |
| <u>Item 14. Principal Accounting Fees and Services</u>  | 97          |
| <b>PART IV</b>  |             |
| <u>Item 15. Exhibits, Financial Statement Schedules</u>   | 99          |
| <u>Signatures</u>   | 100         |

Unless the context indicates otherwise, the terms AcelRx, AcelRx Pharmaceuticals, we, us and our refer to AcelRx Pharmaceuticals, Inc.

ACELRX, the ACELRX logo, ARX, NANOTAB, ACCELERATE.INNOVATE.ALLEVIATE, and associated logo are trademarks of AcelRx Pharmaceuticals, Inc.

Other trademarks and trade names that are the property of their respective owners are also contained in this report.

## **Table of Contents**

### **Forward-Looking Statements**

This Annual Report on Form 10-K, or Form 10-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. The forward-looking statements in this Form 10-K are contained principally under Item 1. Business, Item 1A. Risk Factors and Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations. 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, could, 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 10-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 and clinical trials;

our ability to obtain and maintain regulatory approval of our 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 the NanoTab System 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;

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 Item 1A. Risk Factors in this Form 10-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 10-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 10-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.

## Table of Contents

### PART I

#### Item 1. 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, the Sufentanil NanoTab PCA System, or the NanoTab System or ARX-01, is designed to improve the management of moderate-to-severe acute post-operative pain in patients in the hospital setting. Although widely used, the current standard of care for patients with post-operative pain, 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.

##### *The Sufentanil NanoTab PCA System*

The Sufentanil NanoTab PCA System is an investigational pre-programmed, non-invasive, handheld system that allows post-operative patients to self-dose with sublingual sufentanil NanoTabs to manage their post-operative pain. The NanoTab System is designed to address the limitations of IV PCA by offering:

**A high therapeutic index opioid:** The NanoTab System uses the high therapeutic index opioid sufentanil; it offers post-operative pain patients 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 the NanoTab System provides rapid onset of analgesia, therefore eliminating the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections. In addition, because patients are not tethered to IV tubing and a pump for pain relief, the NanoTab System allows for ease of patient mobility.

**A simple, pre-programmed PCA solution:** The NanoTab System is a pre-programmed PCA system designed to eliminate the risk of pump programming errors.

Our Phase 3 clinical program for the NanoTab System consists of two placebo-controlled efficacy and safety trials and an open-label active comparator trial, in which the NanoTab System was compared to IV PCA. A summary of Phase 3 trials and results to date is as follows:

In March 2013, we reported top-line data showing that the primary endpoint was achieved in a pivotal, double-blind, placebo-controlled, Phase 3 trial of the NanoTab System for acute post-operative pain in major open abdominal surgery patients.

In November 2012, we reported top-line data showing that the primary endpoint of non-inferiority was met in an open-label active-comparator Phase 3 clinical trial.

In the second quarter of 2013, we expect data from our final planned Phase 3 trial, a pivotal, double-blind, placebo-controlled efficacy and safety trial in patients with acute post-operative pain following hip and knee replacement surgeries.

##### *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 May 2011, we announced that the U.S. Army Medical Research and Materiel Command, or USAMRMC, awarded us a \$5.6 million grant to support the development of ARX-04 for the treatment of moderate-to-severe acute pain. In November 2012, we initiated a Phase 2 placebo-controlled, dose-finding trial and, in February 2013, dosing of the last patient in this trial was

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

completed. This trial enrolled 101 patients and top-line results from the trial are expected during the second quarter of 2013.



## **Table of Contents**

In addition to our NanoTab System 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 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.

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006.

### **Sufentanil NanoTabs**

Sufentanil, a high therapeutic index opioid, which has no active metabolites, is 5 to 10 times more potent than fentanyl and is used intravenously as a primary anesthetic to produce balanced general anesthesia for surgery, and for epidural administration during labor and delivery. Sufentanil has many pharmacological advantages over other opioids. Published studies demonstrate that sufentanil produces significantly less respiratory depressive effects relative to its analgesic effects compared to other opioids, including morphine, alfentanil and fentanyl. These third party clinical results correlate well with preclinical trials demonstrating sufentanil's high therapeutic index, or the ratio of the toxic dose to the therapeutic dose of a drug, used as a measure of the relative safety of the drug for a particular treatment. Accordingly, we believe that sufentanil can be developed to provide an effective and well-tolerated treatment for acute and breakthrough pain. The following table illustrates the difference between the therapeutic index of different opioids.

| <b>Opioid</b> | <b>Therapeutic Index</b> |
|---------------|--------------------------|
| Meperidine    | 5                        |
| Methadone     | 12                       |
| Morphine      | 71                       |
| Hydromorphone | 232                      |
| Fentanyl      | 277                      |
| Sufentanil    | 26,716                   |

In addition, the pharmaceutical attributes of sufentanil, including lipid solubility and ionization, result in rapid cell membrane penetration and onset of action, which we believe make sufentanil an optimal opioid for the treatment of both acute pain and breakthrough pain.

Although the analgesic efficacy and safety of sufentanil have been well established, the product's use has been historically limited due to its short duration of action when delivered intravenously. We believe that sublingual delivery of sufentanil avoids the high peak plasma levels and short duration of action of IV administration.

## **Table of Contents**

Our portfolio of product candidates leverages the inherent advantages of sufentanil that are underutilized in medical practice. We believe our non-invasive, proprietary NanoTab sublingual dosage form overcomes the limitations of the current treatment options available for both acute and breakthrough pain.

None of our product candidates have been approved by the United States Food and Drug Administration, or FDA. We have not generated any revenue from the sale of any of our product candidates.

### ***Sublingual Delivery of Sufentanil: Summary of Phase 1 Clinical Studies Results***

We have completed four Phase 1 PK studies with our proprietary sublingual sufentanil NanoTabs to support our four product candidates under development. These studies demonstrated desirable and consistent PK parameters, including:

relatively high bioavailability via the oral mucosa and very low gastrointestinal, or GI, bioavailability;

prolonged plasma levels relative to IV delivery;

PK parameters proportional to dose across a wide range of doses (2.5 mcg to 80 mcg);

lower peak plasma concentration, or  $C_{max}$ , than IV delivery;

time to maximum plasma concentrations, or  $T_{max}$ , range from 30 to 90 minutes;

relatively low patient to patient variability in  $T_{max}$  and  $C_{max}$ ; and

repeat dosing PK that supports a 20 minute minimum re-dosing interval.

## **Table of Contents**

The chart below illustrates the PK profile of sublingual sufentanil NanoTab compared to IV delivery of sufentanil from one of our completed Phase 1 PK studies.

We have demonstrated that sublingual delivery of sufentanil avoids the high peak plasma levels and short duration of action of IV administration, enabling potential for broader use. Our proprietary NanoTab dosage form is a very small disc-shaped tablet with a bioadhesive excipient, or inactive ingredient, that enables the NanoTab to adhere to mucosal tissues. This allows sublingual delivery of sufentanil from the NanoTab by adherence to the sublingual mucosa, or tissues under the tongue. The NanoTab adheres within seconds after administration and full disintegration occurs within minutes. The small size of the NanoTab, pictured above, is designed to minimize the saliva response and amount of sufentanil swallowed, resulting in high oral transmucosal uptake, whereby a majority of the drug is absorbed via the oral tissues directly into the bloodstream, and consistent pharmacokinetics.

We have completed three additional definitive PK studies that will be included in the NDA, as follows:

IAP101 (single vs. multiple dose) Study IAP101 was conducted with the Sufentanil NanoTab PCA System and was designed to characterize the plasma concentration profile of the Sufentanil NanoTab after repeated dosing. Subjects self-administered a single dose from the NanoTab PCA System and, after a washout period, 40 consecutive doses every 20 minutes. Plasma concentration profiles and pharmacokinetic parameters after the single and multiple dosing were compared.

IAP102 (route of delivery) Study IAP102 was conducted to characterize the plasma concentration profile of the Sufentanil NanoTab after transmucosal (sublingual and buccal) and oral administration. The absolute bioavailability of the Sufentanil NanoTab was also calculated.

IAP104 (drug interaction study) Study IAP104 was conducted to determine whether there is a change in the Sufentanil NanoTab plasma concentration profile when a subject is concomitantly receiving a CYP3A4 inhibitor.

**Table of Contents****Our Product Candidates**

The following table summarizes key information about our existing product candidates for which we currently hold worldwide commercialization rights.

| <b>Product Candidate</b> | <b>Description</b>                       | <b>Target Indication</b>                                     | <b>Development Status</b>  |
|--------------------------|--|--|--|
| ARX-01                   | Sufentanil NanoTab PCA System            | Moderate-to-severe acute post-operative pain                 | <p>Three Phase 3 clinical trials were initiated in 2012 as follows:</p> <p>In April 2012, we initiated an open-label active comparator Phase 3 clinical trial comparing ARX-01 to the current standard of care, IV PCA morphine, in patients with acute post-operative pain following open-abdominal surgery or major orthopedic surgery. In November 2012, we reported that this trial met its primary endpoint of non-inferiority.</p> <p>In March 2012, we initiated a double-blind placebo-controlled efficacy and safety Phase 3 clinical trial in patients with acute post-operative pain following open-abdominal surgery. In March 2013, we reported that this trial met its primary endpoint.</p> <p>In August 2012, we initiated a double-blind placebo-controlled efficacy and safety Phase 3 clinical trial in patients with acute post-operative pain following major orthopedic surgeries. We expect top-line data for this trial in the second quarter of 2013.</p> |
| ARX-02                   | Sufentanil NanoTab BTP Management System | Cancer breakthrough pain                                     | <p>Phase 2 clinical trial and End of Phase 2 meeting successfully completed.</p> <p>Future development contingent upon identification of corporate partnership resources.</p>  |
| ARX-03                   | Sufentanil/Triazolam NanoTab             | Mild sedation for painful procedures in a physician's office | <p>Phase 2 clinical trial and End of Phase 2 meeting successfully completed.</p> <p>Future development contingent upon identification of corporate partnership resources.</p>  |
| ARX-04                   | Sufentanil Single-Dose NanoTab           | Moderate-to-severe acute pain                                | <p>Phase 2 clinical trial initiated in November 2012 pursuant to grant from USAMRMC. In February 2013, we completed enrollment of this trial and we expect top-line data in the second quarter of 2013.</p>  |

## **Table of Contents**

### **ARX-01 Sufentanil NanoTab PCA System**

#### ***The Market Opportunity for the NanoTab System***

This product candidate has not been approved by the FDA. We have not generated any revenue from the sale of any of our product candidates.

According to the 2010 Decision Resources Acute Pain Report, or 2010 DR Report, the post-operative pain market in the United States, Europe and Japan is growing steadily and is expected to reach approximately \$6.5 billion by 2018. Despite its size, this market remains underserved. Studies report that up to 75% of patients experience inadequate pain relief after surgery. Inadequate pain relief can lead to decreased mobility, which increases the risks of other medical complications, including deep vein thrombosis and partial lung collapse, and can result in extended hospital stays. The 2010 DR Report projects that in 2013, 20.7 million in-patient procedures performed in the United States and the five largest European Union member state markets will require post-operative treatment of pain, growing at a rate of approximately 1% per annum. Additionally, based on an analysis of data published in 2008 from the World Health Organization, we estimate that there are approximately 27 million surgical procedures annually in other moderate-to-high per capita healthcare expenditure nations in which patients experience moderate-to-severe pain.

Commissioned market research targeting surgeons and anesthesiologists has identified a consistent positive response to the attributes of the NanoTab System and indicates an interest in using the NanoTab System in at least 75% of their eligible patients. Additional market research indicated that physicians expressed interest in using the NanoTab System for patients who stay in the hospital for less than 24 hours and are not traditionally treated with IV PCA. Pharmacy and Therapeutics, or P&T, committees also indicate strong interest in the NanoTab System, with 91% of the P&T committee members interviewed indicating likely adoption to formulary.

#### ***How the NanoTab System Addresses the Unmet Medical Need in Post-Operative Pain Management***

There are many deficiencies associated with the current use of IV PCA, including:

side effects associated with the most commonly used opioid, morphine, and its active metabolites;

infection risk, analgesic gaps and decreased mobility associated with the invasive nature of IV delivery; and

medication errors, which in some instances may be fatal, due to the complexity of IV PCA pumps, many of which arise from programming errors.

According to published literature, the estimated annual error rate is 407 errors per 10,000 people treated with IV PCA in the United States. Published analysis of Medmarx from 2000 to 2005 reveals that IV PCA errors represent a four-fold higher relative risk of harm compared to all other medication errors. The most recent published analysis of the FDA MAUDE database reports that 5% of IV PCA operator errors reported during a two-year index period, from 2002 to 2003, resulted in patient deaths. Approximately 56,000 adverse events were reported to the FDA between 2005 and 2009, prompting 70 Class II infusion pump recalls of devices that could cause temporary or reversible adverse effects and 14 Class I infusion pump recalls of devices that could cause serious injury or death. These issues with infusion pumps have resulted in the issuance of new draft guidance by the FDA, significantly increasing the data required to be submitted by IV PCA pump manufacturers to address safety problems.



## **Table of Contents**

The NanoTab System has the potential to address many of the key disadvantages of IV PCA, including:

reducing the incidence of drug related side effects;

eliminating the risk of IV PCA related infections, reducing analgesic gaps and enhancing mobility; and

eliminating the risk of programming errors.

We believe that the NanoTab System will provide a favorable safety, efficacy and tolerability profile, enabling the NanoTab System to become the new standard of care for PCA. Further, we believe use of the NanoTab System will result in increased patient satisfaction and reduced overall healthcare costs.

### ***The NanoTab System Description***

The NanoTab System allows patients to self-administer sublingual Sufentanil NanoTabs as needed to manage their post-operative pain in the hospital setting, and provides the record-keeping attributes of a conventional IV PCA pump while avoiding some of the key issues, such as programming errors, associated with conventional IV PCA use.

Our NanoTab System consists of three components:

sufentanil, a high therapeutic index opioid;

NanoTabs, our proprietary, non-invasive sublingual dosage form; and

our novel, pre-programmed, handheld PCA device that enables simple patient-controlled delivery of NanoTabs in the hospital setting and eliminates the risk of programming errors.

The NanoTab System utilizes sufentanil, which has one of the highest therapeutic indices of all commercially available opioids, making it an attractive candidate for the management of post-operative pain. Formulated in our proprietary sublingual NanoTab dosage form, sufentanil provides for relatively high bioavailability, with lower peak drug levels and a longer duration of action compared to IV delivery.

Our NanoTab System consists of the following components: a disposable dispenser tip (Figure A); a disposable dispenser cap (Figure B); an adhesive thumb tag (Figure C); a stack of 40 sufentanil 15 mcg NanoTabs (approximately a two-day supply) in a disposable radio frequency identification and bar-coded cartridge (Figure D); a reusable, rechargeable handheld controller (Figure E); a tether (Figure F); and an authorized access card (Figure G).

This product candidate has not been approved by the FDA. We have not generated any revenue

from the sale of any of our product candidates.

## **Table of Contents**

Our novel handheld PCA device has the following safety features:

an authorized access card, which is a wireless system access key for the healthcare professional;

a wireless, electronic, adhesive thumb tag that acts as a single-patient identification key;

pre-programmed 20-minute lock-out to avoid overdosing;

NanoTab singulation, or dispensing, motion that eliminates runaway motor delivery risk;

a security tether that is designed to prevent theft and misuse; and

fully automated inventory record of NanoTabs usage.

To set up the handheld PCA device, the nurse or healthcare professional turns on the controller and follows the simple step-by-step instructions on the color graphical user interface screen described below:

retrieve the NanoTab cartridge from secure drug storage;

lock the cartridge and dispenser into the controller; and

set up the secure patient access system, which is comprised of a security tether and a wireless, electronic, adhesive thumb tag that acts as a single-patient identification key.

To use the NanoTab System, the patient would:

confirm that the green indicator light is illuminated, meaning the device is available to dose;

place dispenser tip under tongue and push the large button on the controller, which dispenses a single NanoTab;

remove the device from mouth upon hearing a tone confirming delivery of the NanoTab; and

see the blue indicator light illuminate, indicating no new dose can be dispensed for the next 20 minutes.

### ***NanoTab System Clinical Program***

#### ***Summary***



## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Our Phase 3 program for the NanoTab System consists of three Phase 3 clinical trials. We have reported top-line results from two of these three clinical trials and expect to report top-line data from the final planned Phase 3 trial in the second quarter of 2013. Prior to our Phase 3 program, we completed three successful Phase 2 clinical trials of sufentanil NanoTabs in the post-operative setting. These Phase 2 clinical trials demonstrated analgesic efficacy, a low adverse event profile and excellent device functionality. During our End of Phase 2 meeting with the FDA, the FDA stated that the demonstration of efficacy versus placebo in two Phase 3 clinical trials with a total safety database of at least 600 patients exposed to the active drug should suffice to support a new drug application, or NDA. We have designed our Phase 3 clinical trials based on the feedback from the FDA.

### *Phase 3 Clinical Trials for the NanoTab System*

#### Active comparator trial (IAP 309)

In November 2012, we reported top-line data showing that the NanoTab System had met its primary endpoint of non-inferiority in the Phase 3 open-label active comparator trial designed to compare the efficacy and safety of the NanoTab System (15 mcg/dose) to IV PCA with morphine (1mg/dose) for the treatment of moderate-to-severe acute post-operative pain. Utilizing a randomized, open-label, parallel group design, this trial enrolled 359 adult patients at 26 U.S. sites for the treatment of pain immediately following open-abdominal or major orthopedic surgery (hip and knee replacement). Patients were randomized 1:1 to treatment with the NanoTab System or IV PCA morphine and were treated for a minimum of 48 hours and up to 72 hours.

## **Table of Contents**

The primary endpoint for the trial was a comparison of the patient's response using the Patient Global Assessment, or PGA, of method of pain control over the 48-hour trial period between the patients treated with the NanoTab System and IV PCA morphine. The PGA uses a 4-point scale of poor, fair, good or excellent to rate each method of pain control. The primary endpoint was determined by measuring the proportion of patients who responded good or excellent using the PGA to rate their method of pain control. An overview of the top-line primary endpoint results of this Phase 3 clinical trial demonstrates that:

For the primary comparison, the NanoTab System was non-inferior ( $p < 0.001$ ) to IV PCA morphine for the primary endpoint of PGA comparison over the 48-hour study period as determined by the combined percentage of patients with PGA ratings of good or excellent (78.5% vs. 65.6%, respectively). A p-value is a probability with a value ranging from 0 to 1, which indicates the likelihood that a clinical trial is different between treatment and control groups. P-values below 0.05 mean that there is a 95% or greater chance that there is a true difference between the groups, and are typically referred to as statistically significant.

The assessment of non-inferiority was based on a lower limit of 15% for the 95% confidence interval, or CI, around the difference between these percentages. Because the 95% CI was +3.7% to +22.1% for the 48 hour PGA and therefore did not cross the zero difference line, a secondary comparison of the primary endpoint, specifically a statistical analysis of superiority could be performed. In this trial, the NanoTab System was statistically superior to IV PCA morphine for the PGA endpoint ( $p = 0.007$ ). Statistically superior PGA was also seen at the 24 hour and 72 hour timepoints.

A number of secondary endpoints were also evaluated, including comparison of individual PGA ratings, a Healthcare Professional Global Assessment, or HPGA, of method of pain control, drop outs from the trial due to inadequate analgesia and adverse events, and Patient and Nurse Ease of Care Questionnaires using a validated questionnaire methodology specifically to evaluate patient-controlled analgesia systems. The NanoTab System achieved a PGA rating of excellent in 42.9% of treated patients, compared to 30.6% for IV PCA with morphine, with a p-value of 0.016.

The HPGA was measured at 24, 48 and 72 hours, and produced similar results to the Patient Global Assessment. HPGA ratings of good or excellent at 48 hours were 81.4% for the NanoTab System compared to 70.0% for IV PCA morphine. An assessment of non-inferiority was conducted and demonstrated that the NanoTab System was non-inferior to IV PCA morphine ( $p < 0.001$ ) in the trial. Because the 95% CI was +2.6% to +20.2% for the 48 hour HPGA and therefore didn't cross the zero difference line, a statistical analysis for superiority could be performed, which demonstrated that for this trial, the NanoTab System was statistically superior to IV PCA morphine for the HPGA endpoint at 48 hours ( $p = 0.012$ ). Statistically superior HPGA was also seen at the 24 hour and 72 hour timepoints.

Throughout the course of the trial, 7.3% of patients treated with the NanoTab System 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 the NanoTab System 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, one was related to the NanoTab System and two were related to IV PCA morphine.

The Patient Ease of Care Questionnaire, or Patient Questionnaire, asked patients to respond to 21 questions regarding aspects of analgesia and PCA systems using a zero to five rating scale, including statements such as, but not limited to, 'pain woke me up from my sleep', 'the device was easy to use', and 'the device interfered with my ability to get out of bed and walk around'. Answers to the Patient Questionnaire were combined for an Overall Patient Ease of Care score. These Patient Questionnaire statements were also grouped into six validated subscales, such as 'comfort with device', 'impact on movement', and 'knowledge and understanding'. Patients were also asked in this Patient Questionnaire to rate their Overall Satisfaction with the level of pain control and with the way in which the medication was administered during the trial.

## Table of Contents

The Nurse Ease of Care Questionnaire, or Nurse Questionnaire, asked nurses to respond to 21 questions regarding aspects of analgesia and PCA systems using a zero to five rating scale, including statements regarding the set-up and management of the systems and management of the patients. Answers to the Nurse Questionnaire were combined for an Overall Nurse Ease of Care score. These Nurse Questionnaire statements were grouped into two validated subscales entitled time-consuming and bothersome. Nurses were also asked in this Nurse Questionnaire to rate their Overall Satisfaction based on the level of pain control and with their overall satisfaction of the system.

An overview of results of the Patient and Nurse Questionnaires results includes:

Patients in the trial reported that they had significantly greater Overall Satisfaction with the NanoTab System compared to IV PCA morphine (4.15 vs. 3.84, respectively, out of a 0 to 5 scale, with a p-value equal to 0.004).

Patients in the trial reported that they had greater Overall Ease of Care with the NanoTab System compared to IV PCA morphine (4.45 vs. 4.07, respectively, out of a 0 to 5 scale, with a p-value less than 0.001).

Nurses managing patients in the trial reported they had significantly greater Overall Satisfaction with the NanoTab System compared to IV PCA morphine (3.92 vs. 3.35, respectively, out of a 0 to 5 scale, with a p-value less than 0.001).

Nurses managing patients in the trial reported they had greater Overall Ease of Care with the NanoTab System compared to IV PCA morphine (4.27 vs. 3.82, respectively, out of a 0 to 5 scale, with a p-value equal to 0.017).

As noted above, additional subscale analyses were performed related to the Overall Ease of Care with the NanoTab System as reported by both nurses and patients. The results, as detailed in the tables below, demonstrate that all Patient Ease of Care subscales were significantly higher for the NanoTab System than for IV PCA morphine in the trial. For the Nurse Ease of Care subscales, nurses rated the NanoTab System significantly less bothersome than IV PCA morphine and there was a trend towards the NanoTab System being less time consuming than IV PCA morphine.

### Patient Ease of Care

#### Subscale

| (0-5 scale)                 | NanoTab System | IV PCA morphine | P Value |
|-----------------------------|----------------|-----------------|---------|
| Confidence with Device      | 4.69           | 4.51            | 0.015   |
| Comfort with Device         | 4.47           | 4.33            | 0.041   |
| Impact on Movement          | 4.73           | 3.88            | <0.001  |
| Dosing Confidence           | 4.74           | 4.47            | 0.003   |
| Pain Control                | 3.58           | 3.16            | 0.004   |
| Knowledge and Understanding | 4.47           | 4.05            | <0.001  |

#### Nurse Ease of Care

#### Subscale

| (0-5 scale)    | NanoTab System | IV PCA morphine | P Value |
|----------------|----------------|-----------------|---------|
| Time consuming | 0.92           | 1.24            | 0.076   |
| Bothersome     | 0.54           | 1.09            | 0.006   |

## Table of Contents

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

In March 2013, we reported top-line data results demonstrating that the NanoTab System met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of the NanoTab System 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 for the treatment of acute post-operative pain immediately following major abdominal surgery. Patients were treated for post-operative pain for a minimum of 48 hours, and up to 72 hours. Patients were randomized 2:1, with 119 patients randomized to sufentanil treatment and 59 to placebo treatment. Both treatments were delivered by the patient, as needed, using the NanoTab System with a 20-minute lock-out period. Patients in both groups could receive up to 2 mg morphine intravenously per hour as a rescue medication, the primary purpose of this rescue medication being to provide placebo-treated patients access to pain medication to enable them to stay in the trial as long as possible. Pre-rescue pain scores were imputed to minimize the impact of this rescue opioid on efficacy evaluations.

The primary endpoint evaluated pain intensity over the 48-hour study period compared to baseline, or Summed Pain Intensity Difference (SPID-48), in patients following major open abdominal surgery. Patients receiving sufentanil NanoTabs demonstrated a significantly greater SPID-48 compared to placebo-treated patients during the study period (105.6 and 55.6, respectively;  $p=0.001$ ).

A number of secondary endpoints were also evaluated, including SPID at 24 hours and 72 hours, drop outs from the trial due to inadequate analgesia and adverse events, and Patient Ease of Care Questionnaires using a validated questionnaire methodology specifically to evaluate patient-controlled analgesia systems. A summary of the results for the secondary endpoints is as follows:

24 hours and 72 hours after first dose, SPID was significantly greater in the sufentanil-treated patients than in the placebo-treated patients ( $p<0.001$  and  $p=0.004$ , respectively).

A summed pain relief measure over the 48-hour study period, commonly referred to as TOTPAR, was significantly greater for sufentanil-treated patients than placebo-treated patients ( $p=0.002$ ).

Eighty, or 70.2%, of the sufentanil NanoTab-treated patients completed the 48-hour study period, compared to 30, or 51.7%, of placebo-treated patients. Reasons for drop-out in the sufentanil-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 sufentanil-treated patients and 67.2% of placebo-treated patients. Adverse events with an occurrence greater than 5% in either the sufentanil 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 sufentanil group, experienced a serious adverse event, which was determined to be unrelated to the study drug by the investigator.

Patients in the trial who were treated with Sufentanil NanoTabs reported an average Overall Ease of Care of 4.39 out of a 0 to 5 scale. In addition, patients in the placebo arm of the trial also reported favorable Overall Ease of Care scores, with an average score of 4.36. These results are comparable to the results from the active comparator trial, which is summarized above.

## **Table of Contents**

The chart below illustrates the SPID-48 results from the pivotal Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP 310).

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

In August 2012, we initiated a Phase 3 clinical trial with the NanoTab System in a double-blind, placebo-controlled trial for a minimum of 48 hours and up to 72 hours in patients who are undergoing a total hip or knee replacement. The objective is to compare the efficacy and safety of the Sufentanil NanoTab PCA System to placebo in the management of acute post-operative pain after major orthopedic surgery. Up to 440 patients will be randomly assigned to treatment with sufentanil or placebo. The primary endpoint is the sum of pain intensity difference to baseline (SPID) over 48 hours. Dosing of the final subject in this trial is expected around the end of the first quarter of 2013, and we expect to receive top-line data from this trial in the second quarter of 2013. Key secondary endpoints include an assessment of different imputation strategies for the use of rescue opioids, pain intensity and relief scores and patient and healthcare professional Global Assessments and Ease of Care questionnaires.

### *Phase 2 Clinical Results for ARX-01*

We completed three Phase 2 clinical trials in support of sufentanil NanoTabs. Across all trials, the average time interval between doses was approximately 80 minutes. This compares favorably to typical redosing intervals for IV PCA with average period between dosing of 20 to 40 minutes. No SAEs were reported that were considered to be related to the trial drug. Adverse events, or AEs, that were reported were similar to those reported for placebo-treated patients. These results demonstrate that sufentanil NanoTabs are effective and well tolerated by patients undergoing both major orthopedic and abdominal surgical procedures.

## **Table of Contents**

### *Phase 2 Clinical Results in Unilateral Knee Replacement (ARX-C-001)*

In the first Phase 2 clinical trial, we conducted a randomized, double-blind, placebo-controlled, multicenter Phase 2 clinical trial to evaluate the efficacy, safety and tolerability of sublingual sufentanil NanoTabs in patients undergoing elective unilateral knee replacement. The trial enrolled 101 male and female patients 45 to 80 years of age who were undergoing elective knee replacement surgery. This procedure was chosen as it represents one of the most painful procedures patients undergo in the hospital setting. Patients were randomly assigned to treatment with sufentanil NanoTab 5 mcg, 10 mcg, 15 mcg, or placebo. Sufentanil NanoTabs were administered by trial staff at the request of the patient with at least 20 minutes between doses. The primary endpoint was the sum of the pain intensity difference at each evaluation time point compared to baseline over the 12-hour trial duration, or SPID-12.

The trial results demonstrated that sufentanil NanoTab 15 mcg was effective, safe and well-tolerated for the treatment of acute post-operative pain in patients who had undergone unilateral knee replacement. The sufentanil NanoTab 15 mcg SPID-12 was higher than placebo ( $p=0.018$ ) using the last observation carried forward, or LOCF, imputation method. The sufentanil NanoTab 5 mcg or 10 mcg dosage strengths did not achieve a statistically significant separation from placebo overall. However, the 10 mcg dose was statistically significant as compared with placebo for women ( $p<0.05$ ). Throughout the trial there were statistically significant differences in SPID-12 scores between the sufentanil NanoTab 15 mcg dose group and the placebo group, even at the earliest time point of 15 minutes ( $p=0.038$ ). There were no clinically significant changes in laboratory variables, vital signs or oxygen saturation during the trial. The five SAEs reported were all considered unrelated to trial drug and occurred after the end of trial drug dosing.

### *Phase 2 Clinical Results in Open-Abdominal Surgery (ARX-C-005)*

Our second Phase 2 clinical trial tested sufentanil NanoTabs 10 mcg, 15 mcg or placebo in patients undergoing open-abdominal surgery. In all other respects this trial was similar in design to our first trial. Both dosage strengths were significantly more effective than placebo for SPID-12 ( $p<0.001$ ) as well as for all measures of pain intensity and pain relief. Significant differences between the sufentanil NanoTab treatment groups and the placebo group were observed within 2 hours after the first dose of trial drug and continued until the end of the 12-hour treatment period. There were no clinically significant changes in laboratory variables, vital signs or oxygen saturation during the trial. There were no SAEs reported during the trial drug treatment period.

We conducted an open-label functionality, safety and efficacy trial of the ARX-01 NanoTab delivery System in patients undergoing elective unilateral knee replacement surgery. The trial was a prospective, open-label, multicenter trial in 30 male and female patients 45 to 80 years of age with an average age of 66. All patients were treated with sufentanil NanoTab 15 mcg dosage strength. The primary endpoint was the percent of patients who completed the trial without any Sufentanil NanoTab PCA System failures. The trial also collected patient feedback on the design characteristics of the PCA System.

Patients self-administered sufentanil NanoTabs repeatedly over the 12-hour trial using the NanoTab System without any system failures or dosing errors for all 30 patients. Over 80% of the patients reported the two highest scores on the 5-point Likert scale of overall patient satisfaction with the Sufentanil NanoTab PCA System 15 mcg. All 30 enrolled patients indicated that they could handle the Sufentanil NanoTab PCA System easily, that the user instructions were clear, that the dosing tone was loud enough and that the time required for dosing was just right. Ninety percent of the patients indicated that the size and the shape of the dosing tip were also just right. The majority of patients indicated that the other system features (weight, size, shape, dose button function) were acceptable.

The mean pain intensity scores decreased from 5.5 at baseline to the lowest score of 3.0 at 2 hours. Dropout due to inadequate analgesia was 6.7%. There were no clinically significant changes in laboratory variables or vital signs and no SAEs reported during the trial drug treatment period.

## **Table of Contents**

### **ARX-02 Sufentanil NanoTab BTP Management System**

#### ***The Market Opportunity for ARX-02***

This product candidate has not been approved by the FDA. We have not generated any revenue from the sale of any of our product candidates.

According to the American Cancer Society, there were more than 1.5 million new cancer cases in the United States in 2010. It is estimated that over 625,000 of these cases result in patients who experience breakthrough pain. We estimate the prescription volume for oral transmucosal products for the management of cancer breakthrough pain to be 220,000 prescriptions per year. This suggests that less than 10% of cancer patients with cancer breakthrough pain are treated with approved transmucosal breakthrough pain medications. In addition, many physicians use immediate release oral opioids to treat cancer breakthrough pain. We believe that this market is significantly larger than the transmucosal product market. Market research among physicians managing cancer patients indicates that ARX-02 could capture approximately a quarter of the cancer breakthrough pain prescriptions. In this research, ARX-02 was predicted to take share equally from both the immediate release oral products and the transmucosal products.

#### ***How ARX-02 Addresses the Unmet Medical Need in Cancer Breakthrough Pain***

All products approved for the treatment of cancer breakthrough pain available today are fentanyl-based and have a number of limitations, including:

elimination half-lives of 6 to 14 hours to treat a cancer breakthrough pain event that typically lasts 15 to 60 minutes;

inconsistent  $T_{\max}$  that ranges from 20 to 240 minutes, and can result in erratic onset of action and the potential for dose-stacking;

local adverse events, such as dental caries and oral mucosal irritation; and

drug packaging that lacks effective deterrence against abuse and misuse.

We designed ARX-02 to address these problems by:

providing sufentanil, a shorter duration of action opioid with an elimination half-life ranging from 2 to 4 hours, which more closely matches the duration of a cancer breakthrough pain event;

utilizing sufentanil, which provides for a consistent  $T_{\max}$  with a narrow range of 30 to 90 minutes, thereby reducing the risk of dose-stacking;

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

avoiding irritation of the oral mucosa, as demonstrated in our clinical trials; and

packaging technology that enhances patient safety by reducing the possibility of misuse or abuse, while providing healthcare professionals with usage data.

In addition, continual use of any given opioid by a patient creates a risk of tolerance specific to that molecule, reducing the effectiveness of the drug. We believe the availability of ARX-02, as a non-fentanyl based product, will allow physicians to rotate opioids prescribed for cancer breakthrough pain, thereby maintaining the effectiveness of treatment.



## **Table of Contents**

### ***ARX-02 Description***

ARX-02 is a product candidate for the treatment of cancer patients who suffer from breakthrough pain. ARX-02 consists of a magazine containing 30 single dose applicators, or SDAs, loaded into a multiple SDA dispenser, or MSD. Each SDA includes a sufentanil NanoTab that a patient can self-administer to his or her sublingual space for oral transmucosal absorption. The MSD:

protects and dispenses SDAs, one at a time;

displays a recent dose indicator that is designed to mitigate overdosing;

has child-resistant, elderly-friendly features; and

provides electronic date and time stamping of each SDA removal event.

The date and time event log is designed to be retrieved from the MSD by a healthcare professional during an office visit to assist the prescriber in understanding the usage profile of the medication, including diversion or abuse. Overall, our goal is to improve the treatment of cancer breakthrough pain while adding a substantially heightened level of detection and deterrence around prescription opioid use, misuse and abuse. While the initial dispenser for outpatient use is designed for dispensing sufentanil NanoTabs for cancer breakthrough pain events, we believe this concept could be adapted into developing dispensers for other scheduled drugs in the future.

### ***Sufentanil NanoTab BTP Management System ARX-02 Clinical Program Overview***

We have completed a successful Phase 2 clinical trial of ARX-02. The primary endpoint in this trial was achieved and demonstrated that the time-weighted summed pain intensity difference over 30 minutes, or SPID-30, following treatment for sufentanil NanoTab-treated episodes was greater than placebo-treated episodes ( $p < 0.001$ ). In addition, pain intensity and pain relief were included as secondary endpoints. Lower scores for pain intensity were reported at each evaluation time point for sufentanil-treated episodes compared to placebo-treated episodes ( $p = 0.027$  at 15 minutes and  $p < 0.001$  at all other time points). Time reported time-weighted total pain relief, or TOTPAR, was greater at all time points for sufentanil-treated episodes compared to placebo-treated episodes ( $p = 0.049$  and  $p = 0.009$  for the 10 and 15 minute time points, respectively, and  $p < 0.001$  for the remaining time points). The trial also demonstrated a low adverse event profile.

We held an End of Phase 2 meeting with the FDA in July 2010. The FDA stated that the demonstration of efficacy versus placebo in a single Phase 3 clinical trial with a total safety database of 300 to 500 patients exposed to active drug, with at least 100 patients treated for a minimum of three months, may support an indication for the treatment of cancer breakthrough pain with underlying chronic pain.

Further development of the ARX-02 program is contingent on identification of corporate partnership resources.

## **Table of Contents**

### **ARX-03 Sufentanil/Triazolam NanoTab**

#### ***The Market Opportunity for ARX-03***

This product candidate has not been approved by the FDA. We have not generated any revenue from the sale of any of our product candidates.

Each year in the United States, more than 100 million procedures take place in a physician's office that are known to be anxiety-inducing and painful, according to commissioned market research data that was completed in 2010. These include diagnostic procedures such as breast and prostate biopsies, cosmetic procedures such as liposuction and dermal abrasions, interventional radiology procedures, and therapeutic procedures such as vasectomies and endometrial ablation procedures. IV sedative medications are typically not offered to these patients because of the high cost of the specialized personnel and monitoring equipment. Despite the high potential for pain and anxiety, most patients currently undergo these procedures with only a local anesthetic, resulting in unnecessary procedure discomfort. We believe there is significant opportunity for a fast-acting, effective and safe product that can provide mild levels of sedation, anxiety reduction and analgesia for painful procedures conducted in a physician's office without the need for specialized personnel to monitor the patient.

#### ***How ARX-03 Addresses the Unmet Medical Need for Painful Procedures in a Physician's Office***

The Joint Commission on the Accreditation of Healthcare Organizations, or JCAHO, mandates that IV sedation requires specialized monitoring, resuscitative equipment and appropriately trained staff. As a result, many practitioners do not provide any IV sedation to their patients prior to or during painful procedures that take place in a physician's office, and instead rely only on the analgesic benefit of local anesthetics.

The anxiety and pain that an individual experiences during painful procedures in a physician's office without sedation has been studied and reported in peer-reviewed journals. Ninety-six percent of men report moderate pain immediately after prostate biopsy, with only 4% of patients reporting no pain during the biopsy. Similarly, women undergoing breast biopsies have pre-procedural scores averaging 60 to 70 out of 100 for visual analog scale measurements of nervousness, tension and fearfulness. This data highlights the need for a mild sedative with analgesic and anxiety-reducing properties in addition to a local anesthetic for painful procedures in a physician's office.

We believe that ARX-03 can provide physicians with a non-invasive, rapid-acting product for mild sedation, anxiety reduction and pain relief during painful diagnostic and therapeutic procedures in a physician's office. We believe the availability of ARX-03 may increase the number of diagnostic and therapeutic procedures performed in a physician's office, resulting in cost savings because specialized personnel and equipment would not be necessary.

#### ***ARX-03 Description***

ARX-03 Sufentanil/Triazolam NanoTab is a single, fixed-dose sublingual product candidate designed to be administered by a healthcare professional prior to a painful procedure in a physician's office. An important advantage of sufentanil and triazolam over other drugs in their classes is their rapid uptake from the sublingual mucosa. Our Phase 2 clinical data showed that administering ARX-03 via sublingual route prior to a procedure results in a rapid onset of mild sedation and reduction in anxiety in 15 to 30 minutes. Sufentanil and triazolam

## **Table of Contents**

have short half-lives compared to many other agents in the same class of compounds, enabling patients treated with ARX-03 to be discharged immediately following completion of the procedure. The sublingual route of administration avoids the high plasma concentrations associated with IV delivery, thereby obviating the need for specialized personnel and extensive monitoring.

### ***Sufentanil/Triazolam NanoTab ARX-03 Clinical Program Overview***

We have completed a successful Phase 2 clinical trial of ARX-03 demonstrating rapid onset of mild sedation and anxiety reduction, with a low adverse event profile during an abdominal liposuction procedure. In addition, we participated in an End of Phase 2 meeting with the FDA in May 2010 to discuss the Phase 3 clinical program and requirements for an NDA submission. Based on these discussions, two four-arm factorial Phase 3 clinical trials will be required with a minimum of 700 patients exposed to active drug.

Further development of the ARX-03 program is contingent on identification of corporate partnership resources.

### ***ARX-04 Sufentanil Single-Dose NanoTab***

#### ***The Market Opportunity for ARX-04***

This product candidate has not been approved by the FDA. We have not generated any revenue from the sale of any of our product candidates.

We believe that ARX-04 could be useful in a variety of medically supervised settings, including for battlefield casualty treatment, by paramedics during patient transport, in the emergency room, or for post-operative patients, following either short-stay or ambulatory surgery, who do not require more long-term patient-controlled analgesia. According to the Centers for Disease Control and Prevention, or CDC, there were more than 136 million emergency room visits in 2009, of which it is estimated that more than 45 million were injury-related emergency room visits, and analgesics were provided or prescribed during more than 94 million of these visits.

#### ***How ARX-04 Addresses the Unmet Medical Need for Moderate-to-Severe Acute Pain***

ARX-04 is a non-invasive, fast-onset sufentanil product candidate for treatment of patients with moderate-to-severe acute pain, either on the battlefield or in civilian settings of trauma or injury. On the battlefield, in the emergency room and in ambulatory care environments, patients often do not have immediate IV access available. Intramuscular injections are a current standard of care on the battlefield, but they are invasive, painful and present an increased risk of infection to both patient and healthcare professional. In addition, in cases of severe trauma where the patient is often in hypovolemic shock and muscles are not well perfused, pain medication given by intramuscular injection may not readily reach the bloodstream to provide pain relief, rendering this route of delivery suboptimal. Oral pills and liquids generally have slow and erratic onset of analgesia. Even patients with IV access may have undesirable side effects with the commonly used IV opioids morphine and hydromorphone, such as sedation or oxygen desaturation. Moreover, IV dosing results in high peak plasma levels, thereby limiting the opioid dose and requiring frequent redosing intervals to titrate to satisfactory analgesia. Additional treatment options are needed that can safely and rapidly treat acute trauma pain, in both civilian and military settings.

## **Table of Contents**

### ***ARX-04 Description***

ARX-04 is a non-invasive, fast-onset sufentanil product candidate for treatment of patients with moderate-to-severe acute pain, either on the battlefield or in civilian settings of trauma or injury. ARX-04 features sufentanil, a high therapeutic index opioid, in our proprietary NanoTab technology that enables rapid sublingual absorption when the NanoTab is placed under the tongue. As a result, sufentanil NanoTabs can provide rapid onset of analgesia and display a consistent pharmacokinetic profile due to a high percentage of drug being absorbed sublingually instead of through the gastrointestinal tract. In addition to battlefield casualty treatment, if approved, we anticipate that ARX-04 could be useful in a variety of medically supervised settings, including by paramedics during patient transport, in the emergency room, for non-surgical patients experiencing pain in the hospital, or for post-operative patients, following either short-stay or ambulatory surgery, who do not require more long-term patient-controlled analgesia.

### ***Sufentanil Single-Dose NanoTab ARX-04 Clinical Program***

#### ***Summary***

In May 2011, we received a grant from the US Army Medical Research and Materiel Command, or USAMRMC, to conduct a Phase 2 dose finding trial, and to prepare to enter Phase 3. In the Phase 2 clinical trial of ARX-04, two different doses of sufentanil are being evaluated in patients suffering from moderate-to-severe acute pain, with the goal of determining an appropriate dose to take into Phase 3. In November 2012, we initiated the Phase 2 clinical trial and, in February 2013, dosing of the last patient in this trial was completed. This Phase 2 clinical trial enrolled 101 patients and top-line results from the trial are expected during the second quarter of 2013.

#### ***Phase 2 Clinical Trial for ARX-04***

In November 2012, we initiated our ARX-04 Phase 2 dose-finding trial, a prospective, randomized, double-blind multicenter trial in patients 18 to 80 years of age that are undergoing primary, unilateral first metatarsal bunionectomy surgery alone or with ipsilateral hammertoe repair. Patients who meet all inclusion and exclusion criteria following surgery were randomly assigned (2:2:1) to treatment with Sufentanil NanoTab 20 mcg, Sufentanil NanoTab 30 mcg, or placebo. Randomization was stratified within each site by two age groups: 18 – 64 years and 65 – 80. In the trial, 101 patients (40 patients in Sufentanil NanoTab 20 mcg group, 40 patients in Sufentanil NanoTab 30 mcg group and 20 patients in placebo treatment group) received trial drug and provided primary efficacy data for analysis. Efficacy was assessed as follows: 1) patient reports of pain intensity on an NRS, 2) pain relief on a 5-point pain relief scale, 3) percentage of patients requiring rescue analgesics due to inadequate analgesia, and 4) patient global assessment of effectiveness and tolerability. Also, a double stop-watch technique was used to assess onset of perceived and meaningful analgesia after the first dose of trial drug.

The primary endpoint is the SPID-12. Secondary endpoints include: TOTPAR over the 12-hour trial period, proportion of patients requiring rescue analgesics due to inadequate analgesia over the 12-hour trial period, proportion of patients who responded in each category of the Patient Global Assessment, time to onset of perceived and meaningful analgesia and time to first use of rescue analgesics and total number of doses of rescue analgesic used.

### ***Other Potential Applications for Our NanoTab Technology***

We believe that as a platform technology, the NanoTab, either as a standalone dosage form or in conjunction with various forms of dispensing mechanisms, has the potential to enable other product candidates utilizing a number of additional compounds to be delivered sublingually to the oral mucosa. There are numerous compounds used for the treatment of pain as well as other therapeutic indications which are dosed in microgram quantities and possess characteristics that we believe make them potential candidates for sublingual delivery via the NanoTab.

## **Table of Contents**

### **Our Strategy**

Our strategy is to develop and commercialize a portfolio of sufentanil NanoTab-based products and other products in hospital markets in the United States. 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 commercialization efforts. In addition, we plan to enter into partnerships to market our product candidates outside the United States.

Our lead product candidate, the NanoTab System, is currently in Phase 3 development, which consists of three Phase 3 clinical trials. We have completed and reported positive top-line results for two of the trials and expect to report data from the third trial in the second quarter of 2013. Contingent upon receipt of successful data from the final planned NanoTab System Phase 3 clinical trial, we intend to submit an NDA to the FDA in the third quarter of 2013. If our planned NDA is approved, we plan to commercialize the NanoTab System ourselves in the United States, and commercialize it outside the United States with a partner.

Our specific strategy with respect to the NanoTab System is to:

complete the remaining Phase 3 efficacy trial and seek regulatory approval in the United States and other countries;

strengthen our commercial relationships for the manufacturing of the components and assembly of the NanoTab System;

build a targeted hospital-directed sales force in the United States; and

partner with third parties for commercialization outside of the United States.

Further development of ARX-02 and ARX-03 will likely depend on the identification of a partner to support these efforts. Development of ARX-04 beyond the current grant-supported activities is contingent upon the successful results from our Phase 2 clinical trial and identification of additional funding.

### **Sales and Marketing**

We anticipate developing a distribution capability and commercial organization in the United States to market and sell our product candidates alone or with partners, while out-licensing commercialization rights outside of the United States. In executing our strategy, our goal is to have significant control over the development process and commercial execution for our product candidates, while retaining meaningful economics.

We plan to progressively build commercial capability to support introduction of the NanoTab System to the United States market as we move toward potential NDA submission and approval. We foresee two stages of commercial execution to support successful introduction of the NanoTab System in the United States:

In parallel with advancement and completion of our Phase 3 clinical trial program and the planned submission of an NDA for the NanoTab System, we plan to:

highlight the clinical and health economic data identifying the limitations of IV PCA in use today;

increase awareness of the clinical profile of the NanoTab System through publication of our clinical data;

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

create and deploy a focused scientific support team to gather a detailed understanding of individual hospital needs in order to be prepared to present the NanoTab System effectively at the time of commercial launch;

establish advisory boards with anesthesiologists, surgeons, nurses and P&T committees to provide us with input on appropriate commercial positioning for the NanoTab System for each of these key audiences;

## **Table of Contents**

build a marketing organization that can define appropriate segmentation and positioning strategies and tactics for the NanoTab System; and

design a post-approval clinical development program.

Assuming FDA approval, we plan to:

establish the NanoTab System on hospital formularies through deployment of an experienced team to explain the clinical and pharmacoeconomic benefits of the NanoTab System in comparison to IV PCA;

create and progressively deploy a high-quality, customer focused and experienced sales organization dedicated to bringing innovative, highly-valued healthcare solutions to patients, payors and healthcare providers, including progressively building a targeted hospital-directed sales force of approximately 60 people in the United States;

conduct a post-approval clinical program for the NanoTab System;

establish the NanoTab System as the product of choice for traditional post-operative PCA; and

expand the market through deployment of the NanoTab System for 24 hour stay patients, and other in hospital acute pain conditions.

## **Intellectual Property**

We seek patent protection in the United States and internationally for our product candidates. Our policy is to pursue, maintain and defend patent rights developed internally and to protect the technology, inventions and improvements that are commercially important to the development of our business. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology. We also rely on trade secrets to protect our product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see [Risk Factors](#) [Risks Related to Our Intellectual Property](#) appearing elsewhere in this Form 10-K.

Our success will depend significantly on our ability to:

obtain and maintain patent and other proprietary protection for our product candidates;

defend our patents;

preserve the confidentiality of our trade secrets; and

operate our business without infringing the patents and proprietary rights of third parties.

We have established and continue to build proprietary positions for our product candidates and related technology in the United States and abroad.

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

As of January 31, 2013, we are the owner of record of six issued U.S. patents, five of which provide coverage over NanoTabs and one of which provides coverage over the NanoTab System device. Of these six patents, five provide coverage through at least 2027 and one provides coverage through at least 2030. We also hold two issued European patents, including national validation in ten countries, one of which expires in 2027, and one of which expires in 2029. Further, we hold one Mexican patent which expires in 2029. We are pursuing 15 U.S. non-provisional patent applications, and 57 foreign national applications, including five 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.



---

## **Table of Contents**

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 ARX-01, ARX-02, ARX-03 and ARX-04 NanoTabs and formulations, our ARX-01 PCA device, the combination of drugs and our ARX-01 PCA device, our ARX-02, ARX-03 and ARX-04 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. We note that 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.

## **Competition**

Our industry is highly competitive and subject to rapid and significant technological change. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, and medical technology companies. We believe the key competitive factors that will affect the development and commercial success of our product candidates are the safety, efficacy and tolerability profile, the patient and healthcare professional satisfaction with using our product candidates in relation to available alternatives and the reliability, convenience of dosing, price and reimbursement of our product candidates.

Many of our potential competitors, including many of the organizations named below, have substantially greater financial, technical and human resources than we do and significantly greater experience in the development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or may be more effectively marketed and sold, than any drug we may commercialize, which 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 advanced technologies become available.

### ***Potential Competition for the NanoTab System***

We are developing the NanoTab System for the management of moderate-to-severe acute post-operative pain in adult patients during hospitalization. We believe that the NanoTab System would compete with a number of opioid-based treatment options that are currently available. The market for opioids for post-operative pain is large and competitive. The primary competition for the NanoTab System is the IV PCA pump, which is widely used in the post-operative 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 post-operative 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 the NanoTab System include products in

## **Table of Contents**

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.

### ***Potential Competition for ARX-02***

We are developing ARX-02, the Sufentanil NanoTab BTP Management System, for the treatment of breakthrough pain in opioid tolerant patients, with an initial indication in cancer patients. The market for opioids for treatment of cancer breakthrough pain is large and competitive; however, currently there are no sufentanil products approved by the FDA for this indication. 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.

### ***Potential Competition for ARX-03***

We are developing ARX-03, the Sufentanil/Triazolam NanoTab, for use in diagnostic or therapeutic painful procedures of short duration in a physician's office. For these procedures, many practitioners rely primarily on local anesthetics injected to the procedural area to reduce the pain of the procedure, and do not use IV sedatives to manage the anxiety of patients because of the cost of having additional trained staff to monitor the patients. Currently, we are not aware of any products on the market which combine an opioid with a benzodiazepine in a single dosage form to manage the anxiety and pain of procedures in a physician's office. 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.

### ***Potential Competition for ARX-04***

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.

## **Pharmaceutical Manufacturing and Supply**

We currently rely on contract manufacturers to produce sufentanil and sufentanil/triazolam NanoTabs for our clinical trials under current Good Manufacturing Practices, or cGMP, with oversight by our internal managers. Equipment specific to the pharmaceutical manufacturing process was purchased and customized by us and is currently owned by us. We plan to continue to rely on contract manufacturers and, potentially, collaboration partners to manufacture commercial quantities of our product candidates if and when approved for marketing by the FDA. We currently rely on a single manufacturer for the preclinical and clinical supplies of our drug product for each of our product candidates and do not currently have agreements in place for redundant supply or a second source for any of our product candidates. We have identified other manufacturers that could satisfy our commercial supply and packaging requirements and we continue to evaluate those manufacturers.

## **Table of Contents**

In January 2013, we entered into an Manufacturing Services Agreement, or the Services Agreement, with Patheon Pharmaceuticals, Inc, or Patheon, relating to the manufacture of sufentanil NanoTabs for use with the NanoTab System. Under the terms of the Services Agreement, Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to the NanoTab System for sale in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. The term of the Services Agreement extends until December 31, 2017, or the Initial Term, and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months prior written notice; provided, however, that the Services Agreement may not be terminated without cause prior to the end of the Initial Term. In addition, we entered into a related Capital Expenditure and Equipment Agreement, or the Capital Agreement, related to clinical and commercial production of our product candidates. Under the terms of the Capital Agreement, we plan to make certain future modifications to Patheon's Cincinnati facility, the aggregate cost of which is expected to be less than \$3.5 million.

### **Device Manufacturing and Supply**

The NanoTab System handheld PCA device is manufactured by contract manufacturers, component fabricators and secondary service providers. Suppliers of components, subassemblies and other materials are located in Korea, Japan, Germany, China, Taiwan, Canada and the United States. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up the NanoTab System. FDA regulations require that materials be produced under cGMPs or Quality System Regulation, or QSR. We outsource injection molding of all the plastic parts for the cartridge and device and product sub-assemblies; NanoTab cartridge filling and packaging; and assembly, packaging and labeling of the dispenser and controller.

ARX-02 is manufactured by contract manufacturers, component fabricators and secondary service providers. Suppliers of components, subassemblies and other materials are located in Korea, Japan, China, Taiwan, Canada and the United States. All contract manufacturers and component suppliers have been selected for their specific competencies in the manufacturing processes and materials that make up ARX-02. FDA regulations require that materials be produced under cGMPs or QSR, as required for the respective unit operation within the manufacturing process. We outsource injection molding of all the plastic parts for the SDA and MSD and product sub-assemblies; and filling, packaging and labeling of SDAs.

ARX-03 and ARX-04 both utilize SDAs in the delivery of the NanoTab. FDA regulations require that materials be produced under cGMPs or QSR, as required for the respective unit operation within the manufacturing process. We outsource injection molding of all the plastic parts for the SDA, and product sub-assemblies; and filling, packaging and labeling of SDAs.

### **Government Regulation**

Government authorities in the United States at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of products such as those we are developing. Our product candidates must be approved by the FDA through the NDA process before they may legally be marketed in the United States.

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and regulations. The process of obtaining regulatory approvals and complying with applicable laws and regulations requires the expenditure of substantial time and financial resources. Failure to comply at any time during the product development and approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of

## **Table of Contents**

production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug product may be marketed in the United States generally involves the following:

completion of non-clinical laboratory tests, animal trials and formulation studies according to Good Laboratory Practices regulations;

submission to the FDA of an investigational new drug, or IND, application which must become effective before human clinical trials may begin;

performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the clinical safety and efficacy of the proposed drug product for its intended use;

submission to the FDA of an NDA for a new drug product;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug product and the drug substance(s) are produced to assess compliance with cGMP;

payment of user and facility fees; and

FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

*Phase 1.* The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

*Phase 2.* Involves trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted conditions and to determine dosage tolerance and optimal dosage and schedule.

*Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical safety and efficacy in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an institutional review board, or IRB, can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biological product has been associated with unexpected serious harm to patients.

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP and QSR for medical devices requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

## **Table of Contents**

Our product candidates, the NanoTab System, ARX-02, ARX-03 and ARX-04, are regulated under IND applications for clinical development and in the case of the NanoTab System, all device related information is filed under the Chemistry, Manufacturing and Controls Section, or CMC, of an IND.

The results of product development, preclinical trials and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on our drug products, proposed labeling and other relevant information, will be submitted to the FDA as part of an NDA for a new drug product, requesting approval to market the product in the United States. The submission of an NDA is subject to the payment of a substantial user fee; a waiver of such fee may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

If one or more of our product candidates receive regulatory approval, the approval may be limited to specific conditions and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Our product candidates, if approved, will also require Risk Evaluations and Mitigation Strategies, or REMS, that can include a medication guide, patient package insert, a communication plan, elements to assure safe use and implementation system, and must include a timetable for assessment of the REMS. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. In addition, the FDA may require post-approval testing which involves clinical trials designed to further assess a drug product's safety and effectiveness after the NDA.

## **Post-Approval Requirements**

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated clinical safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drug products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drug products must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Drug product manufacturers and other entities involved in the manufacturing and distribution of approved drug products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, packaging, labeling, storage and shipment of the drug product. Manufacturers must establish validated systems to ensure that products meet specifications and regulatory standards, and test each product batch or lot prior to its release. In the case of the NanoTab System, the device component must comply with 21 CFR 820.

## **Table of Contents**

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution or may require substantial resources to correct.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

## **Foreign Regulation**

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products to the extent we choose to sell any products outside of the United States. In October 2012, we received notice from the European Medicines Agency, or EMA, that the NanoTab System was eligible for centralized marketing authorization application in the European Union. This regulatory procedure, reserved for novel products, biotechnology products and new chemical entities, allows for commercialization across 31 European Union and EFTA countries based on approval by EMA. In addition, conformance to the European Medical Device Directive could require CE marking on the NanoTab System device to enable commercialization in the European Union. Outside of Europe, the requirements and approval process vary from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

## **Controlled Substances Regulations**

Sufentanil, a Schedule II controlled substance, is the active pharmaceutical ingredient in the NanoTab System, ARX-02, ARX-03 and ARX-04. Triazolam, a Schedule IV controlled substance, is also an active pharmaceutical ingredient in ARX-03. Controlled substances are governed by the Drug Enforcement Administration, or DEA, of the U.S. Department of Justice. The handling of controlled substances and/or drug product by us, our contract manufacturers, analytical laboratories, packagers and distributors, are regulated by the Controlled Substances Act and Title 21 CFR, Part 1300-1399.

Unforeseen delays to the drug substance and drug product manufacture and supply chain may occur due to delays, errors or other unforeseen problems with the permitting process. Also, any one of our suppliers, contract manufacturers, laboratories, packagers and/or distributors could be the subject of DEA violations and enforcement could lead to delays or even loss of DEA license by the contractors.

## **Health Law Compliance**

In addition to FDA laws and regulations, we must comply with a variety of federal and state laws governing, among other things, the privacy of healthcare information, our relationships with healthcare providers and the reimbursement of prescription drug products. Although the federal health care program anti-kickback statute has a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed

## **Table of Contents**

under Medicaid and other state programs, or, in several states, apply regardless of the payer. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations.

In March 2010, the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA, was enacted, which includes measures to significantly change the way health care is financed by both governmental and private insurers. Many of the details regarding the implementation of the PPACA are yet to be determined, and at this time, it remains unclear the full effect that the PPACA would have on our business.

## **Research and Development**

Conducting research and development is central to our business model. We have invested and expect to continue to invest significant time and capital in our research and development operations. Our research and development expenses were \$24.9 million, \$13.6 million and \$8.2 million during the years ended December 31, 2012, 2011 and 2010, respectively. We anticipate that quarterly research and development expenses during the first half of 2013 will be in line with or modestly higher than the fourth quarter of 2012 as we conduct and complete the Phase 3 clinical trials for the NanoTab System and the ARX-04 Phase 2 clinical trial. However, we plan to incur significant expenditures for the foreseeable future as we seek to continue commercial preparations for the NanoTab System and development of ARX-04, and subsequently advance the development of ARX-02 and ARX-03 contingent upon additional funding or identification of corporate partnership resources.

## **Employees**

As of December 31, 2012, we employed 25 full-time employees, all of whom are located at our headquarters in Redwood City, California. None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.



## **Table of Contents**

### **Item 1A. Risk Factors**

*This Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by or on behalf of us, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our revenues, expenses, net loss and loss per share. We believe the risks described below are the risks that are material to us as of the date of this Form 10-K. If any of the following risks comes to fruition, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected.*

#### **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, the Sufentanil NanoTab PCA System, or the NanoTab System or ARX-01. 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 December 31, 2012, we had an accumulated deficit of \$122.0 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 the NanoTab System 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 US 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:

completing the clinical development of the NanoTab System, initially for the treatment of post-operative pain in the hospital setting;

obtaining regulatory approval for the NanoTab System, which will require additional funding;

launching and commercializing the NanoTab System, including building 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.

## **Table of Contents**

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 required by the United States Food and Drug Administration, or FDA, to perform trials in addition to those that we currently anticipate.

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 the completion of our Phase 3 clinical trials, preparation for potential commercialization of the NanoTab System and future advancement of other product candidates. As of December 31, 2012, we had working capital of \$47.4 million.

We believe that our current cash, cash equivalents and investment balances will be sufficient to fund our current operations into the third quarter 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 substantial additional funds 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 our existing cash resources, based on our current estimates of clinical trial expenditures and enrollment pace, are adequate to complete our ongoing NanoTab System Phase 3 clinical trials, to submit our planned New Drug Application, or NDA, to the FDA for the NanoTab System, and to begin preparation for commercialization and manufacturing of the NanoTab System in the United States. However, our clinical trials may encounter technical, enrollment 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 the NanoTab System. Raising funds in the current economic environment, when the capital markets have been affected by the global recession, may present additional challenges. 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.

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;

## **Table of Contents**

seek corporate partners for the NanoTab System 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.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will not be able to continue our planned level of operations beyond the third quarter of 2014 and will not have sufficient capital to complete the regulatory approval process for the NanoTab System in the United States, which would have a material adverse effect on our business, operating results and prospects. 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.

***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 all of our stockholders or impose restrictive covenants that 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. Since entering into the agreement with Hercules, we have been making monthly interest-only payments to Hercules of approximately \$140,000 per month until June 30, 2012. 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 December 31, 2012, the outstanding principal owed to Hercules was \$16.3 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. In order to continue our planned operations and satisfy our debt obligations with Hercules, we will need to raise additional capital in the future. 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.

## **Table of Contents**

### **Risks Related to Clinical Development and Regulatory Approval**

*We depend substantially on the success of our NanoTab System, which is still under clinical development, and may not obtain 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 the NanoTab System for the treatment of acute post-operative pain. We recently completed two of three planned Phase 3 NanoTab System clinical trials, with one Phase 3 NanoTab System clinical trial ongoing.

Contingent upon receipt of successful data from the remaining Phase 3 clinical trial, we intend to submit an NDA for the NanoTab System to the FDA in the third quarter of 2013. There is no guarantee that the remaining Phase 3 NanoTab System clinical trial or the Human Factors studies to be included in the planned NDA, will be completed on schedule or if at all, or if completed, will be successful. 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.

Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing the NanoTab System, generating revenues and achieving profitability. If any of these events occur, we may be forced to abandon our development efforts for the NanoTab System, which would have a material adverse effect on our business and could potentially cause us to cease operations.

*We depend substantially on the successful completion of Phase 3 clinical trials for our product candidates. The positive clinical results obtained to date for our product candidates may not be repeated in the future.*

In March 2013, we announced positive top-line data from our double-blind, placebo-controlled, Phase 3 trial for the NanoTab System in patients following abdominal surgery. In addition, in November 2012, we announced positive top-line data from our active comparator NanoTab System Phase 3 clinical trial. Subsequent analyses of clinical trial data may lead to different, including less favorable, interpretations of the results than the analyses conducted to date or may identify important implications of the trial that are not currently known, or be subject to differing interpretations by the regulatory agencies. In addition, we are still awaiting conclusion and results of our one remaining NanoTab System Phase 3 clinical trial, which are expected to be released during the second quarter of 2013. There is no guarantee that the results of the remaining Phase 3 clinical trial will be positive, and the positive results to date from our Phase 3 clinical trials are not an indication or guarantee that the remaining Phase 3 clinical trial results will be positive.

Our product candidates are subject to the risks of failure inherent in pharmaceutical and medical device development. Before obtaining regulatory approval for the commercial sale of any product candidate, we must successfully complete all required Phase 3 clinical trials. Negative or inconclusive results of a Phase 3 clinical trial could cause the FDA to require that we repeat it or conduct additional clinical trials. Even if we believe that the data from required Phase 3 clinical trials is positive, the FDA could analyze our data using alternative imputation strategies and determine that any trial was negative or inconclusive. Furthermore, while we have completed multiple Phase 2 clinical trials for the NanoTab System, ARX-02 and ARX-03 and have obtained positive safety and efficacy results for our sufentanil-based product candidates during our prior clinical trials, we cannot be certain that these results will be duplicated when our product candidates are tested in a larger number of patients in our Phase 3 clinical trials, including in our ongoing Phase 3 clinical trial of the NanoTab System.

*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. We are conducting three Phase 3 clinical trials for the NanoTab System, and recently announced top-line results from two of these Phase 3 clinical trials. The remaining Phase 3 clinical trial is currently underway. In November

## **Table of Contents**

2012, we initiated a Phase 2 clinical trial for ARX-04 and expect data in the second quarter of 2013. Our current and planned 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 our clinical trials, including our ongoing Phase 3 clinical trial for the NanoTab System or Phase 2 clinical trial for ARX-04, 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 NanoTab System clinical trial, 7.9% of NanoTab System treated patients dropped out of the trial prematurely due to an adverse event, and we observed one

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

serious adverse event, or SAE, that was assessed as possibly or probably related to the NanoTab System. In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial, 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 a serious adverse event, which was determined to be unrelated to the study drug. Phase 2 clinical trials conducted by us with our NanoTab System, ARX-02 and ARX-03 product candidates have generated some AEs, but no SAEs, related to the trial drug.

The analysis of the full data set from our active comparator and abdominal NanoTab System Phase 3 clinical trials or the analysis of the data set from our remaining Phase 3 NanoTab System trial, when available, could result in identification of additional AEs or SAEs, related to the trial drug. Additional SAEs related to the trial drug observed in any of our clinical trials, including in our ongoing Phase 3 clinical trial, may adversely impact our ability to obtain regulatory approval for our product candidates.

## **Table of Contents**

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 our NanoTab System product candidate because it is a drug/device combination.***

The NanoTab System 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 the NanoTab System 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 the NanoTab System. As a result, we have in the past and may in the future experience delays for the NanoTab System 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 the NanoTab System, 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 the NanoTab System. Additional delays may result if the NanoTab System 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 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 that resulted from such trials. The rejection of data from clinical trials required to support an NDA could 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



---

## **Table of Contents**

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.

***Even if we obtain regulatory approval for the NanoTab System 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 the NanoTab System and our other product candidates will likely include restrictions on use due to the opioid nature of sufentanil. The NanoTab System and our other product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion,

## **Table of Contents**

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 the NanoTab System 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 the NanoTab System 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.



## **Table of Contents**

### ***The NanoTab System and our other product candidates will require Risk Evaluation and Mitigation Strategies, or REMS.***

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 the NanoTab System, we cannot predict the specific REMS to be required as part of the FDA's approval of the NanoTab System. Depending on the extent of the REMS requirements, our costs to commercialize the NanoTab System 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

## **Table of Contents**

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.

Currently, we use one supplier of triazolam for our ARX-03 NanoTabs. Switching triazolam suppliers may involve substantial cost and is likely to result in a delay in our desired clinical and commercial timelines. These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

### ***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 proceed with our planned clinical trials and 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, the FDA or other regulatory agencies may require that a bioequivalence study 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 study could fail the FDA's bioequivalence requirements which would adversely affect our clinical and commercial plans.

## **Table of Contents**

***Our designs for the PCA device components of our NanoTab System for Phase 3 clinical trials may not be fully functional or commercially viable.***

The NanoTab System device we are using in Phase 3 clinical trials and plan to use commercially, or the Phase 3 device, 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 Phase 3 device and we plan to conduct additional Human Factors studies prior to submitting the planned NDA for the NanoTab System. However, we cannot predict if the Phase 3 device will be fully functional or acceptable throughout all Phase 3 clinical trials or for commercial use. If we need to modify the Phase 3 device either during or after the remaining Phase 3 clinical trials, we may incur higher costs and experience delay in regulatory approval and commercialization of the NanoTab System. 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 NanoTab System Phase 3 device on a clinical scale, no experience on a commercial scale and do not own or operate a manufacturing facility.***

We have manufactured the NanoTab System devices and supplies on a small scale, including those needed for our Phase 3 clinical trials. We continue to rely on contract manufacturers, component fabricators and secondary service providers to produce the necessary NanoTab System devices for the remaining Phase 3 clinical trials and the commercial marketplace. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the NanoTab System device to third parties and intend to continue to do so. These purchases of Phase 3 devices 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 the NanoTab System 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 the NanoTab System 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 have selected and executed agreements with CROs to conduct our three Phase 3 clinical trials for the NanoTab System and for the Phase 2 clinical trial for ARX-04. We will rely on these 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 ongoing clinical programs for the NanoTab System 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

## **Table of Contents**

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. In addition, our Phase 3 clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of the NanoTab System. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, 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 the NanoTab System, or our other product candidates. As a result, our financial results and the commercial prospects for the NanoTab System and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

### ***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 our ongoing Phase 2 dose-finding trial for the treatment of moderate-to-severe pain, and to prepare to enter into planned Phase 3 development. The period of research under the grant ends January 31, 2014. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research.

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.



## **Table of Contents**

### **Risks Related to Commercialization of Our Product Candidates**

*The commercial success of the NanoTab System 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 the NanoTab System;

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 the NanoTab System 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 the NanoTab System 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

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

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 the NanoTab System 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.

## **Table of Contents**

Until we are able to negotiate a strategic partnership or obtain additional financial resources for ARX-02 or ARX-03, we will not progress development or generate any revenue from these product candidates. We are developing ARX-04 under a grant from USAMRMC and if new funding from USAMRMC to cover Phase 3 costs is not obtained, we may be required to curtail all activities associated with ARX-04. In addition, without a partnership or additional grant funding, we would bear all the risk related to the development of ARX-02, ARX-03 and ARX-04. If we elect to increase our expenditures to fund development or commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring ARX-02, ARX-03 or ARX-04 to market or generate product revenue.

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 our product candidates are approved for commercialization, we intend to enter into agreements with third parties to market the NanoTab System 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.***

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

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 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.

## **Table of Contents**

We believe that the NanoTab System would compete with a number of opioid-based treatment options that are currently available. The market for opioids for post-operative pain is large and competitive. The primary competition for the NanoTab System is the IV PCA pump, which is widely used in the post-operative 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 post-operative 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 the NanoTab System 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/analgic 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 post-operative pain or breakthrough pain could render the NanoTab System and ARX-02, respectively, non-competitive or obsolete. These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

---

## **Table of Contents**

***Hospital formulary approval and reimbursement may not be available for the NanoTab System 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 the NanoTab System, 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 the NanoTab System, 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 the NanoTab System, 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 the NanoTab System 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 the NanoTab System 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 the NanoTab System 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 the NanoTab System or any of our other product candidates. This could have a material adverse effect on our business, results of operations, financial condition and prospects.

## **Table of Contents**

***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 out of this facility and we may encounter difficulties in production at the new facility, or otherwise, which may adversely affect our clinical and commercial plans.

In January 2013, we entered into an Manufacturing Services Agreement, or the Services Agreement, with Patheon Pharmaceuticals, Inc, or Patheon, for use with the NanoTab System. Under the terms of the Services Agreement, Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to the NanoTab System for sale 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, however, 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, we entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement, 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, the aggregate cost of which is expected to be less than \$3.5 million. If equipment manufacture or modifications do not meet expected deadlines, the timing for our planned NDA submission for the NanoTab System may be delayed.

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 the NanoTab System and our other product candidates. We do not 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 the NanoTab System. 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.

---

## **Table of Contents**

### ***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 December 31, 2012, we only 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. 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 the NanoTab System 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.





## **Table of Contents**

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 January 31, 2013, we are the owner of record of one issued European patent, including national validation in ten countries, which expires in 2027, one issued European patent, including national validation in ten countries, which expires in 2029, one Mexican patent which expires in 2029, five issued U.S. patents which provide coverage through at least 2027, and one issued U.S. patent which provides coverage through at least 2030. In addition, we are pursuing 15 U.S. non-provisional patent applications, and 57 foreign national applications, including five 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 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. 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 a re-examination or other post-grant review, 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.

---

## **Table of Contents**

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 be 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, will not become effective until March 16, 2013. Accordingly, 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.

## **Table of Contents**

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/or 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



## **Table of Contents**

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. 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.***

Prior to our initial public offering, or IPO, in February 2011, there was no public market for our common stock. An active public trading market for our common stock has not developed and may never develop or, if developed, may not be sustained. Moreover, the trading price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

adverse results or delays in clinical trials;

inability to obtain additional funding, including funding necessary for the planned commercialization and manufacturing of the NanoTab System in the United States and advancement of clinical trials for other product candidates;

any delay in submitting an NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's filing or review of that NDA;

failure to successfully develop and commercialize our product candidates;



**Table of Contents**

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.

***Our common stock is 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.***

To date, we have 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 fourth quarter of 2012 was approximately 250,000 shares per day. 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.



## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

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.

## **Table of Contents**

***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 owned approximately 52% of our outstanding voting stock as of January 31, 2013. 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 plan to continue to assess our internal controls and procedures and intend to take further action as necessary or appropriate to address any other matters we identify. However, our independent registered public accounting firm is not currently required to deliver an attestation report on the effectiveness of our internal control over financial reporting as we qualify for an exemption as a non-accelerated filer under the applicable SEC rules and regulations.

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 January 31, 2013, we had 37,059,802 shares of common

## **Table of Contents**

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.

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. 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 our 2011 Equity Incentive Plan, or 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. Our public offering in December 2012, together with 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.

## **Table of Contents**

*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.

## **Item 1B. Unresolved Staff Comments**

None.

## **Item 2. Properties**

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

We lease approximately 13,787 square feet of office and laboratory space in Redwood City, California under an agreement that expires in May 2016. We believe that our facilities are adequate to meet our current needs.

**Table of Contents**

**Item 3. Legal Proceedings**

From time to time we may be involved in legal proceedings arising in the ordinary course of business. We believe there is no litigation currently pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

**Item 4. Mine Safety Disclosures**

Not Applicable.

**Table of Contents****PART II****Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities****Market Information**

Our common stock has been trading on the NASDAQ Global Market under the symbol **ACRX** since our IPO on February 11, 2011. Prior to this date, there was no public market for our common stock. The following table sets forth the high and low intraday sales prices of our common stock for the periods indicated as reported by the NASDAQ Global Market:

|   | Price   |         |
|---|---------|---------|
|   | High    | Low     |
| Year ended 2012                             |         |         |
| Fourth Quarter                              | \$ 5.25 | \$ 2.27 |
| Third Quarter                               | \$ 3.88 | \$ 2.54 |
| Second Quarter                              | \$ 4.00 | \$ 2.77 |
| First Quarter                               | \$ 3.76 | \$ 1.89 |
| Year ended 2011                             |         |         |
| Fourth Quarter                              | \$ 3.32 | \$ 1.76 |
| Third Quarter                               | \$ 4.70 | \$ 2.90 |
| Second Quarter                              | \$ 5.00 | \$ 2.90 |
| First Quarter (beginning February 11, 2011) | \$ 5.09 | \$ 2.97 |

## **Table of Contents**

### **Stock Price Performance Graph**

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since February 11, 2011, which is the date our common stock first began trading on the NASDAQ Global Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

*The above Stock Price Performance Graph and related information shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.*

### **Holders of Record**

As of January 31, 2013, there were 32 holders of record of our common stock. This number does not include street name or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

### **Dividend Policy**

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.



**Table of Contents****Item 6. Selected Financial Data**

The selected financial data set forth below should be read together with the financial statements and related notes, Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations, and the other information contained in this Form 10-K. The selected financial data is not intended to replace our audited financial statements and the accompanying notes. Our historical results are not necessarily indicative of our future results.

|  | Year Ended December 31, |             |             |             |             | Period from July 13, 2005 (Inception) Through December 31, 2012 |
|--|-------------------------|-------------|-------------|-------------|-------------|---|
|  | 2012                    | 2011        | 2010        | 2009        | 2008        |   |
| (in thousands, except share and per share data)                                |                         |             |             |             |             |   |
| <b>Statements of Operations Data:</b>  |                         |             |             |             |             |   |
| Research grant revenues  | \$ 2,394                | \$ 1,072    | \$          | \$          | \$          | \$ 3,466  |
| Operating Expenses:  |                         |             |             |             |             |   |
| Research and development   | \$ 24,908               | \$ 13,624   | \$ 8,193    | \$ 15,502   | \$ 18,325   | \$ 92,329   |
| General and administrative   | 7,199                   | 6,800       | 3,993       | 3,529       | 2,365       | 26,493  |
| Total operating expenses   | 32,107                  | 20,424      | 12,186      | 19,031      | 20,690      | 118,822   |
| Loss from operations   | (29,713)                | (19,352)    | (12,186)    | (19,031)    | (20,690)    | (115,356)   |
| Interest expense   | (2,283)                 | (2,309)     | (1,397)     | (1,242)     | (404)       | (7,722)   |
| Other income (expense), net  | (1,367)                 | 1,560       | (761)       | 154         | 432         | 1,051   |
| Net loss   | \$ (33,363)             | \$ (20,101) | \$ (14,344) | \$ (20,119) | \$ (20,662) | \$ (122,027)  |
| Net loss per share of common stock, basic and diluted                          | \$ (1.51)               | \$ (1.16)   | \$ (21.84)  | \$ (34.93)  | \$ (43.69)  |   |
| Shares used in computing net loss per share of common stock, basic and diluted | 22,124,637              | 17,344,727  | 656,650     | 576,021     | 472,914     |   |

|   | 2012      | 2011      | As of December 31, 2010 (in thousands) | 2009      | 2008      |
|---|-----------|-----------|--|-----------|-----------|
| <b>Balance Sheet Data:</b>                        |           |           |  |           |           |
| Cash, cash equivalents and short-term investments | \$ 59,763 | \$ 35,785 | \$ 3,682                               | \$ 12,546 | \$ 20,207 |
| Working capital (deficit)                         | 47,435    | 30,301    | (7,632)                                | 6,931     | 16,450    |
| Total assets                                      | 64,520    | 40,835    | 6,830                                  | 14,491    | 22,679    |
| Total debt, net, including convertible notes      | 15,973    | 19,079    | 12,009                                 | 9,734     | 12,334    |
| Convertible preferred stock warrant liability     |           |           | 2,529                                  | 169       | 240       |
| Convertible preferred stock                       |           |           | 55,941                                 | 55,871    | 41,156    |
| Total stockholders' equity (deficit)              | 33,847    | 17,468    | (65,892)                               | (52,994)  | (33,335)  |

## **Table of Contents**

### **Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations**

*The following discussion and analysis should be read in conjunction with our audited financial statements and the related notes that appear elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking 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. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under Item 1A. Risk Factors and elsewhere in this Annual Report on Form 10-K. Please refer to the section entitled Forward-Looking Statements in this Annual Report on Form 10-K.*

#### **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, the Sufentanil NanoTab PCA System, or the NanoTab System, or ARX-01, is designed to improve the management of moderate-to-severe acute post-operative pain in patients in the hospital setting. Although widely used, the current standard of care for patients with post-operative pain, 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 morphine, the invasive IV needle route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps.

#### *Sufentanil NanoTab System*

The NanoTab System is an investigational pre-programmed, non-invasive, handheld system that allows post-operative patients to self-dose with sublingual Sufentanil NanoTabs to manage their post-operative pain. The NanoTab System is designed to address the limitations of IV PCA by offering:

**A high therapeutic index opioid:** The NanoTab System uses the high therapeutic index opioid sufentanil; it offers post-operative pain patients 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 the NanoTab System provides rapid onset of analgesia, therefore eliminating the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections. In addition, because patients are not tethered to IV tubing and a pump for pain relief, the NanoTab System allows for ease of patient mobility.

**A simple, pre-programmed PCA solution:** The NanoTab System is a pre-programmed PCA system designed to eliminate the risk of pump programming errors.

Our Phase 3 clinical program for the NanoTab System consists of two placebo-controlled efficacy and safety trials and an open-label active comparator trial, in which the NanoTab System was compared to IV PCA. A summary of Phase 3 trials and results to date is as follows:

In March 2013, we reported top-line data showing that the primary endpoint was achieved in a pivotal, double-blind, placebo-controlled, Phase 3 trial of the NanoTab System for post-operative pain in major open abdominal surgery patients.

In November 2012, we reported top-line data showing that the primary endpoint of non-inferiority was met in an open-label active-comparator Phase 3 clinical trial.

In the second quarter of 2013, we expect data from our final planned pivotal Phase 3 trial, a double-blind, placebo-controlled efficacy and safety trial in patients with acute post-operative pain following hip and knee replacement surgeries.

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

In the third quarter of 2013, we intend to submit an NDA to the FDA, contingent upon receipt of successful data from the remaining NanoTab System Phase 3 clinical trial.

## **Table of Contents**

### ***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 May 2011, we announced that the U.S. Army Medical Research and Materiel Command, or USAMRMC, awarded us a \$5.6 million grant to support the development of ARX-04 for the treatment of moderate-to-severe acute pain. In November 2012, we initiated our ARX-04 Phase 2 dose-finding trial, a prospective, randomized, double-blind multicenter trial in patients that are undergoing primary, unilateral first metatarsal bunionectomy surgery alone or with ipsilateral hammertoe repair. In February 2013, dosing of the last patient in this trial was completed. This trial enrolled 101 patients and top-line results from the trial are expected during the second quarter of 2013.

In addition to our NanoTab System 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 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 upon identification of corporate partnership resources.

Development of therapeutic products is costly and is subject to a lengthy and uncertain regulatory process by the United States Food and Drug Administration, or FDA. Adverse events in both our own clinical program and other programs may have a negative impact on regulatory approval, the willingness of potential commercial partners to enter into agreements and the perception of the public.

### **Financial Overview**

We are a development stage company with a limited operating history. We have incurred net losses and generated negative cash flows from operations since inception and expect to incur losses in the future as we continue our research and development activities. We believe that continued investment in research and development is critical to attaining our strategic objectives. In order to develop our product candidates as commercially viable therapeutics, we expect to expend significant resources for expertise in the manufacturing, regulatory affairs, clinical research and other aspects of pharmaceutical development. In addition, as we pursue commercial development of our product candidates we expect the business aspects of our company to become more complex. We may be required in the future to add personnel and incur additional costs related to the maturation of our business.

Our net losses were \$33.4 million and \$20.1 million during the years ended December 31, 2012 and 2011, respectively. As of December 31, 2012, we had an accumulated deficit of \$122.0 million. As of December 31, 2012, we had cash, cash equivalents and investments totaling \$59.8 million compared to \$35.8 million as of December 31, 2011.

To date, we have funded our operations primarily through the sale of equity securities and the issuance of debt instruments. In December 2012, we completed an underwritten public offering, pursuant to which we sold 14,375,000 shares of our common stock at a public offering price of \$3.31 per share for an aggregate offering price of \$47.6 million. As a result of the offering, we received net proceeds of \$44.1 million, after underwriting discounts, commissions and offering expenses totaling \$3.5 million. 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. Since entering into the agreement with Hercules, we have been making monthly interest-only payments to Hercules of approximately \$140,000 per month until June 30, 2012.

## **Table of Contents**

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. As of December 31, 2012, the outstanding principal owed to Hercules was \$16.3 million.

Since our inception in July 2005, we have not generated any revenue from the sale of our products and do not anticipate generating any product revenues for the foreseeable future, if at all. We have recognized revenue associated with our grant from the USAMRMC of \$3.5 million since inception of the grant, but continued funding from the USAMRMC is contingent upon their review and approval of our continued research and development activities associated with the grant. In addition, there can be no assurance that we will receive other research-related grant awards or produce other collaborative agreement revenues in the future.

## **Critical Accounting Estimates**

The accompanying discussion and analysis of our financial condition and results of operations are based upon our financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain. Management has discussed the development, selection and disclosure of the following estimates with the Audit Committee.

### ***Revenue Recognition***

We recognize revenue when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured.

In May 2011, we entered into an award contract with the US Army Medical Research and Materiel Command, or USAMRMC, to support the development of the Company's product candidate, ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain on the battlefield, in the emergency room or in ambulatory care facilities. The grant provides for the reimbursement of qualified expenses for research and development activities as defined under the terms of the grant agreement. Revenue under the grant agreement is recognized when the related qualified research expenses are incurred.

### ***Research and Development Expenses***

We expense research and development expenses as incurred. Research and development expenses consist primarily of direct and research-related allocated overhead costs such as facilities costs, salaries and related personnel costs, and material and supply costs. In addition, research and development expenses include costs related to clinical trials to validate our testing processes and procedures and related overhead expenses. Expenses resulting from clinical trials are recorded when incurred based in part on factors such as estimates of work performed, patient enrollment, progress of patient studies and other events. We make good faith estimates that we believe to be accurate, but the actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

## **Table of Contents**

### ***Share-Based Compensation***

We measure and recognize compensation expense for all share-based payment awards made to our employees and directors, including employee stock options and employee stock purchases related to the Employee Share Purchase Plan, or ESPP, on estimated fair values. The fair value of equity-based awards is amortized over the vesting period of the award using a straight-line method.

To estimate the value of an award, we use the Black-Scholes option pricing model. This model requires inputs such as expected life, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. Estimates of expected life are primarily determined using the simplified method in accordance with guidance provided by the Securities and Exchange Commission, or SEC. Volatility is derived from historical volatilities of several public companies within our industry that are deemed to be comparable to our business because we have limited information on the volatility of our common stock since we had no trading history prior to completion of our IPO in February 2011. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. We review our valuation assumptions quarterly and, as a result, it is likely we will change our valuation assumptions used to value share based awards granted in future periods. Further, we are required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. If factors change and different assumptions are employed in determining the fair value of stock based awards, the stock based compensation expense recorded in future periods may differ significantly from what was recorded in the current period.

Prior to the IPO, we were also required to estimate the fair value of the common stock underlying our stock-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. The fair values of the common stock underlying our stock-based awards were estimated on each grant date by our board of directors, with input from management. In valuing our common stock, our board of directors determined the equity value of our business by taking a weighted combination of the value indications under two valuation approaches, an income approach and a market approach. The income approach estimates the present value of future estimated cash flows, based upon forecasted revenue and costs. These future cash flows were discounted to their present values using a discount rate derived from an analysis of the cost of capital of comparable publicly traded companies in our industry or similar lines of business as of each valuation date and was adjusted to reflect the risks inherent in our cash flows. The market approach estimated the fair value by applying market multiples of comparable publicly traded companies in our industry or similar lines of business which were based on key metrics implied by the enterprise values or acquisition values of our comparable publicly traded companies.

### ***Liabilities Associated with Warrants***

#### ***Warrants to Purchase Common Stock***

In connection with the private placement equity financing in June 2012, or PIPE, the Company issued PIPE warrants to purchase up to 2,630,103 shares of common stock. Under the terms of the PIPE warrants, upon certain transactions, including a merger, tender offer, sale of all or substantially all of the assets of the Company or if a person or group shall become the owner of 50% of the Company's issued and outstanding common stock, which is outside of the Company's control, each PIPE warrant holder may elect to receive a cash payment in exchange for the warrant, in an amount determined by application of the Black-Scholes option-pricing model. Accordingly, the PIPE warrants are recorded as a liability at fair value at the end of each reporting period, as determined by the Black-Scholes option-pricing model and changes to the fair value are recorded in other income (expense). The inputs for the Black-Scholes option-pricing model include exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants. These inputs are subjective and generally require significant analysis and judgment to develop. Changes to the inputs could significantly impact the estimated fair value of the PIPE warrants.

## **Table of Contents**

### *Warrants to Purchase Convertible Preferred Stock*

Freestanding warrants to purchase shares of our convertible preferred stock were classified as liabilities on our balance sheets at fair value because the warrants could have conditionally obligated us to redeem the underlying convertible preferred stock. The warrants were subject to remeasurement at each balance sheet date, and any change in fair value was recognized as a component of other income (expense), net, in the statements of operations. We estimated the fair value of these warrants at the respective balance sheet dates using the Black-Scholes option-pricing model. We used assumptions to estimate the fair value of the warrants including the remaining contractual terms of the warrants, risk-free interest rates, expected dividend yields and the fair value and expected volatility of the underlying stock. These assumptions were subjective and the fair value of the warrants to purchase convertible preferred stock could have differed significantly had we used different assumptions.

Upon the completion of our IPO in February 2011, all of our warrants to purchase convertible preferred stock had been exercised or converted into warrants to purchase common stock. At that time, the then-current aggregate fair value of these warrants was reclassified from liabilities to additional paid-in capital and we will no longer remeasure the liability associated with these warrants to purchase convertible preferred stock to fair value.

### *Bridge Loan*

On September 14, 2010, we entered into a bridge loan financing, in which we issued notes to certain existing investors for an aggregate purchase price of \$8.0 million, or the 2010 notes. The 2010 notes could not be prepaid without the written consent of the holders of the 2010 notes, bore interest at a rate of 4.0% per annum and had a maturity date of the earliest of (1) September 14, 2011 or (2) an event of default. The principal and the interest under the 2010 notes were converted into common stock in connection with our IPO at a conversion price equal to 80% of the IPO price, or \$4.00 per share.

Under the terms of the bridge loan agreement, upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 notes, we agreed to issue an additional \$4.0 million of the 2010 notes. This additional \$4.0 million was determined to be a call option that was recorded at its fair value of \$0.5 million as a debt discount that was amortized to interest expense during the period when the notes were outstanding until conversion in connection with our IPO. The fair value of the call option was determined by evaluating multiple potential outcomes using a market approach and an income approach depending on the scenario and discounted these values back to December 31, 2010 while applying estimated probabilities to each scenario value. As of December 31, 2010, these scenarios included a potential IPO, merger or sale at different times during 2011 and 2012 as well as remaining private. During the quarter ending March 31, 2011, the 2010 notes were amended so that the call option expired upon the closing of our IPO.

Also in connection with the bridge loan financing, we issued warrants, or the 2010 warrants, with a fair value of \$1.3 million, which was recorded as a debt discount that was amortized to interest expense during the period where the warrants were outstanding until exercised at the time of the IPO as detailed above in *Warrants to Purchase Convertible Preferred Stock*.

We used considerable judgment in determining the fair value of these instruments and had we used different assumptions, the resulting fair values could have been materially different.

Subsequent to December 31, 2010, and in conjunction with our IPO, the principal and accrued interest under the 2010 notes converted into 2,034,438 shares of common stock and the 2010 warrants were exercised on a net issuance basis for 107,246 shares of Series C convertible preferred stock, which such shares of Series C convertible preferred stock were automatically converted into 107,246 shares of common stock immediately prior to the closing of our IPO.

## **Table of Contents**

### ***Income Taxes***

Significant management judgment is required in determining our provision or benefit for income taxes, any uncertain tax positions, deferred tax assets and liabilities, and any valuation allowance recorded against our net deferred tax assets. We make these estimates and judgments about our future taxable income that are based on assumptions that are consistent with our future plans. As of December 31, 2012, 2011 and 2010, we have recorded a full valuation allowance on our net deferred tax assets due to uncertainties related to our ability to utilize our deferred tax assets in the foreseeable future. These deferred tax assets primarily consist of certain net operating loss carryforwards and research and development tax credits. Should the actual amounts differ from our estimates, the amount of our valuation allowance could be materially impacted.

Since inception, we have incurred operating losses and, accordingly, we have not recorded a provision for income taxes for any of the periods presented. Accordingly, there have not been significant changes to our provision or benefit for income taxes during the years ended December 31, 2012, 2011 or 2010.

As of December 31, 2012, 2011 and 2010, we had federal net operating loss carryforwards of \$89.7 million, \$82.2 million and \$63.8 million, respectively, and state net operating loss carryforwards of \$89.7 million, \$80.6 million and \$63.7 million, respectively. We also had \$1.3 million, \$1.3 million and \$1.1 million of federal research credit carryforwards, and \$1.1 million, \$0.9 million and \$0.7 million of state research credit carryforwards as of December 31, 2012, 2011 and 2010. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. If not utilized, the federal net operating loss and tax credit carryforwards will expire beginning in 2025 and the state net operating loss will begin expiring in 2015. 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.

### **Results of Operations**

#### ***Years Ended December 31, 2012, 2011 and 2010***

##### ***Revenue***

To date, we have not generated any product revenue. We do not expect to receive any revenues from any product candidates that we develop until we obtain regulatory approval and commercialize our products or enter into collaborative agreements with third parties. In May 2011, we received a grant award of \$5.6 million from the USAMRMC for the development of ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain. Revenue related to this grant award is recognized as the related research and development expenses are incurred.

Revenue for the year ended December 31, 2012 and 2011 was \$2.4 and \$1.1 million, respectively, and was generated from our grant with the USAMRMC. We did not generate any revenue for the year ended December 31, 2010.

##### ***Research and Development Expenses***

Conducting research and development is central to our business model. The majority of our operating expenses to date have been for research and development activities related to the NanoTab System. Research and development expenses included the following:

expenses incurred under agreements with contract research organizations and clinical trial sites;

employee- and consultant-related expenses, which include salaries, benefits and stock-based compensation;



**Table of Contents**

payments to third party pharmaceutical and engineering development contractors;

payments to third party manufacturers; and

depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, depreciation of leasehold improvements and equipment and laboratory and other supply costs.

Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late stage clinical trials. We anticipate that quarterly research and development expenses during the first half of 2013 will be in line with or modestly higher than the fourth quarter of 2012 as we conduct and complete the Phase 3 clinical trials for the NanoTab System and the ARX-04 Phase 2 clinical trial. However, we will incur substantial future expenditures as we seek to continue development of the NanoTab System, including the requisite preparatory activities to submit an NDA to the FDA and activities associated with preparing for the potential commercialization of the NanoTab System. We do not plan to continue development of ARX-04 beyond the current grant-supported activities, and ARX-02 and ARX-03, unless additional funding or corporate partnership resources are available to support these programs.

We track external development expenses on a program-by-program basis. Our development resources are shared among all of our programs. Compensation and benefits, facilities, depreciation, stock-based compensation, and development support services are not allocated specifically to projects and are considered research and development overhead. Below is a summary of our research and development expenses during the years ended December 31, 2012, 2011 and 2010 (in thousands):

|   | Years Ended December 31, |           |          |
|---|--------------------------|-----------|----------|
|   | 2012                     | 2011      | 2010     |
| ARX-01 (NanoTab System)                 | \$ 17,100                | \$ 7,823  | \$ 1,289 |
| ARX-02                                  |                          |           | 507      |
| ARX-03                                  |                          |           | 1,555    |
| ARX-04                                  | 1,547                    | 523       |          |
| Overhead                                | 6,261                    | 5,278     | 4,842    |
| Total research and development expenses | \$ 24,908                | \$ 13,624 | \$ 8,193 |

Due to the inherently unpredictable nature of product development, development timelines and the probability of success, development costs can differ materially from expectations. While we are currently focused on advancing the NanoTab System and ARX-04, and subsequently ARX-02 and ARX-03, our future research and development expenses will depend on the clinical success of each product candidate as well as ongoing assessments of the commercial potential of our product candidates. In addition, we cannot predict which product candidates may be subject to future collaborations, when these arrangements will be secured, if at all, and to what degree these arrangements would affect our development plans and capital requirements.

Total research and development expenses for each of the three years ended December 31, 2012 were as follows (in thousands, except percentages):

|                                   | Years Ended December 31, |           |          | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 | Percentage<br>Increase/<br>(Decrease)<br>2012 vs. 2011 | Percentage<br>Increase/<br>(Decrease)<br>2011 vs. 2010 |
|-----------------------------------|--------------------------|-----------|----------|--|--|--|--|
|                                   | 2012                     | 2011      | 2010     |  |  |  |  |
| Research and development expenses | \$ 24,908                | \$ 13,624 | \$ 8,193 | \$ 11,284                                | \$ 5,431                                 | 83%  | 66%  |

**Table of Contents**

The \$11.3 million increase during the year ended December 31, 2012 was primarily attributable to an increase of \$9.3 million in expenses related to our NanoTab System development program, particularly related to conducting three Phase 3 trials, and a \$1.0 million increase related to activities under our grant with the USAMRMC for ARX-04. The remaining increase primarily relates to an increase in headcount-related expenses, including stock-based compensation, due to an increase in headcount.

The \$5.4 million increase during the year ended December 31, 2011 was primarily attributable to an increase of \$6.5 million in development expenses related to our ARX-01 development program related to the planned Phase 3 trials and a \$0.5 million increase related to activities under our grant with the USAMRMC for ARX-04, partially offset by a decrease in development expenses of \$2.1 million related to the completion in 2010 of Phase 2 clinical trials for our ARX-02 and ARX-03 programs.

*General and Administrative Expenses*

General and administrative expenses consisted primarily of salaries, benefits and stock-based compensation for personnel in administration and finance and business development activities. Other significant expenses included legal expenses to pursue patent protection of our intellectual property, allocated facility costs and professional fees for general legal, audit and consulting services. We expect general and administrative expenses to continue to increase in connection with operating as a public company and as we continue to build our corporate infrastructure in support of continued development of our product candidates.

Total general and administrative expenses for each of the three years ended December 31, 2012 were as follows (in thousands, except percentages):

|                                     | Years Ended December 31, |          |          |  |  | Percentage                               | Percentage                               |
|-------------------------------------|--------------------------|----------|----------|--|--|--|--|
|                                     | 2012                     | 2011     | 2010     | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 |
| General and administrative expenses | \$ 7,199                 | \$ 6,800 | \$ 3,993 | \$ 399                                   | \$ 2,807                                 | 6%                                       | 70%                                      |

The \$0.4 million increase during the year ended December 31, 2012 was primarily due to an increase in legal expenses, primarily associated with our increasing patent portfolio and other corporate-related expenses associated with operations as a public company.

The \$2.8 million increase during the year ended December 31, 2011 was primarily due to an increase in legal, audit and consulting fees in connection with costs associated with our operations as a public company as well as non-equity incentive plan expenses.

*Interest Expense*

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Total interest expense for each of the three years ended December 31, 2012, were as follows (in thousands, except percentages):

|                  | Years Ended December 31, |            |            |  |  | Percentage                               | Percentage                               |
|------------------|--------------------------|------------|------------|--|--|--|--|
|                  | 2012                     | 2011       | 2010       | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 |
| Interest expense | \$ (2,283)               | \$ (2,309) | \$ (1,397) | \$ (26)                                  | \$ 912                                   | (1%)                                     | 65%                                      |

There were no significant changes in interest expense during the year ended December 31, 2012, compared to the year ended December 31, 2011.

**Table of Contents**

The \$912,000 increase during the year ended December 31, 2011 was primarily attributable to interest and the debt discount amortization related to the \$8.0 million principal amount of convertible promissory notes issued in September 2010. The \$1.1 million in unamortized debt discounts was recognized as interest expense in connection with conversion of these notes immediately prior to the IPO in February 2011.

*Interest Income and Other Income (Expense), net*

Interest Income and Other income (expense), net during the year ended December 31, 2012 consisted primarily of the change in the fair value of our warrants, or PIPE warrants, issued in connection with our private placement of our common stock, which was completed in June 2012, and our contingent put option liability associated with the loan and security agreement with Hercules. During the years ended December 31, 2011 and 2010 Interest Income and Other income (expense) consisted primarily of the change in the fair value our then-outstanding warrants to purchase convertible preferred stock. Our warrants to purchase convertible preferred stock were classified as liabilities and, as such, were remeasured to fair value at each balance sheet date with the corresponding gain or loss from the adjustment recorded as other income (expense), net. Upon the completion of our IPO, all of our warrants to purchase convertible preferred stock were remeasured to fair value and were either exercised or converted into warrants to purchase common stock. At that time, the then-current aggregate fair value of these warrants was reclassified from liabilities to additional paid-in capital and we no longer remeasure the liability associated with these warrants to fair value. Total interest income and other income (expense) for each of the three years ended December 31, 2012, were as follows (in thousands, except percentages):

|   | Years Ended December 31, |          |          | Increase/<br>(Decrease)<br>2012 vs. 2011 | Increase/<br>(Decrease)<br>2011 vs. 2010 | Percentage<br>Increase/<br>(Decrease)<br>2012 vs. 2011 | Percentage<br>Increase/<br>(Decrease)<br>2011 vs. 2010 |
|---|--------------------------|----------|----------|--|--|--|--|
|   | 2012                     | 2011     | 2010     |  |  |  |  |
| Interest and Other income<br>(expense), net | \$ (1,367)               | \$ 1,560 | \$ (761) | \$ (2,927)                               | \$ 2,321                                 | NA%  | NA%  |

The \$2.9 million change in interest and other income (expense) during the year ended December 31, 2012 was primarily attributable to the increase in the fair value of our PIPE warrants, which is recorded as an expense. The income generated in 2011 was primarily attributable to the decrease in fair value of our warrants to purchase convertible preferred stock and the elimination of the call option liability related to the convertible promissory notes issued in September 2010 which expired upon closing of the IPO in February 2011.

The \$2.3 million increase in other income (expense), net during the year ended December 31, 2011 was primarily attributable to the change in the decrease in fair value of our warrants to purchase convertible preferred stock and the elimination of the call option liability related to the convertible promissory notes issued in September 2010 which expired upon closing of the IPO in February 2011.

**Liquidity and Capital Resources***Liquidity*

We have incurred losses and generated negative cash flows from operations since inception, and we expect to continue to incur significant and increasing losses and negative cash flows for the foreseeable future. We have funded our operations primarily through the issuance of equity securities and debt financings. From inception through December 31, 2012, we have received net proceeds of \$54.9 million from the sale of convertible preferred stock, \$88.1 million from the sale of common stock and \$41.4 million from our debt arrangements.

As of December 31, 2012, we had cash, cash equivalents and investments totaling \$59.8 million compared to \$35.8 million as of December 31, 2011. The increase was primarily attributable to proceeds from two equity financings conducted in 2012. In December 2012, we sold 14,375,000 shares of our common stock at \$3.31 per share in a public offering and received net proceeds of \$44.1 million, after underwriting discounts, commissions and offering expenses. In June 2012, we completed a private placement of our common stock, in which we sold 2,922,337 shares for net proceeds of \$9.1 million, after commissions and offering expenses.

**Table of Contents**

Our cash and investment balances are held in a variety of interest bearing instruments, including obligations of U.S. government agencies, money market funds and time deposits. Cash in excess of immediate requirements is invested with a view toward capital preservation and liquidity.

***Cash Flows***

|   | Years Ended December 31, |             |             |
|---|--------------------------|-------------|-------------|
|   | 2012                     | 2011        | 2010        |
|   | (in thousands)           |             |             |
| Net cash used in operating activities               | \$ (24,582)              | \$ (15,287) | \$ (12,225) |
| Net cash (used in) provided by investing activities | 14,955                   | (29,579)    | 4,765       |
| Net cash provided by financing activities           | 49,765                   | 49,605      | 3,365       |

***Cash Flows from Operating Activities***

The primary use of cash for our operating activities during these periods was to fund the development of our product candidates. Our cash used for operating activities also reflected changes in our working capital and adjustments for non-cash charges, such as depreciation and amortization of our fixed assets, stock-based compensation, interest expense related to our debt financings, and the revaluation of our warrant liabilities.

Net cash used in operating activities of \$24.6 million during the year ended December 31, 2012 reflected a net loss of \$33.4 million, partially offset by aggregate non-cash charges of \$5.3 million and a net change of \$3.5 million in our net operating assets and liabilities. Non-cash charges primarily included \$2.2 million in stock-based compensation and \$1.4 million for the revaluation of the PIPE warrant liability and the contingent put option liability. The net change in our operating assets and liabilities was primarily a result of an increase in accounts payable and accrued liabilities of \$2.7 million due to increased research and development activities during 2012.

Net cash used in operating activities of \$15.3 million during the year ended December 31, 2011 reflected a net loss of \$20.1 million, partially offset by aggregate non-cash charges of \$2.6 million and a net change of \$2.2 million in our net operating assets and liabilities. Non-cash charges primarily included \$1.6 million for interest on our debt and \$1.8 million in stock-based compensation, partially offset by \$1.5 million for the revaluation of the warrant liability and the call option liability. The net change in our operating assets and liabilities was primarily a result of an increase in accounts payable and accrued liabilities of \$2.8 million due to increased research and development activities during 2011.

Net cash used in operating activities of \$12.2 million during the year ended December 31, 2010 reflected a net loss of \$14.3 million, partially offset by aggregate non-cash charges of \$3.9 million and a net change of \$1.8 million in our net operating assets and liabilities. Non-cash charges primarily included \$0.7 million for interest on our debt, \$1.3 million for the revaluation of the warrant liability and the call option liability, \$0.5 million of depreciation and amortization and \$1.4 million in stock-based compensation. The net change in our operating assets and liabilities was primarily a result of an increase in prepaid expense of \$1.5 million.

***Cash Flows from Investing Activities***

Our investing activities have consisted primarily of our capital expenditures and purchases and sales and maturities of our available-for-sale investments.

During the year ended December 31, 2012, cash provided by investing activities of \$15.0 million was primarily a result of \$42.9 million in maturities of investments, partially offset by \$27.2 million in purchases of investments and \$0.8 million in purchases of property and equipment.

## **Table of Contents**

During the year ended December 31, 2011, cash used in investing activities of \$29.6 million was primarily a result of \$39.4 million in purchases of investments and \$2.0 million in property and equipment purchases, partially offset by \$11.8 million in proceeds from sales and maturities of investments.

During the year ended December 31, 2010, cash provided by investing activities of \$4.8 million was primarily a result of \$9.7 million in proceeds from sale of investments, partially offset by \$4.9 million used for purchases of our investments.

### *Cash Flows from Financing Activities*

Cash flows from financing activities primarily reflect proceeds from the sale of our securities and proceeds from our debt financings, reduced by payments made on such debt financings. As of December 31, 2012, our balance of outstanding principal was \$16.3 million associated with our loan and security agreement with Hercules.

During the year ended December 31, 2012, cash provided by financing activities was primarily a result of the receipt of \$44.1 million in proceeds from an underwritten public offering in December 2012, net of offering costs and underwriting discounts, and proceeds of \$9.1 million from a private placement of our common stock, in June 2012, net of offering costs. During the year ended December 31, 2012, we made payments of \$3.7 million associated with our loan and security agreement with Hercules.

During the year ended December 31, 2011, cash provided by financing activities was primarily a result of the receipt of \$34.9 million in proceeds from our IPO, net of offering costs, and proceeds of \$19.8 million from our loan and security agreement with Hercules, partially offset by principal repayments on our long-term debt of \$5.3 million, including payment in full of our remaining obligations under the Pinnacle agreement, which was terminated upon executing the Hercules loan and security agreement in June 2011.

During the year ended December 31, 2010, cash provided by financing activities of \$3.4 million was primarily a result of the receipt of \$8.0 million in borrowings received from the convertible note agreement entered into in September 2010, partially offset by principal repayments on our long-term debt of \$4.7 million.

### *Operating Capital and Capital Expenditure Requirements*

We expect our rate of cash usage to increase in the future, in particular to support our product development activities. We believe that our available cash resources, will be sufficient to fund our operations into the third quarter of 2014, including support for our continuing development of our product candidates, clinical trials and commercial readiness activities. Future capital requirements will be substantial and we will need to raise additional capital to fund our operations, including product candidate development activities. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. Additional capital may not be available in terms acceptable to us, or at all. If adequate funds are not available, or if the terms underlying potential funding sources are unfavorable, our business and our ability to develop our technology and product candidates would be harmed.

Our future capital requirements will depend on many forward looking factors and are not limited to the following:

the initiation, progress, timing and completion of clinical trials for our product candidates and potential product candidates;

the outcome, timing and cost of regulatory approvals;

delays that may be caused by changing regulatory requirements;

the number of product candidates that we pursue;

the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;

**Table of Contents**

the timing and terms of future in-licensing and out-licensing transactions;

the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;

the cost of procuring clinical and commercial supplies of our product candidates;

the extent to which we acquire or invest in businesses, products or technologies; and

the possible costs of litigation.

**Contractual Obligations**

The following table and disclosure summarizes our outstanding contractual obligations and commitments as of December 31, 2012 (in thousands):

| Contractual Obligations:             | Total     | Payment by Period |           |           |                   |
|--------------------------------------|-----------|-------------------|-----------|-----------|-------------------|
|                                      |           | Less than 1 year  | 1-3 years | 3-5 years | More than 5 years |
| Operating Lease <sup>(1)</sup>       | \$ 1,319  | \$ 381            | \$ 796    | \$ 142    |                   |
| Principal Payments on Long-Term Debt | 16,345    | 7,804             | 8,541     |           |                   |
| Interest Payments on Long-Term Debt  | 1,710     | 1,105             | 605       |           |                   |
| Total                                | \$ 19,374 | \$ 9,290          | \$ 9,942  | \$ 142    |                   |

<sup>(1)</sup> Operating lease include base rent for facilities we occupy in Redwood City, California.

In January 2013, we entered into a Services Agreement with Patheon, relating to the manufacture of Sufentanil NanoTabs, for use with the NanoTab System. Under the terms of the Services Agreement, the Company has agreed to purchase, subject to Patheon's continued material compliance with the terms of the Services Agreement, all of its Sufentanil NanoTabs requirements for the United States, Canada and Mexico from Patheon during the Initial Term of the Services Agreement (as defined below), and at least eighty percent (80%) of its Sufentanil NanoTabs requirements for such territories after the Initial Term. The term of the Services Agreement extends until December 31, 2017, or the Initial Term, and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months' prior written notice; provided, however, that the Services Agreement may not be terminated without cause prior to the end of the Initial Term.

We have also entered into a Capital Agreement, with Patheon. Under the terms of the Capital Agreement, we have the option to make certain future modifications to Patheon's Cincinnati facility, the aggregate cost of which is expected to be less than \$3.5 million and which would be the responsibility of the Company. The Capital Agreement also requires that we make payments in 2013 totaling \$480,000 to Patheon to partially offset taxes incurred and paid by Patheon in connection with facility modifications already completed by Patheon. We can seek reimbursement from Patheon for these payments if it receives approval from the U.S. Food and Drug Administration for the NanoTab System. The Capital Agreement further requires that we pay a maximum overhead fee of \$200,000 annually during the term of the Services Agreement, which amount may be reduced to \$0 based on the amount of annual revenues earned by Patheon under the Services Agreement and pre-existing development agreements with Patheon.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for our products, which are currently in development stage; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

**Off-Balance Sheet Arrangements**

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Through December 31, 2012, we have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.



**Table of Contents**

**Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

Not applicable.

**Table of Contents**

**Item 8. Financial Statements and Supplementary Data**

The financial statements required by this item are attached to this Form 10-K beginning with page F-1.

## **Table of Contents**

### **Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure**

None.

### **Item 9A. Controls and Procedures**

#### **Evaluation of Disclosure Controls and Procedures**

We have carried out an evaluation, under the supervision, and with the participation, of management including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e)) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on their evaluation, our principal executive officer and principal financial officer concluded that, subject to the limitations described below, our disclosure controls and procedures were effective as of December 31, 2012.

*Limitations on the Effectiveness of Controls.* A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were sufficiently effective to provide reasonable assurance that the objectives of our disclosure control system were met. We continue to implement, improve and refine our disclosure controls and procedures and our internal control over financial reporting.

#### **Changes in Internal Control over Financial Reporting**

There have been no significant changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, internal control over financial reporting during the fiscal quarter ended December 31, 2012.

#### **Management's Report on Internal Control over Financial Reporting**

The following report is provided by management in respect of AcetRx Pharmaceuticals' internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act):

1. AcetRx Pharmaceuticals' management is responsible for establishing and maintaining adequate internal control over financial reporting.
2. AcetRx Pharmaceuticals management has used the Committee of Sponsoring Organizations of the Treadway Commission, or COSO framework to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of AcetRx Pharmaceuticals' internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of AcetRx Pharmaceuticals' internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.
3. Management has assessed the effectiveness of AcetRx Pharmaceuticals' internal control over financial reporting as of December 31, 2012 and has concluded that such internal control over financial reporting was effective.

**Table of Contents**

4. This annual report does not include an attestation report of AcetRx Pharmaceuticals' independent registered public accounting firm regarding the effectiveness of AcetRx Pharmaceuticals' internal controls over financial reporting pursuant to temporary rules of the Securities and Exchange Commission that permit AcetRx Pharmaceuticals to provide only management's report in this annual report.

**Item 9B. Other Information**

None.

## **Table of Contents**

### **PART III**

#### **Item 10. Directors, Executive Officers and Corporate Governance**

##### **Board of Directors**

Our board of directors is divided into three classes designated as Class I, Class II and Class III, with each class having a three-year term.

The following is a brief biography of each member of our board of directors with each biography including information regarding the experiences, qualifications, attributes or skills of each current board member.

##### ***Class I Directors***

**Adrian Adams**, age 62, has served as our Chairman since February 2013. Mr. Adams has been Chief Executive Officer and President of Auxilium Pharmaceuticals Inc. since December, 2011. Prior to joining Auxilium, Mr. Adams served as Chairman and Chief Executive Officer of Neurologix, a company focused on development of multiple innovative gene therapy development programs. Before Neurologix, Mr. Adams served as President and Chief Executive Officer of Inspire Pharmaceuticals, Inc., where he oversaw the commercialization and development of prescription pharmaceutical products and led the company through a strategic acquisition by global pharmaceutical leader Merck & Co., Inc. in May 2011. Prior to Inspire, Mr. Adams served as President and Chief Executive Officer of Sepracor Inc. from December 2006 until February 2010. Under his leadership, Sepracor conducted multiple strategic corporate development activities, including the in-licensing of seven products and out-licensing deals with two major pharmaceutical companies, prior to its acquisition by Dainippon Sumitomo Pharma Co. Prior to joining Sepracor, Mr. Adams was President and Chief Executive Officer of Kos Pharmaceuticals, Inc. from 2002 until the acquisition of the company by Abbott Laboratories in December 2006. During his tenure he led the transformation of Kos into a fully integrated and profitable pharmaceutical company with annual revenues approaching \$1 billion. Mr. Adams graduated from the Royal Institute of Chemistry at Salford University in the U.K. Mr. Adams has extensive national and international experience and has been instrumental in launching major global brands in addition to driving successful corporate development activities encapsulating financing, product and company acquisitions, in-licensing and company M&A activities, all of which provide him with the qualifications and skills to serve as a director.

**Guy P. Nohra**, age 52, has served as our director since August 2006. Mr. Nohra co-founded Alta Partners, a venture capital firm investing in life science companies, in 1996, and has served as Managing Director of Alta Partners since 1996. Mr. Nohra was also a partner at Burr, Egan, Deleage & Co., a venture capital firm, which he joined in 1989. From January 1984 until June 1987, Mr. Nohra was Product Manager of Medical Products with Security Pacific Trading Corporation, a consumer and commercial bank. Currently, Mr. Nohra serves on the board of directors of numerous private companies, including Carbylan Biosurgery, Inc., Coapt Systems, PneumRx, Inc. and Vertiflex, Inc., and is the Chairman of the board of USGI Medical, Inc. In addition, Mr. Nohra previously served on the boards of directors of ATS Medical, Inc., a company focused on the manufacture of cardiac surgery products that was acquired by Medtronic, Inc., a medical device company, in 2010 and Cutera, Inc., a global medical device company. Mr. Nohra also serves on the board of directors of the Medical Device Manufacturing Association, a national trade organization that advocates for entrepreneurial medical technology companies. Mr. Nohra holds a B.A. in History from Stanford University and an M.B.A. from the University of Chicago. Mr. Nohra's medical technology and venture capital industry experience provides him with the qualifications and skills to serve as a director.

**Mark G. Edwards**, age 55, has served as our director since September 2011. Mr. Edwards is Managing Director of Bioscience Advisors Inc., a biopharmaceutical consulting firm he founded in 2011. From July 2008 until December 2010, he was Managing Director and a Principal of Deloitte Recap LLC, a wholly-owned subsidiary of Deloitte Touche Tohmatsu, an audit and financial consulting services firm. Mr. Edwards was previously the Managing Director and founder of Recombinant Capital, Inc. (Recap), a consulting and database firm based in

## **Table of Contents**

Walnut Creek, California, from 1988 until the sale of Recap to Deloitte in 2008. Prior to founding Recap in 1988, Mr. Edwards was Manager of Business Development at Chiron Corporation, a biotechnology company. He received his B.A. and M.B.A. degrees from Stanford University. Mr. Edwards' financial and business expertise, including his background as a business advisor to pharmaceutical and biotechnology companies, provides him with the qualifications and skills to serve as a director.

### ***Class II Directors***

**Stephen J. Hoffman**, Ph.D., M.D., age 58, has served as our director since February 2010. Dr. Hoffman has served as a managing director at Skyline Ventures, a venture capital firm, since May 2007. From January 2003 to March 2007, Dr. Hoffman was a general partner at TVM Capital, a venture capital firm. Prior to that, he served as President, Chief Executive Officer and a director of Allos Therapeutics, a biopharmaceutical company, from 1994 to 2002. From 1990 to 1994, Dr. Hoffman completed a fellowship in clinical oncology and a residency/fellowship in dermatology, both at the University of Colorado. Dr. Hoffman was the scientific founder of Somatogen Inc., a biotechnology company that was acquired by Baxter International, Inc., a global medical products and services company, in 1998, where he held the position of Vice President of Science and Technology from 1987 until 1990. He serves on the board of directors of several biopharmaceutical companies: Allos Therapeutics, Inc., Concert Pharmaceuticals, Inc., Collegium Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Genocera Biosciences, Inc., and Proteon Therapeutics, Inc. Previously, Dr. Hoffman served on the board of directors of Sirtris Pharmaceuticals, Inc., a pharmaceutical company that was acquired by GlaxoSmithKline, a global pharmaceutical company, in 2008. Dr. Hoffman holds a Ph.D. in bio-organic chemistry from Northwestern University and an M.D. from the University of Colorado School of Medicine. Dr. Hoffman's scientific, financial and business expertise, including his diversified background as an executive officer and investor in public pharmaceutical companies, provides him with the qualifications and skills to serve as a director.

**Richard A. King**, age 48, has served as our director and President and Chief Executive Officer since May 2010. From April 2009 until May 2010, Mr. King acted as an independent consultant to a number of private and public biotechnology and venture capital companies. From October 2008 to April 2009, Mr. King served as President and General Manager of Tercica, Inc., a biotechnology company that was acquired by Ipsen, SA in 2008, and from February 2008 to October 2008, Mr. King served as President and Chief Operating Officer of Tercica, Inc., and from February 2007 until February 2008, he served as Chief Operating Officer of Tercica, Inc. From January 2002 to October 2006, Mr. King served as Executive Vice President of Commercial Operations of Kos Pharmaceuticals, Inc., a pharmaceutical company that was acquired by Abbott Laboratories, a global, broad-based health care company, in 2006. From January 2000 to January 2002, Mr. King served as Senior Vice President of Commercial Operations at Solvay Pharmaceuticals, a pharmaceutical company that was acquired by Abbott Laboratories in 2009. From April 1992 to January 2000, Mr. King held various marketing positions at SmithKline Beecham Pharmaceuticals, now known as GlaxoSmithKline, a global pharmaceutical company. Mr. King holds a B.Sc. in Chemical Engineering from University of Surrey and an M.B.A. from Manchester Business School. Mr. King's extensive experience as an executive officer of public pharmaceutical companies and his knowledge of the day-to-day operations of our company provide him with the qualifications and skills to serve as a director.

**Pamela P. Palmer, M.D., Ph.D.**, age 50, has served as our director and Chief Medical Officer since she co-founded the company in July 2005. Dr. Palmer has been on faculty at the University of California, San Francisco since 1996 and is currently a Clinical Professor of Anesthesia and Perioperative Care. Dr. Palmer was Director of UCSF PainCARE-Center for Advanced Research and Education from 2005 to 2009, and was Medical Director of the UCSF Pain Management Center from 1999 to 2005. Dr. Palmer has been a consultant of Omeros Corporation, a biopharmaceutical company, since she co-founded that company in 1994. Dr. Palmer holds an M.D. from Stanford University and a Ph.D. from the Stanford Department of Neuroscience. Dr. Palmer's extensive clinical and scientific experience in the treatment of acute and chronic pain as well as historical knowledge of our company provide her with the qualifications and skills to serve as a director.

**Table of Contents*****Class III Directors***

**Howard B. Rosen**, age 54, has served as our director since 2008. Since 2008, Mr. Rosen has served as a consultant to several companies in the biotechnology industry. He has also served as a lecturer at Stanford University in Chemical Engineering since 2008 and in Management since 2011. Mr. Rosen served as interim President and Chief Executive Officer of Pearl Therapeutics, Inc., a company focused on developing combination therapies for the treatment of highly prevalent chronic respiratory diseases, from June 2010 to March 2011. From 2004 to 2008, Mr. Rosen was Vice President of Commercial Strategy at Gilead Sciences, Inc., a biopharmaceutical company. Mr. Rosen was President of ALZA Corporation, a pharmaceutical and medical systems company that merged with Johnson & Johnson, a global healthcare company, in 2001, from 2003 until 2004. Prior to that, from 1994 until 2003, Mr. Rosen held various positions at ALZA Corporation. Mr. Rosen is also a member of the board of directors of a number of private biotechnology companies as follows: PavVax, Inc., NTF Therapeutics, Inc., Pearl Therapeutics, Inc., Entrega, Inc. and ALDEA Pharmaceuticals. Previously, Mr. Rosen served on the board of directors of a number of public companies, as follows: Pharsight Corporation, a company focused on providing software products and consulting services to biopharmaceutical companies that was acquired by Tripos International in 2008 and CoTherix, Inc., a biopharmaceutical company that was acquired by Actelion Pharmaceuticals Ltd. in 2007. Mr. Rosen holds a B.S. in Chemical Engineering from Stanford University, an M.S. in Chemical Engineering from the Massachusetts Institute of Technology and an M.B.A. from the Stanford Graduate School of Business. Mr. Rosen's experience in the biopharmaceutical industry, including his specific experience with commercialization of pharmaceutical products, provides him with the qualifications and skills to serve as a director.

**Mark Wan**, age 47, has served as our director since August 2006. Mr. Wan is a founding general partner of Three Arch Partners, a venture capital firm. Prior to co-founding Three Arch Partners in 1993, Mr. Wan was a general partner at Brentwood Associates, a private equity firm from 1987 until 1993. Since 1999, Mr. Wan has served on the board of directors of Epocrates, Inc., a company focused on providing mobile drug reference tools. Mr. Wan also serves on the board of directors of numerous private companies. Mr. Wan holds a B.S. in Engineering from Yale University and an M.B.A. from the Stanford Graduate School of Business. Mr. Wan's financial experience and extensive knowledge of our company provides him with the qualifications and skills to serve as a director.

**Executive Officers of the Registrant**

The following table sets forth certain information concerning our executive officers as of January 31, 2013:

| <b>Name</b>                   | <b>Age</b> | <b>Position</b>                                 |
|-------------------------------|------------|---|
| Richard A. King               | 48         | Director, President and Chief Executive Officer |
| James H. Welch                | 55         | Chief Financial Officer                         |
| Pamela P. Palmer, M.D., Ph.D. | 50         | Director, Chief Medical Officer and Co-Founder  |
| Lawrence G. Hamel             | 61         | Chief Development Officer                       |
| Badri Dasu                    | 49         | Chief Engineering Officer                       |

**Richard A. King**, Mr. King's biography is included above under the section titled "Board of Directors" Class II Directors.

**James H. Welch** has served as our Chief Financial Officer since October 1, 2010. From June 2006 until September 2010, Mr. Welch served as Chief Financial Officer and Corporate Secretary for Cerimon Pharmaceuticals, a biopharmaceutical company. Mr. Welch served as Vice President, Chief Financial Officer and Corporate Secretary for Rigel Pharmaceuticals, Inc., a drug development company from October 2000 until May 2006, and as Vice President, Finance and Administration for Rigel Pharmaceuticals, Inc. from May 1999 until October 2000. From June 1998 until May 1999, Mr. Welch served as an independent consultant at various companies. Mr. Welch served as Chief Financial Officer of Biocircuits Corporation, a company focused on

## **Table of Contents**

developing immunodiagnostic testing systems from February 1997 until June 1998, and from June 1992 until February 1997, he served as Corporate Controller of Biocircuits Corporation. Mr. Welch holds a B.A. in Business Administration from Whitworth College and an M.B.A. from Washington State University.

**Pamela P. Palmer, M.D., Ph.D.** Dr. Palmer's biography is included above under the section titled Board of Directors Class II Directors.

**Lawrence G. Hamel** has served as our Chief Development Officer since September 2006. From 1986 until September 2006, Mr. Hamel served as Product Development Manager, Director Project Management, Executive Director Oral Product Development, and Vice President Oral Products Development at ALZA Corporation. From 1977 until 1985, Mr. Hamel held a number of other positions at ALZA Corporation, including Senior Chemist, Research Scientist, and Senior Research Fellow. Mr. Hamel holds a B.S. in Biology from the University of Michigan.

**Badri Dasu** has served as our Chief Engineering Office since September 2007. From December 2005 until September 2007, Mr. Dasu served as Vice President of Medical Device Engineering at Anesiva, Inc., a biopharmaceutical company. From March 2002 until December 2005, Mr. Dasu served as Vice President for Manufacturing and Device Development at AlgoRx Pharmaceuticals, Inc., an emerging pain management company, which merged with Corgentech Inc., a biotechnology company, in December 2005. From January 2000 until March 2002, Mr. Dasu served as Vice President of Manufacturing and Process Development at PowderJect Pharmaceuticals, a vaccine, drug and diagnostics delivery company that was acquired by Chiron Corporation in 2003 and later acquired by Novartis AG, a global healthcare and pharmaceutical company, in 2006. Previously, Mr. Dasu served in various capacities in process development at Metrika, Inc., a company focused on the manufacture and marketing of disposable diabetes monitoring products that was acquired by Bayer HealthCare, LLC in 2006, and at Cygnus, Inc., a drug delivery and specialty pharmaceuticals company. Mr. Dasu holds a B.E. in Chemical Engineering from the University of Mangalore, India and a M.S. in Chemical Engineering from the University of Tulsa.

## **Section 16(a) Beneficial Ownership Reporting Compliance**

Section 16(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, requires our directors and executive officers, and persons who own more than ten percent of a registered class of our equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of common stock and other equity securities of our company. Officers, directors and greater than ten percent stockholders are required by SEC regulation to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based solely on a review of the copies of such reports furnished to us and written representations that no other reports were required, during the fiscal year ended December 31, 2012, our officers, directors and greater than ten percent beneficial owners complied with all applicable Section 16(a) filing requirements.

## **Certain Corporate Governance Matters**

### ***Code of Business Conduct and Ethics***

The AcelRx Pharmaceuticals, Inc. Code of Business Conduct and Ethics applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is available on our website at [www.acelrx.com](http://www.acelrx.com). Stockholders may request a free copy of the Code of Business Conduct and Ethics by submitting a written request to: AcelRx Pharmaceuticals, Inc., Attention: Investor Relations, 351 Galveston Drive, Redwood City, CA 94063. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website.



## Table of Contents

### Director Nominations

The nominating and corporate governance committee of the board of directors, to date, has not adopted a formal policy with regard to the consideration of director candidates recommended by stockholders and will consider director candidates recommended by stockholders on a case-by-case basis, as appropriate. Stockholders wishing to recommend individuals for consideration by the nominating and corporate governance committee may do so by delivering a written recommendation to our Secretary at 351 Galveston Drive, Redwood City, CA 94063 and providing the candidate's name, biographical data and qualifications and a document indicating the candidate's willingness to serve if elected. The nominating and corporate governance committee does not intend to alter the manner in which it evaluates candidates based on whether the candidate was recommended by a stockholder. To date, the nominating and corporate governance committee has not received any such nominations nor has it rejected a director nominee from a stockholder or stockholders holding more than 5% of our voting stock.

### Audit Committee

Our audit committee consists of Messrs. Edwards and Rosen and Dr. Hoffman, each of whom is a non-employee member of our board of directors. Mr. Edwards serves as the chair of our audit committee. Our board of directors has determined that each of the directors serving on our audit committee meets the requirements for financial literacy under applicable rules and regulations of the SEC and NASDAQ. Our Board has also determined that Mr. Edwards qualifies as an audit committee financial expert within the meaning of SEC regulations. In making this determination, our Board considered the overall knowledge, experience and familiarity of Mr. Edwards with accounting matters, in analyzing and evaluating financial statements and in managing private equity investments. The composition of the audit committee satisfies the independence and other requirements of NASDAQ and the SEC. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ and is available on our website at [www.ancelrx.com](http://www.ancelrx.com).

## Item 11. Executive Compensation

### Summary Compensation Table

The following table sets forth certain summary information for the years indicated with respect to the compensation earned by our Chief Executive Officer, our Chief Financial Officer and each of our three other most highly compensated executive officers as of December 31, 2012. We refer to these individuals as our named executive officers elsewhere in this Form 10-K.

**Summary Compensation Table**

| Name and Principal Position                  | Year | Salary<br>(\$) | Bonus<br>(\$) | Stock<br>Awards<br>\$(1) | Option<br>Awards<br>\$(2) | Non-Equity<br>Incentive<br>Plan<br>Compensation<br>\$(3) | Total (\$) |
|--|------|----------------|---------------|--------------------------|---------------------------|--|------------|
| Richard A. King                              | 2012 | 426,006        |               |                          | 616,203                   | 170,400  | 1,212,609  |
| <i>President and Chief Executive Officer</i> | 2011 | 411,600        |               | 425,927                  | 279,955                   | 100,842  | 1,218,324  |
| James H. Welch                               | 2012 | 299,000        |               |                          | 170,561                   | 95,232   | 564,793    |
| <i>Chief Financial Officer</i>               | 2011 | 290,000        |               |                          | 60,750                    | 67,425   | 418,175    |
| Pamela P. Palmer, M.D., Ph.D.                | 2012 | 396,550        |               |                          | 544,991                   | 134,034  | 1,075,575  |
| <i>Chief Medical Officer</i>                 | 2011 | 385,000        |               | 233,199                  | 243,000                   | 89,513   | 950,712    |
| Lawrence G. Hamel                            | 2012 | 292,800        |               |                          | 120,600                   | 95,160   | 508,560    |
| <i>Chief Development Officer</i>             | 2011 | 283,000        |               | 58,302                   | 75,330                    | 70,892   | 487,524    |
| Badri Dasu                                   | 2012 | 278,000        |               |                          | 120,600                   | 93,964   | 492,564    |
| <i>Chief Engineering Officer</i>             | 2011 | 270,500        |               | 51,305                   | 127,575                   | 59,645   | 509,025    |

(1) The dollar amounts in this column represent the aggregate grant date fair value calculated in accordance with Financial Accounting Standards Board Accounting Standards Codification Topic 718, or ASC 718, for all restricted stock unit awards granted during the indicated year. The estimated fair value of restricted stock unit awards is calculated based on the market price of our common stock on the date of grant.



## **Table of Contents**

- (2) The dollar amounts in this column represent the aggregate grant date fair value of all option awards granted during the indicated year. These amounts have been calculated in accordance with ASC 718, using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 1 to our financial statements and the discussion under Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Estimates Stock-Based Compensation included elsewhere in this Form 10-K. These amounts do not necessarily correspond to the actual value that may be recognized from the option awards by the named executive officers.
- (3) The dollar amounts reflect the cash awards made to the named executive officers under the Company's 2012 Cash Bonus Plan and 2011 Cash Bonus Plan, respectively.

## **Employment Agreements and Arrangements**

### ***Executive Employment Agreements and Termination Benefits***

#### ***Offer Letter Agreements***

We have entered into offer letter agreements with each of our named executive officers, in connection with each named executive officer's commencement of employment with us. These offer letter agreements provide for the named executive officer's initial base salary, eligibility to participate in our standard benefit plans and in certain cases, the named executive officer's initial stock option grant along with vesting provisions with respect to that initial stock option grant. We amended and restated these offer letter agreements in December 2010 to clarify certain terms for compliance with tax laws, to specify the terms of the option to be granted to Mr. King upon achievement of certain milestones and to provide additional change of control severance benefits to Mr. Welch and Dr. Palmer.

Under Mr. King's, Mr. Welch's and Dr. Palmer's respective offer letter agreements, in the event that Mr. Welch's or Dr. Palmer's employment is terminated by us without cause, or in a manner that constitutes an involuntary termination, or Mr. King's employment is terminated by us without cause or he resigns for good reason, in each case within one year following a change in control, as these terms are defined in the offer letters, each will be entitled to base salary and health benefits continuation for a period of twelve months in the case of Mr. King, and six months in the case of each of Mr. Welch and Dr. Palmer. Mr. King is also entitled to base salary and health benefits continuation for a period of twelve months in connection with a termination by us without cause that is not in connection with a change of control. In order to receive severance benefits, each such executive must sign a waiver and release of claims, and in the case of Mr. King and Dr. Palmer, each such executive must resign from our board of directors if so requested by the board of directors. Please refer to Long-Term Equity Incentive Award Vesting Acceleration below for descriptions of the current stock option and restricted stock unit, or RSU, vesting acceleration for each of our executive officers.

Mr. King's and Mr. Welch's offer letters also provide for an opportunity to earn a target annual bonus of 35% and 30% of base salary, respectively, and Mr. King was entitled to an additional option grant covering 115,208 shares of our common stock upon achievement of one of the following corporate milestones prior to June 30, 2011: (i) completion by the company of a qualifying partnering transaction, (ii) completion of our IPO, or (iii) completion of a private financing raising at least \$15 million from new investors. Mr. Welch was entitled to an additional option grant covering 25,000 shares if we completed our IPO or a private financing raising at least \$15 million from new investors prior to June 30, 2011. In December 2010, our board of directors approved a bonus payment of \$94,500 to Mr. King in connection with his annual target bonus pursuant to his employment agreement. In March 2011, our board of directors approved a bonus payment of \$21,750 to Mr. Welch in connection with his annual target bonus pursuant to his employment agreement. In March 2011, our board of directors also granted Messrs. King and Welch options to purchase 115,208 and 25,000 shares of our common stock in connection with the completion of our IPO pursuant to each of their employment agreements.

Each of our executive officers are employed at-will, and each such executive officer's employment may be terminated at any time by us or the named executive officer.

**Table of Contents***Long-Term Equity Incentive Award Vesting Acceleration*

Each of our executive officers are entitled to full double-trigger stock option and RSU vesting acceleration benefits (for all currently outstanding stock options and RSUs and any stock options and RSUs that may be granted in the future) in the event their service with us is terminated by us without cause or, in the case of acceleration of stock options only for Messrs. Welch, Hamel and Dasu and Dr. Palmer, in a manner that constitutes an involuntary termination, or, in the case of acceleration of RSUs only for Messrs. Welch, Hamel and Dasu and Dr. Palmer and for acceleration of stock options and RSUs for Mr. King, such executive resigns for good reason, in each case within 18 months following a change in control, subject to signing an effective release of claims, and in the case of acceleration of stock options for Mr. King and Dr. Palmer, resignation from our board of directors if so requested by the board of directors.

*Cash Bonus Plan*

Our annual Cash Bonus Plan is designed to reward executive officers and other employees for attaining our corporate performance objectives, as well as to reward them for their individual contributions to the achievement of those objectives. Target bonus levels under the annual Bonus Plan are assigned based on various categories of employees. The actual bonus awarded in any year, if any, may be more or less than the target, depending primarily on the achievement of our corporate objectives, and an individual employee's achievement of his or her objectives. Whether or not a bonus is paid for any year is within the discretion of our Compensation Committee, and our Compensation Committee has the discretion to award bonuses even if the applicable performance criteria set forth under the annual Bonus Plan have not been met or to award a bonus based on other criteria.

**2012 Cash Bonus Plan**

Target bonuses for our named executive officers under the 2012 Cash Bonus Plan, or the 2012 Bonus Plan, ranged from 32.5% to 40% of such executive's 2012 base salary based on market data established for each executive position. The amount of cash bonus, if any, for each named executive officer was based on both the named executive officer achieving his or her individual performance goals and on our attainment of the 2012 corporate objectives approved by our board of directors. Our 2012 corporate objectives were primarily related to product development, clinical trial milestones and financial objectives. The target bonuses for our named executive officers for 2012 were as follows:

| <b>Named Executive Officer</b> | <b>Target Bonus<br/>(as a percentage of<br/>FY 2011 Base<br/>Salary)</b> |
|--------------------------------|--|
| Richard A. King                | 40%  |
| James H. Welch                 | 32.5%  |
| Pamela P. Palmer, M.D., Ph.D.  | 32.5%  |
| Lawrence G. Hamel              | 32.5%  |
| Badri Dasu                     | 32.5%  |

Mr. King's cash bonus under the 2012 Bonus Plan was based 100% on the achievement of the 2012 corporate objectives. The cash bonus for all other named executive officers was based 40% on the achievement of his or her individual performance goals, as determined by our board of directors, and 60% on the achievement of the 2012 corporate objectives. The named executive officers' actual bonuses could have exceeded 100% of target in the event performance exceeded the predetermined goals.

In February 2013, the Compensation Committee determined, and the Board of Directors confirmed, that the Company had achieved a 100% attainment level of the 2012 corporate objectives. At that same time, the Board of Directors also confirmed the attainment levels of each named executive officers' individual performance goals for 2012. Pursuant to the 2012 Bonus Plan, the Board of Directors awarded cash bonuses to our executives based on the confirmed attainment level of the 2012 corporate objectives and the confirmed attainment level of their respective individual performance goals for 2012. All bonus amounts were paid on February 15, 2013.

**Table of Contents**

The table below sets forth the target and actual non-equity incentive plan awards for our named executive officers for fiscal 2012 performance:

| <b>Name</b>                   | <b>Target Award</b> | <b>Actual Award</b> |
|-------------------------------|---------------------|---------------------|
| Richard A. King               | \$ 170,400          | \$ 170,400          |
| James H. Welch                | \$ 97,175           | \$ 95,232           |
| Pamela P. Palmer, M.D., Ph.D. | \$ 128,879          | \$ 134,034          |
| Lawrence G. Hamel             | \$ 95,160           | \$ 95,160           |
| Badri Dasu                    | \$ 90,350           | \$ 93,964           |

**2011 Cash Bonus Plan**

Target bonuses for our named executive officers under the 2011 Cash Bonus Plan, or the 2011 Bonus Plan, ranged from 30% to 35% of such executive's 2011 base salary based on market data established for each executive position. The amount of cash bonus, if any, for each named executive officer was based on both the named executive officer achieving his or her individual performance goals and on our attainment of the 2011 corporate objectives approved by our board of directors. Our 2011 corporate objectives were primarily related to product development, clinical trial milestones and financial objectives. The target bonuses for our named executive officers for 2011 were as follows:

| <b>Named Executive Officer</b> | <b>Target Bonus<br/>(as a percentage of<br/>FY 2011 Base<br/>Salary)</b> |
|--------------------------------|--|
| Richard A. King                | 35%  |
| James H. Welch                 | 30%  |
| Pamela P. Palmer, M.D., Ph.D.  | 30%  |
| Lawrence G. Hamel              | 30%  |
| Badri Dasu                     | 30%  |

Mr. King's cash bonus under the 2011 Bonus Plan was based 25% on the achievement of his individual performance goals, as determined by our board of directors, and 75% on the achievement of the 2011 corporate objectives. The cash bonus for all other named executive officers was based 40% on the achievement of his or her individual performance goals, as determined by our board of directors, and 60% on the achievement of the 2011 corporate objectives. The named executive officers' actual bonuses could have exceeded 100% of target in the event performance exceeded the predetermined goals.

In February 2012, the Compensation Committee determined, and the Board of Directors confirmed, that the Company had achieved a 62.5% attainment level of the 2011 corporate objectives. At that same time, the Board of Directors also confirmed the attainment levels of each executive's individual performance goals for 2011. Pursuant to our 2011 Cash Bonus Plan, the Board of Directors awarded cash bonuses to our executives based on the confirmed attainment level of the 2011 corporate objectives and the confirmed attainment level of their respective individual performance goals for 2011. All bonus amounts were paid on February 15, 2012.

The table below sets forth the target and actual non-equity incentive plan awards for our named executive officers for fiscal 2011 performance:

| <b>Name</b>                   | <b>Target Award</b> | <b>Actual Award</b> |
|-------------------------------|---------------------|---------------------|
| Richard A. King               | \$ 144,060          | \$ 100,842          |
| James H. Welch                | \$ 87,000           | \$ 67,425           |
| Pamela P. Palmer, M.D., Ph.D. | \$ 115,500          | \$ 89,513           |
| Lawrence G. Hamel             | \$ 84,900           | \$ 70,892           |
| Badri Dasu                    | \$ 81,150           | \$ 59,645           |

**Table of Contents****Outstanding Equity Awards at December 31, 2012**

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2012.

**Outstanding Equity Awards at December 31, 2012**

| Name                          | Number of Securities Underlying Unexercised Options (#) Exercisable | Option Awards   |                            |                        | Stock Awards   |   |
|-------------------------------|---|---|----------------------------|------------------------|--|---|
|                               |   | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price (\$) | Option Expiration Date | Number of Shares or Units of Stock That Have Not Vested (#) <sup>(1)</sup> | Market Value of Shares or Units of Stock That Have Not Vested (\$) <sup>(2)</sup> |
| Richard A. King               |   | 262,214 <sup>(3)</sup>  | 3.39                       | 02/13/2022             |  |   |
|                               | 50,403  | 64,805 <sup>(4)</sup>   | 3.45                       | 03/02/2021             |  |   |
|                               | 28,538 <sup>(5)</sup>   |   | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               | 285,381   | 142,690 <sup>(7)</sup>  | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               |   |   |                            |                        | 61,729   | 262,966   |
| James H. Welch                |   | 72,579 <sup>(3)</sup>   | 3.39                       | 02/07/2022             |  |   |
|                               | 10,937  | 14,063 <sup>(4)</sup>   | 3.45                       | 03/02/2021             |  |   |
|                               | 70,312  | 54,688 <sup>(8)</sup>   | 5.32                       | 11/04/2020             |  |   |
| Pamela P. Palmer, M.D., Ph.D. |   | 231,911 <sup>(3)</sup>  | 3.39                       | 02/07/2022             |  |   |
|                               | 43,749  | 56,251 <sup>(4)</sup>   | 3.45                       | 03/02/2021             |  |   |
|                               | 250,000   |   | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               | 37,500  |   | 5.52                       | 03/25/2019             |  |   |
|                               | 37,500  |   | 4.00                       | 08/14/2018             |  |   |
|                               | 25,000  |   | 1.32                       | 04/03/2017             |  |   |
|                               |   |   |                            |                        | 33,797   | 143,975   |
| Lawrence G. Hamel             |   | 51,319 <sup>(3)</sup>   | 3.39                       | 02/07/2022             |  |   |
|                               | 13,562  | 17,438 <sup>(4)</sup>   | 3.45                       | 03/02/2021             |  |   |
|                               | 62,500  |   | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               | 12,500  |   | 5.52                       | 03/25/2019             |  |   |
|                               | 18,750  |   | 1.20                       | 12/05/2017             |  |   |
|                               | 25,000  |   | 1.20                       | 04/03/2017             |  |   |
|                               | 12,500  |   | 1.20                       | 04/03/2017             |  |   |
|                               |   |   |                            |                        | 8,450  | 35,997  |
| Badri Dasu                    |   | 51,319 <sup>(3)</sup>   | 3.39                       | 02/07/2022             |  |   |
|                               | 22,968  | 29,532 <sup>(4)</sup>   | 3.45                       | 03/02/2021             |  |   |
|                               | 30,000  |   | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               | 18,750  | 6,250   | 2.56 <sup>(6)</sup>        | 06/15/2020             |  |   |
|                               | 6,250   |   | 5.52                       | 03/25/2019             |  |   |
|                               | 37,500  |   | 1.20                       | 10/25/2017             |  |   |
|                               |   |   |                            |                        | 7,436  | 31,677  |

(1) The shares subject to these restricted stock units vested as to 1/4 of the shares on September 2, 2011, with the remaining shares vesting as to 1/4 of the shares subject to the award on each of the 1-, 2-, and 3-year anniversary of the March 2, 2011 stock award grant date.

(2) The dollar amounts in this column represent the aggregate grant date fair value of all restricted stock unit awards granted that have not vested. The estimated fair value of restricted stock unit awards is calculated based on the market price of our common stock as of December 31, 2012, which is \$4.26.

(3) The shares subject to this stock option vested as to 1/4 of the shares on February 13, 2013, with the remaining shares vesting on an equal monthly basis over the following 36 months.



## **Table of Contents**

- (4) The shares subject to this stock option vested as to 1/4 of the shares on March 2, 2012, with the remaining shares vesting on an equal monthly basis over the following 36 months.
- (5) The shares subject to this stock option were fully vested as of the June 15, 2010 grant date.
- (6) The dollar amounts reflect the increase in the exercise price of the options, effective December 27, 2010, we granted to our named executive officers on June 15, 2010 from an original estimated fair value of \$1.20 to a revised estimate of fair value of \$2.56 in consideration of IRC Section 409a.
- (7) The shares subject to this stock option vested as to 28,538 shares on June 15, 2010, and another 85,614 shares vested on March 3, 2011, with the remaining shares vesting on an equal monthly basis over the following 36 months.
- (8) The shares subject to this stock option will vest as to 1/4 of the shares on September 30, 2011, with the remaining shares vesting on an equal monthly basis over the following 36 months.

### ***Employee Benefits and Stock Plans***

#### ***2011 Equity Incentive Plan***

Our board of directors adopted, and our stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan, in January 2011 as a successor to the 2006 Equity Incentive Plan, or 2006 Plan. The 2011 Incentive Plan became effective immediately upon the execution and delivery of the underwriting agreement for our IPO and, on that date, the 51,693 shares that were available for future grant under the 2006 Plan as of such date became available for future grant under the 2011 Incentive Plan, and no additional shares remain available for grant under the 2006 Plan. The 2011 Incentive Plan will terminate on January 4, 2021, unless sooner terminated by our board of directors.

*Administration.* The board of directors has delegated its authority to administer the 2011 Incentive Plan to the compensation committee. Subject to the terms of the 2011 Incentive Plan, the board of directors or an authorized committee determines recipients, dates of grant, the numbers and types of stock awards to be granted, and the terms and conditions of the stock awards, including the period of their exercisability and vesting. Our board of directors may amend or suspend the 2011 Incentive Plan at any time, although no such action may impair the rights under any then-outstanding award without the holder's consent.

*Stock awards.* The 2011 Incentive Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation, or collectively, stock awards, all of which may be granted to employees, including officers, and to non-employee directors and consultants.

*Share reserve.* The initial aggregate number of shares of our common stock that may be issued pursuant to stock awards under the 2011 Incentive Plan was 1,875,000 shares. The number of shares of our common stock reserved for issuance under the 2011 Incentive Plan will automatically increase on January 1st each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by our board of directors. The maximum number of shares that may be issued pursuant to the exercise of incentive stock options under the 2011 Incentive Plan is 10,000,000 shares.

*Changes to capital structure.* In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, the plan administrator shall appropriately and proportionately adjust: (a) the class(es) and maximum number of shares reserved for issuance under the 2011 Incentive Plan and the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (b) the class(es) and maximum number of shares that may be issued upon the exercise of incentive stock options, (c) the class(es) and maximum number of shares subject to stock awards that can be granted in a calendar year (as established under the 2011 Incentive Plan pursuant to Section 162(m) of the Code) and (d) the class(es) and number of shares and price per share of stock subject to outstanding stock awards.



## **Table of Contents**

*Corporate transactions.* In the event of certain specified significant corporate transactions, unless otherwise provided in the instrument evidencing the stock award or any other written agreement between us or any affiliate and the holder of the stock award, the plan administrator has the discretion to take any of the following actions with respect to stock awards:

arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;

arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;

accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;

arrange for the lapse of any reacquisition or repurchase right held by us;

cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our board of directors may deem appropriate; or

make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

Our board of directors is not obligated to treat all stock awards, even those that are of the same type, in the same manner.

*Change in control.* The plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us, that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a certain specified change in control. However, in the absence of such a provision, no such acceleration of the stock award will occur.

### *2011 Employee Stock Purchase Plan*

Our board of directors adopted, and our stockholders approved, the 2011 Employee Stock Purchase Plan, or ESPP, in January 2011. The ESPP became effective immediately upon the execution and delivery of the underwriting agreement for our IPO. The ESPP is intended to qualify as an employee stock purchase plan within the meaning of section 423 of the Code. Under the ESPP, all regular employees of the company (including the named executive officers) may participate and may contribute, normally through payroll deductions, up to 15% of their earnings for the purchase of our ordinary shares under the ESPP. The ESPP is implemented through a series of offerings of purchase rights to eligible employees. Under the ESPP, we may specify offerings with a duration of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which our common stock will be purchased for employees participating in the offering. Unless otherwise determined by the plan administrator, common stock will be purchased for participating employees at a price per share equal to the lower of (a) 85% of the fair market value of a share of our common stock on the first date of an offering, or (b) 85% of the fair market value of a share of our common stock on the date of purchase. Initially, 250,000 shares of our common stock were authorized to be issued under the ESPP pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by our board of directors.

### *2006 Stock Plan*

Our board of directors adopted, and our stockholders approved, the 2006 Stock Plan, or 2006 Plan, in August 2006. The 2006 Plan was subsequently amended by our board of directors and approved by our stockholders in



## **Table of Contents**

each of February 2008 and November 2009. The 2006 Plan provides for the grant of incentive stock options, nonstatutory stock options and rights to acquire restricted stock. Effective upon the execution and delivery of the underwriting agreement for our IPO, no additional stock options or other stock awards may be granted under the 2006 Plan. All outstanding stock options and other stock awards previously granted under the 2006 Plan remain subject to the terms of the 2006 Plan.

*Administration* . Our board of directors administers our 2006 Plan. Subject to the terms of the 2006 Plan, the board of directors or an authorized committee determines recipients, dates of grant, the numbers and types of stock awards to be granted, and the terms and conditions of the stock awards, including the period of their exercisability and vesting.

*Stock awards*. The 2006 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation, or collectively, stock awards, all of which may be granted to employees, including officers, and to non-employee directors and consultants.

*Changes to capital structure*. In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, appropriate adjustments will be made to the number of shares and price per share of all outstanding options and stock awards under the 2006 Plan.

*Change in control*. In the event of certain change in control transactions involving us, such as our liquidation or dissolution or an event that results in a material change in the ownership of our company, the plan administrator has the discretion to take any of the following actions with respect to stock awards under the 2006 Plan:

accelerate the vesting of a stock award;

arrange for the assumption, continuation or substitution of a stock award by the surviving or acquiring entity or its parent company;  
or

cancel or arrange for the cancellation of the stock award in exchange for a payment in (1) cash, (2) stock, or (3) other property, and in any such case in an amount equal to the fair market value of the consideration to be paid per share of stock in the change of control over the exercise price per share.

Stock awards that are neither assumed or continued by the surviving or acquiring entity or its parent company nor exercised as of the effective time of the change in control will terminate and cease to be outstanding as of the effective time of the change in control.

### *401(k) Plan*

We maintain a tax-qualified 401(k) retirement plan for all employees who satisfy certain eligibility requirements, including requirements relating to age and length of service. Under our 401(k) plan, employees may elect to defer a portion of their eligible compensation subject to applicable annual Code limits. We provide a discretionary safe harbor profit sharing contribution equal to 3% of a participant's compensation to our eligible participants, which is 100% vested when made. We intend for the 401(k) plan to qualify under Section 401(a) and 501(a) of the Code so that contributions by employees to the 401(k) plan, and income earned on those contributions, are not taxable to employees until withdrawn from the 401(k) plan.

### *Pension Benefits*

We do not maintain any pension or retirement plans.

### *Nonqualified Deferred Compensation*

We do not maintain any nonqualified deferred compensation plans.



## **Table of Contents**

### **Director Compensation**

#### ***Non-Employee Director Compensation***

##### *Cash Compensation Arrangements*

In January 2011, our board of directors adopted a non-employee director compensation policy, which became effective for all of our non-employee directors upon the execution and delivery of the underwriting agreement for our IPO and remained effective through December 31, 2012. Pursuant to the non-employee director compensation policy, each member of our board of directors who is not our employee received an annual retainer of \$30,000 plus \$2,000 as a meeting fee for each board meeting attended by the non-employee director in person. In addition, our non-employee directors received the following cash compensation for board services, as applicable:

the board chair received an additional annual retainer of \$25,000;

the audit committee chair received an additional annual retainer of \$10,000;

the compensation committee chair received an additional annual retainer of \$5,000;

the nominating and corporate governance committee chair received an additional annual retainer of \$5,000; and

each committee member received \$1,000 as a meeting fee for each committee meeting attended by the non-employee director in person.

In February 2013, our board of directors revised the non-employee director compensation policy, which became effective January 1, 2013. Pursuant to the revised non-employee director compensation policy, each member of our board of directors, who is not our employee, receives an annual retainer of \$40,000. In addition, our non-employee directors receive the following cash compensation for board services, as applicable:

the board chair receives an additional annual retainer of \$20,000;

the audit committee chair receives an additional annual retainer of \$15,000;

the compensation committee chair receives an additional annual retainer of \$7,500;

the nominating and corporate governance committee chair receives an additional annual retainer of \$6,000;

an audit committee member receives an additional annual retainer of \$7,500;

a compensation committee member receives an additional annual retainer of \$3,750; and

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

a nominating and corporate governance committee member receives an additional retainer of \$3,000

All board and committee retainers accrue and are payable on a quarterly basis at the end of each calendar quarter of service. We continue to reimburse our non-employee directors for travel, lodging and other reasonable expenses incurred in connection with their attendance at board of director or committee meetings.

### *Equity Compensation Arrangements*

Our non-employee director compensation policy provides for automatic grants of stock options to our non-employee directors under our 2011 Incentive Plan. Upon election or appointment to our board, each non-employee director will receive an initial grant of a stock option to purchase 15,000 shares of our common stock, which will vest as to 1/36<sup>th</sup> of the shares subject to the option on an equal monthly basis over a three-year period. Additionally, on the date of each annual meeting of stockholders, each non-employee director who is then serving as a director or who is elected to our board of directors on the date of such annual meeting was eligible to receive a grant of a stock option to purchase 12,500 shares of our common stock, prior to our amended director

**Table of Contents**

compensation policy, effective January 1, 2013, which vest as to 1/24<sup>th</sup> of the shares subject to the option on an equal monthly basis over a two-year period. Beginning with our 2013 annual meeting, each non-employee director who is then serving as a director or who is elected to our board of directors on the date of such annual meeting was eligible to receive a grant of a stock option to purchase 15,000 shares of our common stock, which will vest as to 1/24<sup>th</sup> of the shares subject to the option on an equal monthly basis over a two-year period. All these options will be granted with an exercise price equal to the fair market value of our common stock on the date of the grant, and shall be entitled to full vesting acceleration as of immediately prior to the effective date of certain change in control transactions involving us, such as our liquidation or a dissolution of or an event that results in a material change in the ownership of our company. For a description of the terms of the 2011 Incentive Plan, see Employment Agreements and Arrangements Employee Benefits and Stock Plans 2011 Equity Incentive Plan.

*Director Compensation Table*

The following table sets forth certain summary information for the year ended December 31, 2012 with respect to the compensation of our non-employee directors. Neither Mr. King nor Dr. Palmer, each of whom are executive officers, received or receives any additional compensation for serving on our board of directors or its committees.

**2012 Director Compensation Table**

| <b>Name</b>                    | <b>Fees Earned or<br/>Paid in Cash<br/>(\$)</b> | <b>Option<br/>Awards<br/>\$(1)(2)</b> | <b>Total<br/>(\$)</b> |
|--------------------------------|---|---------------------------------------|-----------------------|
| Thomas A. Schreck              | 63,058  | 25,125                                | 88,183                |
| Howard B. Rosen                | 41,187  | 25,125                                | 66,312                |
| Stephen J. Hoffman Ph.D., M.D. | 43,926  | 25,125                                | 69,051                |
| Guy P. Nohra                   | 43,000  | 25,125                                | 68,125                |
| Mark Wan                       | 44,286  | 25,125                                | 69,411                |
| Mark G. Edwards                | 51,000  | 25,125                                | 76,125                |

- (1) The dollar amount in this column represents the grant date fair value of the stock option award granted to each of the directors on July 24, 2012, the date of our Annual Meeting of Shareholders. This amount has been calculated in accordance with ASC 718 using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 1 to our financial statements and the discussion under Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Estimates Share-Based Compensation included elsewhere in this Form 10-K. These amounts do not necessarily correspond to the actual value that may be recognized from the option award.
- (2) As of December 31, 2012, the following directors held options to purchase the following number of shares of the Company's common stock: Mr. Schreck, 337,500; Mr. Rosen, 51,250; Dr. Hoffman, 12,500; Mr. Nohra, 12,500; Mr. Wan, 12,500 Mr. Edwards, 27,500.

**Table of Contents****Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters****Equity Compensation Plan Information**

The following table provides certain information with respect to our equity compensation plans in effect as of December 31, 2012.

| Plan Category  | Number of securities to be<br>issued upon<br>exercise<br>of outstanding<br>options,<br>warrants and rights<br>(a)(2) | Weighted-average exercise<br>price of outstanding options,<br>warrants and<br>rights<br>(b)(3) | Number of securities<br>remaining available for future issuance<br>under equity<br>compensation plans<br>(excluding securities<br>reflected in column<br>(a))(c)(4)(5) |
|--|--|--|--|
| Equity compensation plans<br>approved by security holders <sup>(1)</sup> | 3,560,905  | \$ 3.18  | 1,251,034  |
| Equity compensation plans not<br>approved by security holders            |  | \$   |  |
| <b>Total</b>   | <b>3,560,905</b>   |  | <b>1,251,034</b>   |

(1) Consists of the 2006 Plan, the 2011 Plan and the ESPP.

(2) Includes 161,096 shares subject to outstanding restricted stock units that will entitle the holder to one share of common stock for each unit that vests over the holder's period of continued service with us.

(3) The calculation does not take into account the 161,096 shares of common stock subject to outstanding restricted stock units. Such shares will be issued at the time the restricted stock units vest, without any cash consideration payable for those shares.

(4) Consists of shares available for future issuance under the 2011 Incentive Plan, including shares that were previously available for future issuance under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for our IPO, and the ESPP. As of December 31, 2012, 725,719 shares of common stock were available for issuance under the 2011 Incentive Plan and 525,315 shares of common stock were available for issuance under the ESPP.

(5) The initial aggregate number of shares of our common stock that may be issued pursuant to stock awards under the 2011 Incentive Plan was 1,875,000 shares, which number was the sum of (i) 51,693 shares remaining available for future grant under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for our IPO, and (ii) an additional 1,823,307 new shares. The number of shares of our common stock reserved for issuance under the 2011 Incentive Plan will automatically increase on January 1st each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by our board of directors. The initial aggregate number of shares of common stock that may be issued pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates under the ESPP was 250,000 shares. The number of shares of our common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (i) 2% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, and (ii) a number of shares of common stock as determined by our board of directors.



**Table of Contents****Security Ownership of Certain Beneficial Owners and Management**

The following table sets forth certain information regarding the ownership of our common stock as of January 31, 2013 by: (i) each director; (ii) each named executive officer; (iii) all of our executive officers and directors as a group; and (iv) all those known by us to be beneficial owners of more than five percent of our common stock.

| Name of Beneficial Owner   | Beneficial Ownership <sup>(1)</sup> |            |
|--|-------------------------------------|------------|
|  | Number of Shares                    | % of Total |
| <b>5% Stockholders:</b>  |                                     |            |
| Funds affiliated with Three Arch Entities <sup>(2)</sup>                     | 10,623,269                          | 28.5%      |
| Fund affiliated with Skyline Venture Partners <sup>(3)</sup>                 | 4,428,161                           | 11.9%      |
| Fund affiliated with Alta Partners <sup>(4)</sup>                            | 2,794,907                           | 7.5%       |
| Fund affiliated with Perceptive Advisors LLC <sup>(5)</sup>                  | 5,008,400                           | 13.5%      |
| <b>Named Executive Officers and Directors:</b>                               |                                     |            |
| Richard A. King <sup>(6)</sup>   | 575,277                             | 1.5%       |
| James H. Welch <sup>(7)</sup>  | 130,281                             | 0.4%       |
| Pamela P. Palmer, M.D., Ph.D. <sup>(8)</sup>                                 | 780,653                             | 2.1%       |
| Badri Dasu <sup>(9)</sup>  | 147,970                             | 0.4%       |
| Lawrence G. Hamel <sup>(10)</sup>  | 180,243                             | 0.5%       |
| Thomas A. Schreck <sup>(11)</sup>  | 712,578                             | 1.9%       |
| Mark Wan <sup>(12)</sup>   | 10,627,435                          | 28.5%      |
| Stephen J. Hoffman, Ph.D., M.D. <sup>(13)</sup>                              | 4,432,327                           | 11.9%      |
| Guy P. Nohra <sup>(14)</sup>   | 2,799,073                           | 7.6%       |
| Howard B. Rosen <sup>(15)</sup>  | 46,212                              | 0.1%       |
| Mark G. Edwards <sup>(16)</sup>  | 61,666                              | 0.2%       |
| All executive officers and directors as a group (11 persons) <sup>(17)</sup> | 20,493,714                          | 52.1%      |

(1) This table is based upon information supplied by officers, directors and principal stockholders. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned. Applicable percentages are based on 37,059,802 shares outstanding on January 31, 2013, adjusted as required by rules promulgated by the SEC. The number of shares beneficially owned includes shares of common stock issuable pursuant to the exercise of stock options and warrants that are exercisable within 60 days of January 31, 2013, and RSUs which have or are scheduled to vest within 60 days of January 31, 2013. Shares issuable pursuant to the exercise of stock options and warrants that are exercisable within 60 days of January 31, 2013 and RSUs which have or are scheduled to vest within 60 days of January 31, 2013 are deemed to be outstanding and beneficially owned by the person to whom such shares are issuable for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

(2) Includes 199,174 shares held by Three Arch Associates III, L.P., 139,621 shares held by Three Arch Associates IV, L.P., 3,704,712 shares held by Three Arch Partners III, L.P. and 6,323,534 shares held by Three Arch Partners IV, L.P. The number also includes 256,228 shares of common stock issuable pursuant to the exercise of stock warrants that are exercisable within 60 days of January 31, 2013. The voting and dispositive decisions with respect to the shares held by Three Arch Associates III, L.P. and Three Arch Partners III, L.P., are made by the following Managing Members of their general partner, Three Arch Management III, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The voting and dispositive decisions with respect to the shares held by Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P. are made by the following Managing Members of their general partner, Three Arch Management IV, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The address for the funds affiliated with Three Arch Partners is 3200 Alpine Road, Portola Valley, CA 94028.

(3) Includes 4,171,933 shares held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. and 256,228 shares of common stock issuable pursuant to the exercise of stock warrants that are exercisable within 60 days of January 31, 2013. John G. Freund and Yasunori Kaneko are the Managing Members of Skyline Venture Management IV, LLC, which is the general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P., and as such Drs. Freund and Kaneko may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. In addition, Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Each of Drs. Freund, Kaneko and Hoffman disclaims beneficial ownership of such shares. The address for the funds affiliated with Skyline Venture Partners is 525 University Avenue, Ste. 610, Palo Alto, CA 94301.

(4) The 2,794,907 shares are held by ACP IV, L.P., or ACPIV. ACMP IV, LLC, or ACMPIV, is the general partner of ACPIV. Dan Janney, David Mack and Guy Nohra are directors of ACMPIV and they exercise shared voting and investment power with respect to the securities held by ACPIV. Each of Messrs. Janney, Mack and Nohra disclaims beneficial ownership of such securities, except to the extent of their pecuniary interest therein. The address for funds affiliated with Alta Partners is One Embarcadero Center, Suite 3700, San Francisco, CA 94111.



## **Table of Contents**

- (5) The indicated ownership is based on a Schedule 13G filed with the SEC by the reporting persons on December 13, 2012, reporting beneficial ownership as of December 7, 2012. According to the Schedule 13G, the reporting persons beneficially own a total of 5,008,400 shares of Common Stock held by a private investment fund to which Perceptive Advisors LLC serves as the investment manager. Mr. Edelman is the managing member of Perceptive Advisors LLC. The Schedule 13G filed by the reporting persons provides information only as of December 7, 2012, and, consequently, the beneficial ownership of the above-mentioned reporting persons may have changed between December 7, 2012 and January 31, 2013.
- (6) Includes 469,293 shares issuable pursuant to stock options exercisable, and 92,592 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.
- (7) Includes 110,281 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2013.
- (8) Includes 462,809 shares issuable pursuant to stock options exercisable, and 50,696 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.
- (9) Includes 134,210 shares issuable pursuant to stock options exercisable, and 8,288 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.
- (10) Includes 160,648 shares issuable pursuant to stock options exercisable, and 9,595 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.
- (11) Includes 337,500 shares issuable pursuant to stock options exercisable, and 59,145 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013, and 16,482 shares held in trust for Mr. Schreck's children. Mr. Schreck disclaims beneficial ownership of the shares held in trust for Mr. Schreck's children.
- (12) Includes 4,166 shares issuable pursuant to stock options exercisable, within 60 days of January 31, 2013. Mr. Wan, one of our directors, is a managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares. The address of Mr. Wan is c/o Three Arch Partners, 3200 Alpine Road, Portola Valley, CA 94028.
- (13) Includes 4,166 shares issuable pursuant to stock options exercisable, within 60 days of January 31, 2013. Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of such shares. The address for Dr. Hoffman is c/o Skyline Ventures, 525 University Avenue, Suite 610, Palo Alto, CA 94301.
- (14) Includes 4,166 shares issuable pursuant to stock options exercisable, within 60 days of January 31, 2013. Mr. Nohra, one of our directors, is a director of ACMPIV, and in such capacity he may be deemed to beneficially own the shares owned by ACMPIV. Mr. Nohra disclaims beneficial ownership of these shares. The address for Mr. Nohra is c/o Alta Partners, One Embarcadero Center, Suite 3700, San Francisco, CA 94111.
- (15) Represents 42,916 shares issuable pursuant to stock options exercisable, and 3,296 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.
- (16) Includes 11,666 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2013.
- (17) Includes 1,741,821 shares issuable pursuant to stock options exercisable, 512,456 shares issuable pursuant to warrants exercisable and 223,610 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2013.

## **Item 13. Certain Relationships and Related Transactions and Director Independence**

### **Policy and Procedures for Review of Related Party Transactions**

In January 2011, our board of directors adopted an audit committee charter, which charter became effective in connection with our IPO. The audit committee charter provides that the audit committee will review and approve all related party transactions. This review will cover any material transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, and a related party had or will have a direct or indirect material interest, including, purchases of goods or services by or from the related party or entities in which the related party has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related party.

In addition, in January 2011, our board of directors adopted a related party transactions policy, which became effective in connection with our IPO. The policy sets forth the procedures for the identification, review, consideration and approval or ratification of transactions involving the Company and its related persons. The policy is designed to prevent transactions between the Company and any of its related persons that may interfere with the performance of the Company's employees' and directors' duties to the Company or deprive the Company of a business opportunity. Any such transactions with related persons may present actual or potential conflicts of interests. However, the Company recognizes that whether or not a conflict exists is often unclear and, in many circumstances, transactions with related persons may, on balance, be beneficial to the Company and its stockholders.

## **Table of Contents**

None of the transactions below were required to be approved under the terms of the audit committee charter, because the audit committee charter was not effective until our IPO.

### **Certain Transactions With or Involving Related Persons**

The following is a summary of transactions since January 1, 2011 to which we have been a party in which the amount involved exceeded the lesser of \$120,000 or one percent of the average of our total assets at fiscal years ended 2010 and 2011 and in which any of our executive officers, directors or holders of more than 5% of our capital stock, or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than compensation arrangements which are described under Item 11. Executive Compensation appearing elsewhere in this Form 10-K.

#### *Bridge Note and Warrant Transfer*

In February 2011, ACP IV, L.P., a participant in our 2010 bridge loan and warrant financing, agreed to transfer a 37% interest in its note and the associated portion of its warrant for nominal consideration to funds affiliated with Three Arch Partners, Skyline Venture Partners and Kaiser Foundation Hospitals pro rata among them based on each entity's affiliated funds' then-current beneficial ownership of our outstanding capital stock, with such transfer effective immediately prior to the closing of our IPO. As a result of the foregoing transfer, effective immediately prior to the closing of our IPO:

funds affiliated with Three Arch Partners acquired warrants which were subsequently exercised, on a net issuance basis, for an aggregate of 5,236 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and notes in an aggregate principal amount of \$390,704;

funds affiliated with Skyline Venture Partners acquired a warrant which was subsequently exercised, on a net issuance basis, for 2,730 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and a note in a principal amount of \$203,676;

funds affiliated with Kaiser Foundation Hospitals acquired warrants which were subsequently exercised, on a net issuance basis, for an aggregate of 672 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and notes in an aggregate principal amount of \$50,176; and

funds affiliated with ACP IV, L.P. continued to hold a warrant which was subsequently exercised, on a net issuance basis, for 14,713 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and a note in a principal amount of \$1,097,487.

**Table of Contents****Participation in Our Initial Public Offering**

Entities affiliated with Three Arch Partners, Skyline Venture Partners and Alta Partners, each a holder of more than 5% of our capital stock, purchased an aggregate of 4,495,552 shares of our common stock in our IPO, as follows:

| Name   | Common Stock<br>Purchased in<br>Initial Public<br>Offering | Aggregate Purchase<br>Price |
|--|--|-----------------------------|
| Funds affiliated with Three Arch Partners <sup>(1)</sup>     | 2,579,579  | \$ 12,897,895               |
| Fund affiliated with Skyline Venture Partners <sup>(2)</sup> | 1,235,943  | 6,179,715                   |
| Fund affiliated with Alta Partners <sup>(3)</sup>            | 680,000  | 3,400,000                   |
| Price per share  | \$ 5.00  |                             |
| Date of purchase   | 2/11/11  |                             |

- (1) Includes 65,806 shares of common stock purchased by Three Arch Associates III, L.P., 27,863 shares of common stock purchased by Three Arch Associates IV, L.P., 1,223,983 shares of common stock purchased by Three Arch Partners III, L.P. and 1,261,927 shares of common stock purchased by Three Arch Partners IV, L.P. Mark Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares.
- (2) These shares were purchased by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Stephen Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of stock purchased by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of these shares.
- (3) These shares were purchased by ACP IV, L.P. Guy Nohra is one of our directors and is a director of ACP IV, LLC, the general partner of ACP IV, L.P., and shares voting and investment power with respect to such shares. Mr. Nohra disclaims beneficial ownership of these shares.

**2012 Private Placement**

On May 29, 2012, we entered into a securities purchase agreement, or the Purchase Agreement, with certain accredited investors, including entities affiliated with certain members of our board of directors, providing for a private placement, or the Private Placement, of up to \$10.0 million of our securities. At the closing of the Private Placement on June 1, 2012, and pursuant to the Purchase Agreement, we sold shares of common stock and warrants to purchase common stock in immediately separable units, with each unit consisting of (i) one share of common stock and (ii) a warrant to purchase 0.9 of a share of common stock. The per share exercise price of the warrants was \$3.40. The offering price per unit was \$3.40 for non-affiliated investors, and \$3.5125 for affiliated investors, which equals the sum of (i) \$3.40, the closing consolidated bid price of our common stock on May 29, 2012, plus (ii) \$0.1125 (which is equal to \$0.125 per warrant share, multiplied by 0.9), for an aggregate amount of \$10.0 million. The warrants issued in the Private Placement become exercisable six months after the issuance date, and expire on the five year anniversary of the initial exercisability date. Entities affiliated with Three Arch Partners and Skyline Venture Partners purchased an aggregate of 569,396 shares of our common stock and 512,456 warrants in the Private Placement, as follows:

| Name   | Common Stock<br>Purchased in<br>Private Placement | Warrants<br>Purchased in<br>Private<br>Placement | Aggregate<br>Purchase Price |
|--|---|--|-----------------------------|
| Funds affiliated with Three Arch Partners <sup>(1)</sup>     | 284,698   | 256,228  | \$ 1,000,001.73             |
| Fund affiliated with Skyline Venture Partners <sup>(2)</sup> | 284,698   | 256,228  | \$ 1,000,001.73             |

- (1) Includes 3,631 shares of common stock and 3,268 shares of common stock underlying warrants purchased by Three Arch Associates III, L.P., 4,613 shares of common stock and 4,151 shares of common stock underlying warrants purchased by Three Arch Associates IV, L.P., 67,543 shares of common stock and 60,789 shares of common stock underlying warrants purchased by Three Arch Partners III, L.P. and 208,911 shares of common stock and 188,020 shares of common stock underlying warrants purchased by Three Arch Partners IV, L.P. Mark A. Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares.



## Table of Contents

(2) These shares and warrants were purchased by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Stephen Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of stock purchased by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of these shares.

Pursuant to the Purchase Agreement, we agreed to register the resale of the shares of our common stock we issued and any common stock issuable upon the exercise of the warrants that we issued in the Private Placement, including the shares and warrants held by the entities affiliated with Three Arch Partners and Skyline Venture Partners. Pursuant to our obligation under the Purchase Agreement, we filed a registration statement with the SEC registering the resale of these shares on June 21, 2012 and it was declared effective by the SEC on July 2, 2012. We agreed to use our commercially reasonable best efforts to keep the registrations statement we filed registering the resale of these shares continuously effective until the earlier of (i) such time as all of the such shares have been sold under the registration statement or Rule 144 or (ii) such time as all of the shares may be sold pursuant to Rule 144 without compliance with Rule 144(c)(1).

### 2012 Public Offering

Entities affiliated with Three Arch Partners, which was a holder of more than 5% of our capital stock, purchased an aggregate of 2,416,918 shares of our common stock in our public offering in December 2012, as follows:

| Name   | Common Stock<br>Purchased in<br>Public<br>Offering | Aggregate Purchase<br>Price |
|--|--|-----------------------------|
| Funds affiliated with Three Arch Partners <sup>(1)</sup> | 2,416,918  | \$ 8,000,000                |
| Price per share  | \$ 3.31  |                             |

(1) Includes 2,364,705 shares of common stock purchased by Three Arch Partners IV, L.P. and 52,213 shares of common stock purchased by Three Arch Associates IV, L.P. Mark Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares.

### Investors Rights Agreements

We entered into an investors rights agreement with certain holders of our previously outstanding preferred stock and previously outstanding warrants to purchase our preferred stock, including our principal stockholders with which certain of our directors are affiliated. Pursuant to the investors rights agreement, these holders will have the right to demand that we file a registration statement or request that the common stock issued upon conversion of our previously outstanding preferred stock and the common stock issuable upon the exercise of outstanding warrants to purchase common stock (which, in connection with our IPO, were converted from previously outstanding warrants to purchase our preferred stock), collectively, the registrable securities, be covered by a registration statement that we are otherwise filing. In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, these holders are entitled to notice of our registration and are entitled to certain piggyback registration rights allowing the holders to include their registrable securities in such registration, subject to certain marketing and other limitations. Pursuant to the investors rights agreement, the holders of registrable securities have the right to require us to file a registration statement under the Securities Act in order to register the resale of their shares of registrable securities, provided that the registration meets certain thresholds. We may, in certain circumstances, defer such registrations. In an underwritten offering, the managing underwriter has the right, subject to specified conditions, to limit the number of registrable securities such holders may include.

### Indemnification Agreements

We have entered into indemnification agreements with each of our current directors and officers. These agreements provide for the indemnification of such persons for all reasonable expenses and liabilities incurred in

## **Table of Contents**

connection with any action or proceeding brought against them by reason of the fact that they are or were serving in such capacity. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. Furthermore, we have obtained director and officer liability insurance to cover liabilities our directors and officers may incur in connection with their services to us and have increased the level upon the completion of the our IPO.

### ***Other Transactions***

We have entered into various employment related agreements and compensatory arrangements with our directors and executive officers that, among other things, provide for compensatory and certain severance and change in control benefits. For a description of these agreements and arrangements, see the sections entitled Item 11. Executive Compensation Employment Agreements and Arrangements and Item 11. Executive Compensation Director Compensation Non-Employee Director Compensation appearing elsewhere in this Form 10-K.

### **Director Independence**

Under the rules of the NASDAQ Stock Market, LLC, or NASDAQ, independent directors must comprise a majority of a listed company's board of directors within a specified period following that company's listing date in conjunction with its IPO. In addition, applicable NASDAQ rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating committees be independent within the meaning of applicable NASDAQ rules. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act.

Our board of directors undertook a review of the independence of each director and considered whether any director has a material relationship with us that could compromise his or her ability to exercise independent judgment in carrying out his responsibilities. As a result of this review, our board of directors determined that all of our directors, other than Messrs. King and Schreck and Dr. Palmer, qualify as independent directors within the meaning of the NASDAQ rules. Accordingly, a majority of our directors are independent, as required under applicable NASDAQ rules. In making this determination, our board considered Mr. Nohra's affiliation with Alta Partners, one of our stockholders, Dr. Hoffman's affiliation with Skyline Ventures, one of our stockholders and Mr. Wan's affiliation with Three Arch Partners, one of our stockholders and determined that it does not interfere with their independent judgment. Our non-employee directors have been meeting, and we anticipate that they will continue to meet, in regularly scheduled executive sessions at which only non-employee directors are present.

### **Item 14. Principal Accounting Fees and Services**

#### **Independent Registered Public Accounting Firm Fees and Services**

In connection with the audit of our 2012 financial statements, we entered into an engagement agreement with Ernst & Young LLP which sets forth the terms by which Ernst & Young LLP will perform audit and interim services for us. That agreement is subject to alternative dispute resolution procedures and an exclusion of punitive damages.



**Table of Contents**

The following table represents aggregate fees billed to our company for the fiscal years ended December 31, 2012 and 2011 by Ernst & Young LLP, our independent registered public accounting firm:

|                    | <b>Fiscal Year Ended</b> |                   |
|--------------------|--------------------------|-------------------|
|                    | <b>2012</b>              | <b>2011</b>       |
| Audit Fees         | \$ 616,375               | \$ 435,825        |
| Audit-Related Fees |                          |                   |
| Tax Fees           |                          |                   |
| All Other Fees     |                          |                   |
| <b>Total Fees</b>  | <b>\$ 616,375</b>        | <b>\$ 435,825</b> |

*Audit Fees:* Consists of fees for professional services rendered for the audit of our financial statements and review of interim financial statements, and fees for assistance with registration statements filed with the SEC, comfort letters and services that are normally provided by Ernst & Young LLP in connection with statutory and regulatory filings or engagements.

**Pre-Approval Policies and Procedures**

Our audit committee pre-approves all audit and permissible non-audit services provided by Ernst & Young LLP. These services may include audit services, audit-related services, tax services and other services. Pre-approval may be given as part of the audit committee's approval of the scope of the engagement of the independent registered public accounting firm or on an individual explicit case-by-case basis.

**Table of Contents**

**PART IV**

**Item 15. Exhibits, Financial Statement Schedules**

(a) The following documents are filed as part of this Form 10-K:

1. Financial Statements:

See Index to Financial Statements in Item 8 of this Form 10-K.

2. Financial Statement Schedules:

No schedules are provided because they are not applicable, not required under the instructions, or the requested information is shown in the financial statements or related notes thereto.

(b) Exhibits The exhibits listed in the accompanying index to exhibits are filed or incorporated by reference as part of this Annual Report on Form 10-K

**Table of Contents****SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 12, 2013

**AcelRx Pharmaceuticals, Inc.**  
(Registrant)

/s/ Richard A. King  
**Richard A. King**

**Chief Executive Officer and Director**

**(Principal Executive Officer)**

/s/ James H. Welch  
**James H. Welch**

**Chief Financial Officer**

**(Principal Financial and Accounting Officer)**

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Richard A. King and James H. Welch, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

| <b>Signature</b>                     | <b>Title</b>  | <b>Date</b>    |
|--------------------------------------|---|----------------|
| /s/ Richard A. King                  | Chief Executive Officer and Director                | March 12, 2013 |
| <b>Richard A. King</b>               | <i>(Principal Executive Officer)</i>                |                |
| /s/ James H. Welch                   | Chief Financial Officer                             | March 12, 2013 |
| <b>James H. Welch</b>                | <i>(Principal Financial and Accounting Officer)</i> |                |
| /s/ Adrian Adams                     | Chairman  | March 12, 2013 |
| <b>Adrian Adams</b>                  |   |                |
| /s/ Pamela P. Palmer, M.D., Ph.D.    | Chief Medical Officer and Director                  | March 12, 2013 |
| <b>Pamela P. Palmer, M.D., Ph.D.</b> |   |                |

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

/s/ Mark G. Edwards

Director

March 12, 2013

**Mark G. Edwards**

/s/ Stephen J. Hoffman, Ph.D., M.D.

Director

March 12, 2013

**Stephen J. Hoffman, Ph.D., M.D.**

**Table of Contents**

| <b>Signature</b>       | <b>Title</b> | <b>Date</b>    |
|------------------------|--------------|----------------|
| /s/ Guy P. Nohra       | Director     | March 12, 2013 |
| <b>Guy P. Nohra</b>    |              |                |
| /s/ Howard B. Rosen    | Director     | March 12, 2013 |
| <b>Howard B. Rosen</b> |              |                |
| /s/ Mark Wan           | Director     | March 12, 2013 |
| <b>Mark Wan</b>        |              |                |

**Table of Contents**

**ACELRX PHARMACEUTICALS, INC.**

**INDEX TO FINANCIAL STATEMENTS**

|  | <b>Page</b> |
|--|-------------|
| <u>Report of Independent Registered Public Accounting Firm</u>   | F-2         |
| <u>Balance Sheets at December 31, 2012 and 2011</u>  | F-3         |
| <u>Statements of Comprehensive Loss for each of the three years in the period ended December 31, 2012, and for the period from July 13, 2005 (inception) through December 31, 2012</u> | F-4         |
| <u>Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit) for the period from July 13, 2005 (inception) through December 31, 2012</u>                            | F-5         |
| <u>Statements of Cash Flows for each of the three years in the period ended December 31, 2012, and for the period from July 13, 2005 (inception) through December 31, 2012</u>         | F-7         |
| <u>Notes to Financial Statements</u>   | F-8         |

**Table of Contents**

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders

AcelRx Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of AcelRx Pharmaceuticals, Inc. (a development stage company) (the Company) as of December 31, 2012 and 2011, and the related statements of comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2012, and for the period from July 13, 2005 (inception) through December 31, 2012. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of AcelRx Pharmaceuticals, Inc. (a development stage company) at December 31, 2012 and 2011, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, and for the period from July 13, 2005 (inception) through December 31, 2012 in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California

March 12, 2013

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Balance Sheets****(in thousands, except share data)**

|   | <b>December 31,<br/>2012</b> | <b>December 31,<br/>2011</b> |
|---|------------------------------|------------------------------|
| <b>ASSETS</b>   |                              |                              |
| <b>CURRENT ASSETS:</b>  |                              |                              |
| Cash and cash equivalents   | \$ 47,932                    | \$ 7,794                     |
| Short-term investments  | 11,831                       | 27,991                       |
| Prepaid expenses and other current assets   | 2,003                        | 2,361                        |
| Total current assets  | 61,766                       | 38,146                       |
| Property and equipment, net   | 2,485                        | 2,306                        |
| Restricted cash   | 205                          | 205                          |
| Other assets  | 64                           | 178                          |
| <b>TOTAL ASSETS</b>   | <b>\$ 64,520</b>             | <b>\$ 40,835</b>             |
| <b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>   |                              |                              |
| <b>CURRENT LIABILITIES:</b>   |                              |                              |
| Accounts payable  | \$ 2,235                     | \$ 1,530                     |
| Accrued liabilities   | 4,653                        | 2,511                        |
| Long-term debt, current portion   | 7,443                        | 3,804                        |
| Total current liabilities   | 14,331                       | 7,845                        |
| Deferred rent   | 312                          | 15                           |
| Long-term debt, net of current portion  | 8,530                        | 15,275                       |
| Contingent put option liability   | 82                           | 232                          |
| Warrant liability   | 7,418                        |                              |
| <b>Total liabilities</b>  | <b>30,673</b>                | <b>23,367</b>                |
| <b>Commitments and Contingencies</b>  |                              |                              |
| <b>STOCKHOLDERS' EQUITY:</b>  |                              |                              |
| Common stock, \$0.001 par value 100,000,000 shares authorized as of December 31, 2012 and 2011;<br>37,055,027 and 19,567,778 shares issued and outstanding as of December 31, 2012 and 2011 |                              |                              |
| Additional paid-in capital  | 37                           | 22                           |
| Deficit accumulated during the development stage  | 155,836                      | 106,110                      |
| Accumulated other comprehensive income  | (122,027)                    | (88,664)                     |
|   | 1                            |                              |
| <b>Total stockholders' equity</b>   | <b>33,847</b>                | <b>17,468</b>                |
| <b>TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY</b>   | <b>\$ 64,520</b>             | <b>\$ 40,835</b>             |

See notes to financial statements.





**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Statements of Comprehensive Loss****(in thousands, except share and per share data)**

|  | Year Ended December 31, |             |             | Period from July 13,<br>2005 (Inception)<br>Through December 31, |
|--|-------------------------|-------------|-------------|--|
|  | 2012                    | 2011        | 2010        | 2012   |
| Research grant revenue   | \$ 2,394                | \$ 1,072    | \$          | \$ 3,466   |
| Operating expenses:  |                         |             |             |  |
| Research and development   | 24,908                  | 13,624      | 8,193       | 92,329   |
| General and administrative   | 7,199                   | 6,800       | 3,993       | 26,493   |
| Total operating expenses   | 32,107                  | 20,424      | 12,186      | 118,822  |
| Loss from operations   | (29,713)                | (19,352)    | (12,186)    | (115,356)  |
| Interest expense   | (2,283)                 | (2,309)     | (1,397)     | (7,722)  |
| Interest income and Other income (expense), net                                | (1,367)                 | 1,560       | (761)       | 1,051  |
| Net loss   | (33,363)                | (20,101)    | (14,344)    | (122,027)  |
| Other comprehensive loss:  |                         |             |             |  |
| Unrealized gains (losses) on available for sale securities                     | 1                       |             |             |  |
|  |                         |             | 2           | 1  |
| Comprehensive loss   | \$ (33,362)             | \$ (20,101) | \$ (14,342) | \$ (122,026)   |
| Net loss per share of common stock, basic and diluted                          | \$ (1.51)               | \$ (1.16)   | \$ (21.84)  |  |
| Shares used in computing net loss per share of common stock, basic and diluted | 22,124,637              | 17,344,727  | 656,650     |  |

See notes to financial statements.

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Statements of Convertible Preferred Stock and Stockholders Equity (Deficit)****(in thousands, except share and per share data)**

|  | Convertible Preferred Stock |        | Common Stock |        | Additional | Deficit     | Other         | Total        |
|--|-----------------------------|--------|--------------|--------|------------|-------------|---------------|--------------|
|  | Shares                      | Amount | Shares       | Amount | Paid-in    | Accumulated | Comprehensive | Stockholders |
|  |                             |        |              |        | Capital    | During the  | Income        | Equity       |
|  |                             |        |              |        |            | Development | (loss)        | (Deficit)    |
|  |                             |        |              |        |            | Stage       |               |              |
| Balance as of July 13, 2005 (Inception)  |                             | \$     |              | \$     | \$         | \$          | \$            | \$           |
| Net loss   |                             |        |              |        |            | (40)        |               | (40)         |
| Balance as of December 31, 2005  |                             |        |              |        |            | (40)        |               | (40)         |
| Issuance of restricted common stock to founders                                  |                             |        | 250,000      | 1      |            |             |               | 1            |
| Issuance of Series A convertible preferred stock, net of issuance costs of \$100 | 2,111,639                   | 21,016 |              |        |            |             |               |              |
| Issuance of common stock upon the exercise of common stock warrants              |                             |        | 25,534       | 1      | 50         |             |               | 51           |
| Stock-based compensation related to restricted stock                             |                             |        | 20,833       |        | 42         |             |               | 42           |
| Change in unrealized gains and losses on investments, net of taxes               |                             |        |              |        |            |             | (1)           | (1)          |
| Net loss   |                             |        |              |        |            | (3,768)     |               | (3,768)      |
| Balance as of December 31, 2006  | 2,111,639                   | 21,016 | 296,367      | 2      | 92         | (3,808)     | (1)           | (3,715)      |
| Stock-based compensation related to restricted stock                             |                             |        | 127,448      | 1      | 116        |             |               | 117          |
| Stock-based compensation related to stock options                                |                             |        |              |        | 33         |             |               | 33           |
| Change in unrealized gains and losses on investments, net of taxes               |                             |        |              |        |            |             | 6             | 6            |
| Net loss   |                             |        |              |        |            | (9,630)     |               | (9,630)      |
| Balance as of December 31, 2007  | 2,111,639                   | 21,016 | 423,815      | 3      | 241        | (13,438)    | 5             | (13,189)     |
| Issuance of Series B convertible preferred stock, net of issuance costs of \$78  | 1,263,635                   | 20,140 |              |        |            |             |               |              |
| Stock-based compensation related to restricted stock                             |                             |        | 97,812       |        | 271        |             |               | 271          |
| Stock-based compensation related to stock options                                |                             |        |              |        | 197        |             |               | 197          |
| Contribution of common stock to a charitable organization                        |                             |        | 2,500        |        | 14         |             |               | 14           |
| Change in unrealized gains and losses on investments, net of taxes               |                             |        |              |        |            |             | 34            | 34           |
| Net loss   |                             |        |              |        |            | (20,662)    |               | (20,662)     |
| Balance as of December 31, 2008  | 3,375,274                   | 41,156 | 524,127      | 3      | 723        | (34,100)    | 39            | (33,335)     |
| Issuance of Series C convertible preferred stock, net of issuance costs of \$99  | 3,757,253                   | 14,715 |              |        |            |             |               |              |
| Stock-based compensation related to restricted stock                             |                             |        | 74,375       |        | 163        |             |               | 163          |
| Stock-based compensation related to stock options                                |                             |        |              |        | 312        |             |               | 312          |
|  |                             |        | 21,614       |        | 26         |             |               | 26           |

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Issuance of common stock upon exercise of stock options

|  |  |  |  |  |  |          |      |          |
|--|--|--|--|--|--|----------|------|----------|
| Change in unrealized gains and losses on investments, net of taxes |  |  |  |  |  |          | (41) | (41)     |
| Net loss   |  |  |  |  |  | (20,119) |      | (20,119) |

|   |           |        |         |   |       |          |     |          |
|---|-----------|--------|---------|---|-------|----------|-----|----------|
| Balance as of December 31, 2009 (carried forward) | 7,132,527 | 55,871 | 620,116 | 3 | 1,224 | (54,219) | (2) | (52,994) |
|---|-----------|--------|---------|---|-------|----------|-----|----------|

F-5

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)****(in thousands, except share and per share data)**

|  | Convertible Preferred Stock |          | Common Stock |        | Additional      | Deficit                                  | Other                       | Total                          |
|--|-----------------------------|----------|--------------|--------|-----------------|--|-----------------------------|--------------------------------|
|  | Shares                      | Amount   | Shares       | Amount | Paid-in Capital | Accumulated During the Development Stage | Comprehensive Income (loss) | Stockholders' Equity (Deficit) |
| Balance as of December 31, 2009  | 7,132,527                   | 55,871   | 620,116      | 3      | 1,224           | (54,219)                                 | (2)                         | (52,994)                       |
| Issuance of Series C convertible preferred stock, net of issuance costs of \$99                            | 19,275                      | 70       |              |        |                 |  |                             |                                |
| Stock-based compensation related to restricted stock   |                             |          | 43,282       |        | 93              |  |                             | 93                             |
| Stock-based compensation related to stock options  |                             |          |              |        | 1,330           |  |                             | 1,330                          |
| Issuance of common stock upon exercise of stock options  |                             |          | 10,955       |        | 21              |  |                             | 21                             |
| Change in unrealized gains and losses on investments, net of taxes   |                             |          |              |        |                 |  | 2                           | 2                              |
| Net loss   |                             |          |              |        |                 | (14,344)                                 |                             | (14,344)                       |
| Balance as of December 31, 2010  | 7,151,802                   | 55,941   | 674,353      | 3      | 2,668           | (68,563)                                 |                             | (65,892)                       |
| Conversion of convertible preferred stock to common stock  | (7,151,802)                 | (55,941) | 8,555,713    | 8      | 55,933          |  |                             | 55,941                         |
| Conversion of Bridge Note and warrants to common stock   |                             |          | 2,141,684    | 2      | 9,579           |  |                             | 9,824                          |
| Issuance of Warrants   |                             |          |              |        | 967             |  |                             | 967                            |
| Stock-based compensation   |                             |          |              |        | 1,833           |  |                             | 1,833                          |
| Issuance of common stock upon exercise of stock options and in connection with restricted stock units      |                             |          | 147,792      | 1      | 60              |  |                             | 61                             |
| Issuance of common stock upon ESPP purchase  |                             |          | 48,236       |        | 139             |  |                             | 139                            |
| Issuance of common stock upon IPO, net of offering-related costs of \$5.1 million                          |                             |          | 8,000,000    | 8      | 34,931          |  |                             | 34,939                         |
| Change in unrealized gains and losses on investments, net of taxes   |                             |          |              |        |                 |  |                             |                                |
| Net loss   |                             |          |              |        |                 | (20,101)                                 |                             | (20,101)                       |
| Balance as of December 31, 2011  |                             |          | 19,567,778   | 22     | 106,110         | (88,664)                                 |                             | 17,468                         |
| Issuance of Warrants   |                             |          |              |        |                 |  |                             |                                |
| Stock-based compensation   |                             |          |              |        | 2,150           |  |                             | 2,150                          |
| Issuance of common stock upon exercise of stock options and in connection with restricted stock units      |                             |          | 122,108      |        | 80              |  |                             | 80                             |
| Issuance of common stock upon ESPP purchase  |                             |          | 67,804       |        | 169             |  |                             | 169                            |
| Issuance of common stock upon private placement offering, net of offering-related costs of \$0.9 million   |                             |          | 2,922,337    | 1      | 3,245           |  |                             | 3,246                          |
| Issuance of common stock upon underwritten public offering, net of offering-related costs of \$3.5 million |                             |          | 14,375,000   | 14     | 44,082          |  |                             | 44,096                         |
|  |                             |          |              |        |                 |  | 1                           | 1                              |

# Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

|  |            |       |            |              |  |          |   |           |  |
|--|------------|-------|------------|--------------|--|----------|---|-----------|--|
| Change in unrealized gains and losses on investments, net of taxes |            |       |            |              |  |          |   |           |  |
| Net loss   |            |       |            |              |  | (33,363) |   | (33,363)  |  |
| Balance as of December 31, 2012                                    | 37,055,027 | \$ 37 | \$ 155,836 | \$ (122,027) |  |          | 1 | \$ 33,847 |  |

See notes to financial statements.

F-6

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Statements of Cash Flows****(in thousands)**

|  | <b>Year Ended December 31,</b> |             |             | <b>Period from July 13,<br/>2005 (Inception)<br/>Through<br/>December 31,<br/>2012</b> |
|--|--------------------------------|-------------|-------------|--|
|  | <b>2012</b>                    | <b>2011</b> | <b>2010</b> |  |
| <b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>   |                                |             |             |  |
| Net loss   | \$ (33,363)                    | \$ (20,101) | \$ (14,344) | \$ (122,027)   |
| Adjustments to reconcile net loss to net cash used in operating activities:                              |                                |             |             |  |
| Depreciation and amortization  | 605                            | 513         | 479         | 2,683  |
| Amortization of premium/discount on investments, net   | 380                            | 195         |             | 575  |
| Interest expense related to debt financing   | 647                            | 1,619       | 717         | 3,474  |
| Stock-based compensation   | 2,150                          | 1,833       | 1,424       | 6,496  |
| Revaluation of convertible preferred stock warrant, call option, put option and PIPE warrant liabilities | 1,439                          | (1,512)     | 1,257       | 1,355  |
| Other  | 43                             |             | 5           | 33   |
| Changes in operating assets and liabilities:   |                                |             |             |  |
| Prepaid expenses and other assets  | 429                            | (434)       | (120)       | (554)  |
| Restricted cash  |                                |             |             | (205)  |
| Accounts payable   | 705                            | 987         | (371)       | 2,234  |
| Accrued liabilities  | 2,029                          | 1,788       | (1,091)     | 2,907  |
| Deferred rent  | 354                            | (175)       | (181)       | 424  |
| Net cash used in operating activities  | (24,582)                       | (15,287)    | (12,225)    | (102,605)  |
| <b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>   |                                |             |             |  |
| Purchase of property and equipment   | (826)                          | (2,019)     | (4)         | (5,214)  |
| Purchase of investments  | (27,167)                       | (39,367)    | (4,922)     | (111,834)  |
| Proceeds from sales of investments   |                                | 2,082       |             | 21,815   |
| Proceeds from maturities of investments  | 42,948                         | 9,725       | 9,691       | 77,664   |
| Net cash provided by (used in) investing activities  | 14,955                         | (29,579)    | 4,765       | (17,569)   |
| <b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>   |                                |             |             |  |
| Proceeds from issuance of common stock in equity offerings, net of offering costs                        | 53,174                         | 34,939      |             | 88,113   |
| Proceeds from the issuance of long-term debt   |                                | 19,762      |             | 32,383   |
| Payment of long-term debt  | (3,655)                        | (5,297)     | (4,726)     | (16,876)   |
| Proceeds from issuance of convertible promissory notes   |                                |             | 8,000       | 9,000  |
| Net proceeds from issuance of common stock through equity plans  | 246                            | 201         | 21          | 545  |
| Proceeds from issuance of convertible preferred stock, net of issuance costs                             |                                |             | 70          | 54,941   |
| Net cash provided by financing activities  | 49,765                         | 49,605      | 3,365       | 168,106  |
| NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS   | 40,138                         | 4,739       | (4,095)     | 47,932   |
| CASH AND CASH EQUIVALENTS Beginning of period  | 7,794                          | 3,055       | 7,150       |  |
| CASH AND CASH EQUIVALENTS End of period  | \$ 47,932                      | \$ 7,794    | \$ 3,055    | \$ 47,932  |
| <b>SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:</b>  |                                |             |             |  |
| Cash paid for interest   | \$ 1,632                       | \$ 1,162    | \$ 584      | \$ 4,534   |

# Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

## NONCASH INVESTING AND FINANCING ACTIVITIES:

|   |          |          |          |          |
|---|----------|----------|----------|----------|
| Issuance of convertible preferred stock warrants                          | \$       | \$       | \$ 1,223 | \$ 1,223 |
| Beneficial conversion features related to convertible notes               | \$       | \$       | \$ 1,699 | \$ 1,699 |
| Issuance of call option related to convertible note                       | \$       | \$       | \$ 476   | \$ 476   |
| Conversion of convertible promissory notes into common stock              | \$       | \$ 8,137 | \$       | \$ 8,137 |
| Issuance of common stock upon cashless exercise of warrants               | \$       | \$ 536   | \$       | \$ 536   |
| Reclassification of warrant liability and call option liability to equity | \$       | \$ 906   | \$       | \$ 906   |
| Issuance of warrants for common stock                                     | \$ 5,828 | \$ 967   | \$       | \$ 6,795 |
| Contingent put option liability   | \$       | \$ 232   | \$       | \$ 232   |

See notes to financial statements.

F-7



## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

## **1. Organization and Summary of Significant Accounting Policies**

### ***The Company***

AcelRx Pharmaceuticals, Inc., or the Company, is a development stage company that was incorporated in Delaware on July 13, 2005 as SuRx, Inc. In January 2006, the Company changed its name to AcelRx Pharmaceuticals, Inc. The Company's operations are based in Redwood City, California.

The Company is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. The Company is in the development stage and since incorporation, primary activities have consisted of establishing facilities, recruiting personnel, conducting research and development of its product candidates, developing intellectual property and raising capital. To date, the Company has not generated any sales revenues.

The Company has one business activity, which is the development and commercialization of product candidates for the treatment of pain, and a single reporting and operating unit structure.

The Company has incurred recurring operating losses and negative cash flows from operating activities since inception and anticipates incurring losses for the next several years. The Company had an accumulated deficit of \$122.0 million and \$88.7 million as of December 31, 2012 and 2011, respectively. Through December 31, 2012, the Company has relied primarily on proceeds from equity and debt offerings to finance its operations. Management believes that the Company's current cash, cash equivalents and investments will be sufficient to fund the Company's current operations into the third quarter of 2014. The Company will need to raise substantial additional funding or otherwise enter into collaborations to support future operations. However, there is no assurance that additional funding will be available to the Company on acceptable terms on a timely basis, if at all, or that the Company will achieve profitable operations. If the Company is unable to raise additional capital to fund its operations, it will need to curtail planned activities to reduce costs. Doing so may affect the Company's ability to operate effectively. The accompanying financial statements do not include any adjustments that might result from the outcome of these uncertainties.

### ***Basis of Presentation***

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. Actual results could differ from those estimates.

### ***Concentration of Risk***

The Company invests cash that is currently not being used for operational purposes in accordance with its investment policy in low risk debt securities of the U.S. Treasury and U.S. government sponsored agencies. The Company is exposed to credit risk in the event of default by the institutions holding the cash equivalents and available-for-sale securities to the extent recorded on the balance sheet.

### ***Cash, Cash Equivalents and Marketable Securities***

The Company considers all highly liquid investments with an original maturity (at date of purchase) of three months or less to be cash equivalents. Cash and cash equivalents consist of cash on deposit with banks and money market instruments.

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

All marketable securities are classified as available-for-sale and consist of U.S. Treasury and U.S. government sponsored enterprise debt securities. These securities are carried at estimated fair value, which is based on quoted market prices or observable market inputs of almost identical assets, with unrealized gains and losses included in accumulated other comprehensive income (loss). The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in interest income or expense. The cost of securities sold is based on specific identification. The Company's investments are subject to a periodic impairment review for other-than-temporary declines in fair value. The Company's review includes the consideration of the cause of the impairment including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. When the Company determines that the decline in fair value of an investment is below its accounting basis and this decline is other-than-temporary, it reduces the carrying value of the security it holds and records a loss in the amount of such decline.

#### ***Property and Equipment***

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the estimated useful life of the improvements or the remaining lease term.

#### ***Impairment of Long-Lived Assets***

The Company periodically assesses the impairment of long-lived assets and, if indicators of asset impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through an analysis of the undiscounted future expected operating cash flows. If impairment is indicated, the Company records the amount of such impairment for the excess of the carrying value of the asset over its estimated fair value. As of December 31, 2012, the Company has not written down any of its long-lived assets as a result of impairment.

#### ***Restricted Cash***

Under the Company's facility lease and corporate credit card agreements, the Company is required to maintain letters of credit as security for performance under these agreements. The letters of credit are secured by certificates of deposit in amounts equal to the letters of credit, which are classified as restricted cash on the balance sheet.

#### ***Revenue Recognition***

The Company recognizes revenue when all of the following criteria are met: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured.

In May 2011, the Company entered into an award contract with the US Army Medical Research and Materiel Command, or USAMRMC, to support the development of the Company's new product candidate, ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain. The grant provides for the reimbursement of qualified expenses for research and development activities as defined under the terms of the grant agreement. Revenue under the grant agreement is recognized when the related qualified research expenses are incurred.

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

#### ***Research and Development Expenses***

Research and development costs are charged to expense when incurred. Research and development expenses include salaries, employee benefits, including stock-based compensation, consultant fees, laboratory supplies, costs associated with clinical trials and manufacturing, including contract research organization fees, other professional services and allocations of corporate costs. The Company reviews and accrues clinical trial expenses based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of patient studies and other events.

#### ***Comprehensive Loss***

Comprehensive loss is comprised of net loss and other comprehensive income (loss). For the Company, other comprehensive income (loss) consists of changes in unrealized gains and losses on the Company's investments. Total comprehensive loss for all periods presented has been disclosed in the statements of convertible preferred stock and stockholders' equity (deficit).

#### ***Fair Value of Financial Instruments***

The Company measures and reports its cash equivalents, investments and financial liabilities at fair value. Fair value is defined as the exchange price that would be received for an asset or an exit price paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The fair value hierarchy defines a three-level valuation hierarchy for disclosure of fair value measurements as follows:

Level I Unadjusted quoted prices in active markets for identical assets or liabilities;

Level II Inputs other than quoted prices included within Level I that are observable, unadjusted quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

Level III Unobservable inputs that are supported by little or no market activity for the related assets or liabilities.

The categorization of a financial instrument within the valuation hierarchy is based upon the lowest level of input that is significant to the fair value measurement.

#### ***Income Taxes***

Deferred tax assets and liabilities are measured based on differences between the financial reporting and tax basis of assets and liabilities using enacted rates and laws that are expected to be in effect when the differences are expected to reverse. The Company records a valuation allowance for the full amount of deferred assets, which would otherwise be recorded for tax benefits relating to operating loss and tax credit carryforwards, as realization of such deferred tax assets cannot be determined to be more likely than not.

#### ***Stock-Based Compensation***

Compensation expense for all share-based payment awards made to employees and directors, including employee stock options, restricted stock units and employee share purchases related to the 2011 Employee Stock Purchase Plan, or ESPP, is based on estimated fair values at grant date. The Company determines the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognizes the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards.

F-10

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

The Black-Scholes option pricing model requires inputs such as expected term, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. Estimates of expected life are primarily determined using the simplified method in accordance with guidance provided by the SEC. Such method was utilized as the Company did not believe its historical option exercise experience, which was limited, provided a reasonable basis upon which to estimate expected term. Volatility is derived from historical volatilities of several public companies within our industry that are deemed to be comparable to our business because we have limited information on the volatility of our common stock since we had no trading history prior to completion of our Initial Public Offering, or IPO, in February 2011. The risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. Further, the Company estimates forfeitures at the time of grant and revises those estimates in subsequent periods if actual forfeitures differ from those estimates.

### ***Net Loss per Share of Common Stock***

The Company's basic net loss per share of common stock is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. The diluted net loss per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, convertible preferred stock, options to purchase common stock, restricted stock subject to repurchase, warrants to purchase convertible preferred stock and warrants to purchase common stock were considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share of common stock as their effect is antidilutive.

### ***Segment Information***

The Company operates in one operating segment and has operations solely in the United States.

### ***Recently Issued Accounting Pronouncements***

In June of 2011, Accounting Standards Codification Topic 220, Comprehensive Income was amended to increase the prominence of items reported in other comprehensive income. Accordingly, a company can present all non-owner changes in stockholders' equity either in a single continuous statement of comprehensive income or in two separate but consecutive statements. The Company adopted this guidance as of January 1, 2012 on a retrospective basis and this adoption did not have a material effect on the Company's financial statements.

In May of 2011, Accounting Standards Codification Topic 820, Fair Value Measurement was amended to develop common requirements for measuring fair value and for disclosing information about fair value measurements in accordance with U.S. generally accepted accounting principles and International Financial Reporting Standards. The Company adopted this guidance as of January 1, 2012 on a retrospective basis and this adoption did not have a material effect on the Company's financial statements.

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements****2. Investments and Fair Value Measurement*****Investments***

The Company classifies its marketable securities as available-for-sale and records its investments at fair value. Available-for-sale securities are carried at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains and losses included in accumulated other comprehensive income. Marketable securities which have maturities beyond one year as of the end of the reporting period are classified as non-current.

The table below summarizes the Company's cash, cash equivalents and investments (in thousands):

|   |                       | <b>As of December 31, 2012</b> |                                |                   |
|---|-----------------------|--------------------------------|--------------------------------|-------------------|
|   | <b>Amortized Cost</b> | <b>Gross Unrealized Gains</b>  | <b>Gross Unrealized Losses</b> | <b>Fair Value</b> |
| Cash and cash equivalents:                          |                       |                                |                                |                   |
| Cash  | \$ 44,440             | \$                             | \$                             | \$ 44,440         |
| Money market funds                                  | 2,086                 |                                |                                | 2,086             |
| U.S. government agency securities                   | 1,406                 |                                |                                | 1,406             |
| <b>Total cash and cash equivalents</b>              | <b>47,932</b>         |                                |                                | <b>47,932</b>     |
| Marketable securities:                              |                       |                                |                                |                   |
| U.S. government agency securities                   | 11,830                | 1                              |                                | 11,831            |
| <b>Total marketable securities</b>                  | <b>11,830</b>         | <b>1</b>                       |                                | <b>11,831</b>     |
| <b>Total cash, cash equivalents and investments</b> | <b>\$ 59,762</b>      | <b>\$ 1</b>                    | <b>\$</b>                      | <b>\$ 59,763</b>  |

|   |                       | <b>As of December 31, 2011</b> |                                |                   |
|---|-----------------------|--------------------------------|--------------------------------|-------------------|
|   | <b>Amortized Cost</b> | <b>Gross Unrealized Gains</b>  | <b>Gross Unrealized Losses</b> | <b>Fair Value</b> |
| Cash and cash equivalents:                          |                       |                                |                                |                   |
| Cash  | \$ 641                | \$                             | \$                             | \$ 641            |
| Money market funds                                  | 6,883                 |                                |                                | 6,883             |
| U.S. government agency securities                   | 270                   |                                |                                | 270               |
| <b>Total cash and cash equivalents</b>              | <b>7,794</b>          |                                |                                | <b>7,794</b>      |
| Marketable securities:                              |                       |                                |                                |                   |
| U.S. government agency securities                   | 27,991                |                                |                                | 27,991            |
| <b>Total marketable securities</b>                  | <b>27,991</b>         |                                |                                | <b>27,991</b>     |
| <b>Total cash, cash equivalents and investments</b> | <b>\$ 35,785</b>      | <b>\$</b>                      | <b>\$</b>                      | <b>\$ 35,785</b>  |

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

None of the available-for-sale securities held by the Company had material unrealized losses and there were no realized losses for the years ended December 31, 2012 and 2011. There were no other-than-temporary impairments for these securities as of December 31, 2012 or December 31, 2011.

As of December 31, 2012 and 2011, the contractual maturity of all investments held was less than one year.

F-12

**Table of Contents**

**AcelRx Pharmaceuticals, Inc.**

**(A Development Stage Company)**

**Notes to Financial Statements**

***Fair Value Measurement***

The Company's financial instruments consist of Level I and Level II assets and Level III liabilities. Level I securities include highly liquid money market funds and are valued based on quoted market prices. For Level II instruments, the Company estimates fair value by utilizing third party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. Such Level II instruments typically include U.S. treasury and U.S. government agency obligations. As of December 31, 2012 and December 31, 2011, the Company held, in addition to Level I and Level II assets, a contingent put option liability associated with the Company's loan and security agreement with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, which was classified as a Level III liability. The Company's estimate of fair value of the contingent put option liability was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default, and discounting such cash flows back to the reporting date using a risk-free rate. As of December 31, 2012, the Company also held a Level III liability associated with warrants, or PIPE warrants, issued in connection with the Company's private placement equity offering, completed in June 2012. For a detailed description, see Note 9 Stockholders Equity. The PIPE warrants are considered a liability and are valued using the Black-Scholes option-pricing model, the inputs for which include exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants. Changes to any of the inputs can have a significant impact to the estimated fair value of the PIPE warrants.

F-13



**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

The following table sets forth the fair value of the Company's financial assets and liabilities by level within the fair value hierarchy (in thousands):

|  | Fair Value | As of December 31, 2012 |           |           |
|--|------------|-------------------------|-----------|-----------|
|  |            | Level I                 | Level II  | Level III |
| <b>Assets</b>                            |            |                         |           |           |
| Money market funds                       | \$ 2,086   | \$ 2,086                | \$        | \$        |
| U.S. government agency obligations       | 13,237     |                         | 13,237    |           |
| Total assets measured at fair value      | \$ 15,323  | \$ 2,086                | \$ 13,237 | \$        |
| <b>Liabilities</b>                       |            |                         |           |           |
| PIPE warrant                             | \$ 7,418   |                         |           | \$ 7,418  |
| Contingent put option                    | \$ 82      |                         |           | \$ 82     |
| Total liabilities measured at fair value | \$ 7,500   | \$                      | \$        | \$ 7,500  |

|  | Fair Value | As of December 31, 2011 |           |           |
|--|------------|-------------------------|-----------|-----------|
|  |            | Level I                 | Level II  | Level III |
| <b>Assets</b>                            |            |                         |           |           |
| Money market funds                       | \$ 6,883   | \$ 6,883                | \$        | \$        |
| U.S. government agency obligations       | 28,261     |                         | 28,261    |           |
| Total assets measured at fair value      | \$ 35,144  | \$ 6,883                | \$ 28,261 | \$        |
| <b>Liabilities</b>                       |            |                         |           |           |
| Contingent put option liability          | \$ 232     |                         |           | \$ 232    |
| Total liabilities measured at fair value | \$ 232     | \$                      | \$        | \$ 232    |

The following table sets forth the assumptions used in the Black-Scholes option-pricing model to estimate the fair value of the PIPE warrants as of December 31, 2012:

|                          |       |
|--------------------------|-------|
| Risk-free interest rate  | 0.72% |
| Expected volatility      | 78.0% |
| Expected life (in years) | 4.9   |
| Expected dividend yield  | 0.0%  |

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

The following table sets forth a summary of the changes in the fair value of the Company's Level III financial liabilities for the years ended December 31, 2012 and 2011 (in thousands):

|   | <b>Year Ended<br/>December 31,<br/>2012</b> |
|---|---|
| Fair value beginning of period                | \$ 232                                      |
| Addition of PIPE warrants in June 2012        | 5,828                                       |
| Change in fair value of PIPE warrants         | 1,590                                       |
| Change in fair value of contingent put option | (150)                                       |
| Fair value end of period                      | \$ 7,500                                    |

|   | <b>Year Ended<br/>December 31,<br/>2011</b> |
|---|---|
| Fair value beginning of period                | \$ 3,125                                    |
| Exercise of warrants                          | (536)                                       |
| Reclassification of warrant liability         | (906)                                       |
| Contingent put option liability               | 62  |
| Change in fair value of Level III liabilities | (1,513)                                     |
| Fair value end of period                      | \$ 232                                      |

**3. Property and Equipment**

Property and equipment consist of the following (in thousands):

|  | <b>As of December 31,<br/>2012</b> | <b>2011</b> |
|--|------------------------------------|-------------|
| Research equipment                             | \$ 2,014                           | \$ 1,350    |
| Leasehold improvements                         | 1,418                              | 2,066       |
| Computer equipment and software                | 167                                | 240         |
| Construction in Process                        |                                    | 309         |
| Tooling  | 337                                | 283         |
| Furniture and fixtures                         | 59                                 | 107         |
| Total property, plant and equipment            | 3,995                              | 4,355       |
| Less accumulated depreciation and amortization | (1,510)                            | (2,049)     |

|          |          |
|----------|----------|
| \$ 2,485 | \$ 2,306 |
|----------|----------|

Depreciation and amortization expense was \$0.6 million, \$0.5 million, \$0.5 million and \$2.7 million during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, respectively.

#### 4. Research Grant Agreement

In May 2011, AcelRx received a grant from the US Army Medical Research and Materiel Command, or USAMRMC, in which the USAMRMC granted \$5.6 million to the Company in order to support the development of a new product candidate, ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain.

F-15

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

Under the terms of the grant, the USAMRMC will reimburse the Company for development, manufacturing and clinical costs necessary to prepare for and complete the planned Phase 2 dose-finding trial in a study of acute moderate-to-severe pain, and to prepare to enter Phase 3 development. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research. The original term of the grant was through August 31, 2012; however, due to a longer than expected administrative review process by the USAMRMC, AcelRx has received no-cost extensions of the grant, whereby the term has been extended to January 31, 2014.

Revenue is recognized based on expenses incurred by AcelRx in conducting research and development activities set forth in the agreement. Revenue attributable to the research and development performed under the USAMRMC grant was \$2.4 million, \$1.1 million, \$0 and \$3.5 million for the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, respectively.

## **5. Long-Term Debt**

### ***Hercules Loan and Security Agreement***

In June 2011, AcelRx entered into a loan and security agreement with Hercules, under which AcelRx borrowed \$20.0 million in two tranches of \$10.0 million each, represented by secured convertible term promissory notes. The Company's obligations associated with the agreement are secured by a security interest in substantially all of its assets, other than its intellectual property.

The Company borrowed the first tranche of \$10.0 million upon the closing of the transaction on June 29, 2011 and borrowed the second tranche of \$10.0 million in December 2011. The Company used a portion of the proceeds from the first tranche to repay the remaining obligations under that certain loan and security agreement between the Company and Pinnacle Ventures, L.L.C., or Pinnacle Ventures, dated September 16, 2008. The agreement with Pinnacle Ventures is described further below. The interest rate for each tranche is 8.50%. The Company made interest only payments until June 30, 2012, followed by equal monthly payments of principal and interest, totaling \$742,000, through the scheduled maturity date on December 1, 2014.

Subject to certain conditions and limitations set forth in the Hercules loan and security agreement, the Company has the right to convert up to \$3.0 million of scheduled principal installments under the notes into that number of freely tradable shares of common stock equal to (x) the product of (A) the principal amount to be so converted and (B) 103%, divided by (y) \$5.73 per share.

In addition, Hercules was granted the right, in their discretion, to participate in certain future private offerings of securities by the Company occurring on or prior to June 29, 2013 by investing up to an aggregate of \$2.0 million on the same terms, conditions and pricing afforded to others participating in such subsequent offerings.

The Hercules loan and security agreement includes customary affirmative and restrictive covenants, but does not include any financial maintenance covenants, and also includes standard events of default.

Upon an event of default, including a change of control, Hercules has the option to accelerate repayment of the loan, including payment of any applicable prepayment charges, which range from 1%-3% of the outstanding loan balance and accrued interest, as well as a final payment fee of \$0.2 million. This option is considered a contingent put option liability as the holder of the loan may exercise the option in the event of default and, is considered an embedded derivative which must be valued and separately accounted for in the Company's financial statements. As of December 31, 2012 and 2011, the estimated fair value of the contingent put option

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

liability was \$82,000 and \$232,000, respectively, which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default, and discounting such cash flows back to the reporting date using a risk-free rate. The contingent put option liability was recorded as a debt discount to the loan and consequently a reduction to the carrying value of the loan. The contingent put option liability will be revalued at the end of each reporting period and any change in the fair value will be recognized in the statement of operations.

In connection with the loan, the Company issued Hercules seven-year warrants to purchase an aggregate of 274,508 shares of common stock at a price of \$3.06 per share. See Note 7 Warrants, for further description.

As of December 31, 2012, the Company had outstanding borrowings under the Hercules loan and security agreement of \$16.0 million, net of debt discounts of \$0.5 million. Amortization of the debt discounts, which was recorded as interest expense, was \$0.5 million for the year ended December 31, 2012. As of December 31, 2011, the Company had outstanding borrowings under the Hercules loan and security agreement of \$19.0 million, net of debt discounts of \$1.0 million. Amortization of the debt discounts, which was recorded as Interest Expense, was \$254,000 for the year ended December 31, 2011.

***Pinnacle Loan and Security Agreement***

In September 2008, the Company entered into a \$12.0 million loan and security agreement with Pinnacle. In November 2008, the Company drew down all \$12.0 million of the loan facility. On June 29, 2011, upon execution of the Hercules loan and security agreement, the Pinnacle agreement was terminated and the outstanding balance of \$2.8 million was repaid. The unamortized portion of the final balloon payment and deferred financing costs were recorded to interest expense upon termination of the agreement.

***Future Payments on Long-Term Debt***

The following table summarizes our outstanding future payments associated with our long-term debt as of December 31, 2012 (in thousands):

| Obligations:                         | Total     | Less than 1<br>year | Payment by Period |           | More than 5<br>years |
|--------------------------------------|-----------|---------------------|-------------------|-----------|----------------------|
|                                      |           |                     | 1-3 years         | 3-5 years |                      |
| Principal Payments on Long-Term Debt | \$ 16,345 | \$ 7,804            | \$ 8,541          | \$        |                      |
| Interest Payments on Long-Term Debt  | 1,710     | 1,105               | 605               | \$        |                      |
| Total                                | \$ 18,055 | \$ 8,909            | \$ 9,146          | \$        |                      |

**6. Convertible Notes*****2010 Convertible Notes***

On September 14, 2010, the Company sold convertible promissory notes, or the 2010 Convertible Notes, to certain existing investors for an aggregate purchase price of \$8.0 million. The 2010 Convertible Notes bore interest at a rate of 4.0% per annum and had a maturity date of the earlier of (1) September 14, 2011 or (2) an

F-17

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

event of default. In connection with the IPO, the outstanding principal and accrued interest under the 2010 Convertible Notes automatically converted into 2,034,438 shares of common stock immediately prior to the closing of the IPO.

Upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 Convertible Notes outstanding, the Company was required to sell an additional \$4.0 million of 2010 Convertible Notes. This additional \$4.0 million was determined to be a call option that was recorded at its fair value of \$476,000 as a debt discount that would have been amortized to interest expense over the one-year term of the 2010 Convertible Notes. The fair value of the call option was determined by evaluating multiple potential scenarios using a market approach and an income approach depending on the scenario and discounting these values back to the appropriate date while applying estimated probabilities to each scenario value. These scenarios included a potential initial public offering, merger or sale of the Company at different times during 2011 and 2012 as well as remaining private. The fair value of the call option as of December 31, 2010 was \$596,000. During the three months ended March 31, 2011, the 2010 Convertible Notes were amended so that the note holders' option to invest the second tranche of \$4.0 million expired upon the closing of the IPO. The call option was revalued to its fair value as of the IPO date and was written off upon its expiration with a benefit of \$596,000 being recognized through other income (expense). In addition, the unamortized debt discount in the amount of \$1.1 million at the time of the IPO was recognized as interest expense in connection with the conversion of the notes.

## **7. Warrants**

### ***Series A Warrants***

In March 2007, the Company entered into an equipment financing agreement in which the Company issued immediately exercisable and fully vested warrants to purchase 2,500 shares of its Series A convertible preferred stock, or the Series A warrants, with an exercise price of \$10.00 per share. The fair value of the Series A warrants on the date of issuance was \$1,000, as determined using the Black-Scholes option-pricing model. This fair value was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The fair value was remeasured at the end of each reporting period. In connection with the IPO, the Series A warrants were automatically converted into warrants to purchase 3,425 shares of common stock. As a result of the conversion, these common stock warrants were no longer recorded as liabilities and were, therefore, no longer remeasured as of the end of each reporting period.

As of December 31, 2012, warrants to purchase 3,425 shares of common stock had not been exercised and were still outstanding. These warrants expire in March 2017.

### ***Series B and Series C Warrants***

In September 2008, the Company entered into a \$12.0 million loan and security agreement with Pinnacle Ventures. In November 2008, the Company drew down all \$12.0 million of the loan facility. In connection with the loan and security agreement, the Company issued immediately exercisable and fully vested warrants, or the Series B warrants, to purchase 56,250 shares of Series B convertible preferred stock with an exercise price of \$16.00 per share. Upon the closing of the Series C convertible preferred stock financing during the year ended December 31, 2009, the Series B warrants underlying the loan and security agreement became exercisable for 228,264 shares of Series C convertible preferred stock with an exercise price of \$3.94 per share, or the Series C warrants. The Company determined the fair value of the Series B warrants and Series C warrants on the dates of issuance to be \$162,000, as determined using the Black-Scholes option-pricing model which was recorded as a

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

convertible preferred stock warrant liability and as a deferred financing cost in other assets. The Company revalued the convertible preferred stock warrant liability related to the Series B warrants and Series C warrants during each reporting period using the Black-Scholes option-pricing model. The fair value of the convertible preferred stock warrant liability related to these Series B warrants and Series C warrants was estimated to be \$894,000 and \$1.2 million as of the IPO date in February 2011 and December 31, 2010.

In connection with the Company's IPO in February 2011, the Series C warrants were automatically converted into warrants to purchase 228,264 shares of common stock with an exercise price of \$3.94 per share. Immediately before the conversion to common stock warrants, the Series C warrants were remeasured to fair value with the change in the fair value of these warrants of \$323,000 being recorded as a benefit through other income (expense), net during the three months ended March 31, 2011. Immediately after the conversion to common stock warrants, the remaining liability of \$894,000 was reclassified to additional paid-in capital. As a result of the conversion, these common stock warrants were no longer recorded as liabilities and were therefore no longer remeasured as of the end of each reporting period.

As of December 31, 2012, warrants to purchase 228,264 shares of common stock had not been exercised and were still outstanding. These warrants expire in September 2018.

### ***2010 Warrants***

The Company issued warrants in connection with the 2010 Convertible Notes in September 2010, or the 2010 Warrants. The 2010 Warrants were exercisable into shares of convertible preferred stock. The 2010 Warrants would have terminated if not exercised immediately prior to the IPO. The 2010 Warrants allowed for cashless exercises.

The Company determined the fair value of the 2010 Warrants to be \$1.2 million upon issuance, as determined using the Black-Scholes option-pricing model which was recorded as a convertible preferred stock warrant liability and a debt discount. As of December 31, 2010, the related warrant liability was \$1.3 million. In connection with the IPO, the 2010 Warrants were net exercised into shares of Series C convertible preferred stock, which shares were automatically converted to 107,246 shares of common stock immediately prior to the IPO. Immediately before the exercise into Series C convertible preferred stock, the 2010 Warrants were remeasured to fair value with the change in the fair value of these warrants of \$763,000 being recorded as a benefit through other income (expense), net during the three months ended March 31, 2011. Immediately after the exercise into Series C convertible preferred stock, the remaining liability of \$536,000 was reclassified to additional paid-in capital.

### ***Hercules Warrants***

In connection with the loan and security agreement with Hercules, the Company issued to Hercules warrants to purchase an aggregate of 274,508 shares of common stock at a price of \$3.06 per share. The warrants may be exercised on a cashless basis. The warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of seven years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the warrants. The Company estimated the fair value of these warrants as of the issuance date to be \$967,000, which was recorded as a debt discount to the loan and consequently a reduction to the carrying value of the loan. The fair value of the warrants was calculated using the Black-Scholes option-valuation model, and was based on the seven-year contractual term of the warrants, a risk-free interest rate of 2.44%, expected volatility of 79% and 0% expected dividend yield.



---

**Table of Contents**

**AcelRx Pharmaceuticals, Inc.**

**(A Development Stage Company)**

**Notes to Financial Statements**

As of December 31, 2012, warrants to purchase 274,508 shares of common stock issued to Hercules had not been exercised and were still outstanding. These warrants expire in June 2018.

***2012 Private Placement Warrants***

In connection with the Private Placement, completed in June 2012, the Company issued PIPE warrants to purchase up to 2,630,103 shares of common stock. The per share exercise price of the PIPE warrants was \$3.40 which equals the closing consolidated bid price of the Company's common stock on May 29, 2012, the effective date of the Purchase Agreement. The PIPE warrants issued in the Private Placement became exercisable six months after the issuance date, and expire on the five year anniversary of the initial exercisability date. Under the terms of the PIPE warrants, upon certain transactions, including a merger, tender offer, sale of all or substantially all of the assets of the Company or if a person or group shall become the owner of 50% of the Company's issued and outstanding common stock, which is outside of the Company's control, each PIPE warrant holder may elect to receive a cash payment in exchange for the warrant, in an amount determined by application of the Black-Scholes option-pricing model. Accordingly, the PIPE warrants were recorded as a liability at fair value, as determined by the Black-Scholes option-pricing model, and then marked to fair value each reporting period, with changes in estimated fair value recorded through the Statement of Comprehensive Loss in other income or expense. The Black-Scholes assumptions used to value the PIPE warrants are disclosed in Note 2.

Upon execution of the Purchase Agreement, the fair value of the PIPE warrants was estimated to be \$5.8 million, which was recorded as a liability. As of December 31, 2012, the fair value of the PIPE warrants was estimated to be \$7.4 million. The change in fair value for the twelve months ended December 31, 2012, which was recorded as other expense, was \$1.6 million.

As of December 31, 2012, PIPE warrants to purchase 2,630,103 shares of common stock issued in connection with the Private Placement had not been exercised and were outstanding. These warrants expire in November 2017.

**8. Commitments and Contingencies**

***Operating Leases***

In December 2011, the Company entered into a non-cancelable lease agreement for approximately 13,787 square feet of office and laboratory facilities in Redwood City, California, which serve as the Company headquarters, effective April 2012. The lease agreement expires in May 2016. Rent expense from the facility lease is recognized on a straight-line basis from the inception of the lease in December 2011, the early access date, through the end of the lease.

Prior to April 2012, the Company was subject to a non-cancelable lease agreement for approximately 11,305 square feet of office and laboratory facilities in Redwood City, California, which served as the Company headquarters for the duration of the lease term. The lease term commenced in April 2007 and expired in April 2012. Rent expense from the facility lease was recognized on a straight-line basis from the inception of the lease in January 2007, the early access date, through the end of the lease.

Rent expense was \$0.3 million, \$0.2 million, \$0.2 million and \$1.3 million during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, respectively.

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

Future minimum payments under the lease agreement as of December 31, 2012 are as follows (in thousands):

|                          |          |
|--------------------------|----------|
| Year Ending December 31: |          |
| 2013                     | 381      |
| 2014                     | 392      |
| 2015                     | 404      |
| 2016                     | 142      |
| Total minimum payments   | \$ 1,319 |

***Litigation***

The Company is not a party to any litigation and does not have contingent reserves established for any litigation liabilities.

***Manufacturing Agreement***

In January 2013, the Company and Patheon Pharmaceuticals Inc., or Patheon, entered into a Manufacturing Services Agreement, or the Services Agreement, and a related Amended and Restated Capital Expenditure and Equipment Agreement, or the Capital Agreement, relating to the manufacture of Sufentanil NanoTabs, or the Product, for use with the Company's Sufentanil NanoTab PCA System, or ARX-01.

Under the terms of the Services Agreement, the Company has agreed to purchase, subject to Patheon's continued material compliance with the terms of the Services Agreement, all of its Product requirements for the United States, Canada and Mexico from Patheon during the Initial Term of the Services Agreement (as defined below), and at least eighty percent (80%) of its Product requirements for such territories after the Initial Term.

The term of the Services Agreement extends until December 31, 2017, or the Initial Term, and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months' prior written notice; provided, however, that the Services Agreement may not be terminated without cause prior to the end of the Initial Term.

The Company also entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement. Under the terms of the Capital Agreement, the Company has the option to make certain future modifications to Patheon's Cincinnati facility, the aggregate cost of which is expected to be less than \$3.5 million and which would be the responsibility of the Company. If additional equipment and facility modifications are required to meet the Company's Product needs, the Company may be required to contribute to the cost of such additional equipment and facility modifications. The Capital Agreement also requires that the Company make payments in 2013 totaling \$480,000 to Patheon to partially offset taxes incurred and paid by Patheon in connection with facility modifications already completed by Patheon. The Company can seek reimbursement from Patheon for this payment if it receives approval from the U.S. Food and Drug Administration for ARX-01. The Capital Agreement further requires that the Company pay a maximum overhead fee of \$200,000 annually during the term of the Services Agreement, which amount may be reduced to \$0 based on the amount of annual revenues earned by Patheon under the Services Agreement and the pre-existing development agreements.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for our products, which are currently in development stage; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.



**Table of Contents**

**AcelRx Pharmaceuticals, Inc.**

**(A Development Stage Company)**

**Notes to Financial Statements**

**9. Stockholders' Equity**

***Common Stock***

***Public Offering***

In December 2012, AcelRx completed an underwritten public offering, in which the Company sold an aggregate of 14,375,000 shares of its common stock at a public offering price of \$3.31 per share, resulting in net proceeds of \$44.1 million, after deducting underwriting discounts and commissions and other offering related expenses totaling \$3.5 million.

***Private Placement Offering***

On June 1, 2012, or the Issuance Date, the Company issued an aggregate of 2,922,337 shares of common stock and warrants to purchase up to 2,630,103 shares of common stock, or the PIPE warrants, for aggregate gross proceeds of \$10.0 million, or the Private Placement. Costs related to the offering were \$0.9 million. The shares of common stock and PIPE warrants issued in the Private Placement were sold pursuant to a Securities Purchase Agreement, or Purchase Agreement, dated May 29, 2012, between the Company and certain purchasers, including certain entities affiliated with Mark Wan and Stephen J. Hoffman, members of the Company's board of directors. Pursuant to the Purchase Agreement, AcelRx sold shares of common stock and PIPE warrants to purchase common stock in immediately separable Units, with each Unit consisting of (i) one share of common stock and (ii) a PIPE warrant to purchase 0.9 of a share of common stock. The per share exercise price of the PIPE warrants was \$3.40. The offering price per Unit was \$3.40 for non-affiliated investors, and \$3.5125 for affiliated investors, which equals the sum of (i) \$3.40, the closing consolidated bid price of our common stock on May 29, 2012, plus (ii) \$0.1125 (which is equal to \$0.125 per PIPE warrant share, multiplied by 0.9), for an aggregate amount of \$10.0 million. The PIPE warrants issued in the Private Placement became exercisable six months after the Issuance Date, and expire on the five year anniversary of the initial exercisability date.

In connection with the Private Placement, the Company filed a registration statement with the U.S. Securities and Exchange Commission, or SEC, registering for resale the shares of common stock and shares of common stock issuable upon exercise of the warrants sold in the Private Placement. The registration statement was declared effective by the SEC in July 2012.

***2012 ATM Agreement***

On August 31, 2012, the Company entered into an At Market Issuance Sales Agreement, or Sales Agreement, or ATM, with MLV & Co. LLC, or MLV, pursuant to which the Company may elect to issue and sell shares of its common stock having an aggregate offering price equal to the lesser of (i) the amount that the Company may continue to offer and sell under the eligibility requirements for use of Form S-3 (including, if applicable, Instruction I.B.6 thereof) or (ii) \$7,500,000. The Company is not obligated to make any sales of common stock under the Sales Agreement. Unless earlier terminated, the Sales Agreement will automatically terminate upon the earlier of (1) the sale of all common stock subject to the Sales Agreement or (2) August 31, 2015. The Company will pay MLV an aggregate commission rate equal to up to 3.0% of the gross proceeds for common stock sold through MLV under the Sales Agreement. The Company has also provided MLV with customary indemnification rights and expense reimbursements for up to \$25,000 of expenses. As of December 31, 2012, the Company has not sold any shares of common stock pursuant to the ATM.

## **Table of Contents**

### **AcelRx Pharmaceuticals, Inc.**

### **(A Development Stage Company)**

### **Notes to Financial Statements**

#### ***Initial Public Offering***

On February 10, 2011, the Company sold 8,000,000 shares of common stock at a price of \$5.00 per share in an IPO. The shares began trading on the NASDAQ Global Market on February 11, 2011. The Company received \$34.9 million in net proceeds from the IPO, after deducting underwriting discounts and commissions and other offering expenses totaling \$5.1 million. Upon the closing of the offering, all outstanding shares of convertible preferred stock converted into common stock. The convertible preferred stock converted into 8,555,713 shares of common stock. In addition, the principal and accrued interest under the 2010 Convertible Notes converted into 2,034,438 shares of common stock upon the closing of the Company's IPO and the 2010 Warrants were net exercised for 107,246 shares of Series C convertible preferred stock, which shares were converted to common stock upon the closing of the Company's IPO. All other outstanding warrants to purchase convertible preferred stock became exercisable into shares of common stock. Concurrently, the Company increased the number of authorized shares of common stock to 100,000,000 with a par value of \$0.001 per share and decreased the number of authorized shares of preferred stock to 10,000,000 with a par value of \$0.001 per share.

#### ***Convertible Preferred Stock***

Upon the closing of the Company's IPO in February 2011, all outstanding shares of convertible preferred stock converted into common stock, as described further above, under *Initial Public Offering*.

During the year ended December 31, 2010, the Company issued 19,275 shares of Series C at \$3.94 per share, resulting in net cash proceeds of \$70,000.

During the year ended December 31, 2009, the Company issued 3,757,253 shares of Series C at \$3.94 per share, resulting in net cash proceeds of \$14.7 million.

During the year ended December 31, 2008, the Company issued 1,263,635 shares of Series B at \$16.00 per share, resulting in net cash proceeds of \$20.1 million.

During the year ended December 31, 2006, the Company completed a private placement of an aggregate of 2,111,639 shares of Series A, which included 102,141 shares issued upon conversion of the 2006 Convertible Notes, at a price of \$10.00 per share, resulting in net cash proceeds of \$21.0 million.

#### ***Stock Plans***

##### ***2011 Equity Incentive Plan***

In January 2011, the board of directors adopted, and the Company's stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan, as a successor to the 2006 Plan. The 2011 Incentive Plan became effective immediately upon the execution and delivery of the underwriting agreement for the IPO on February 10, 2011. As of February 10, 2011, no more awards may be granted under the 2006 Plan, although all outstanding stock options and other stock awards previously granted under the 2006 Plan will continue to remain subject to the terms of the 2006 Plan. The 51,693 shares reserved under the 2006 Plan that remained available for future grant at the time of the IPO were transferred to the share reserve of the 2011 Incentive Plan.

The initial aggregate number of shares of the Company's common stock that may be issued pursuant to stock awards under the 2011 Incentive Plan is 1,875,000 shares, which number was the sum of (i) 51,693 shares remaining available for future grant under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for the Company's IPO, and (ii) an additional 1,823,307 new shares. Then, the number



**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

of shares of common stock reserved for issuance under the 2011 Incentive Plan will automatically increase on January 1st each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by the board of directors. In January 2013 and 2012, an additional 1,482,201 and 782,711 shares, were authorized for issuance under the 2011 Incentive Plan, respectively.

*2011 Employee Stock Purchase Plan*

Additionally, in January 2011, the board of directors adopted, and the Company's stockholders approved, the 2011 Employee Stock Purchase Plan, or the ESPP, which also became effective immediately upon the execution and delivery of the underwriting agreement for the IPO.

Initially, 250,000 shares of the Company's common stock were authorized for issuance under the ESPP pursuant to purchase rights granted to the Company's employees or to employees of any of its designated affiliates. The number of shares of the Company's common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by the board of directors. If a purchase right granted under the ESPP terminates without having been exercised, the shares of the Company's common stock not purchased under such purchase right will be available for issuance under the ESPP. In January 2013, no additional shares were authorized for issuance under the ESPP, and in January 2012, an additional 391,355 were authorized for issuance under the ESPP.

*2006 Stock Plan*

In August 2006, the Company established the 2006 Plan in which 342,000 shares of common stock were originally reserved for the issuance of incentive stock options, or ISOs, and nonstatutory stock options, or NSOs, to employees, directors or consultants of the Company. In February 2008, an additional 375,000 shares of common stock were reserved for issuance under the 2006 Plan and, in November 2009, an additional 1,376,059 shares of common stock were reserved for issuance under the 2006 Plan. Per the 2006 Plan, the exercise price of ISOs and NSOs granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company could not be less than 110% of the fair value per share of the underlying common stock on the date of grant. Effective upon the execution and delivery of the underwriting agreement for the Company's IPO, no additional stock options or other stock awards may be granted under the 2006 Plan.

**10. Stock-Based Compensation**

The Company recorded total stock-based compensation expense for stock options, stock awards and the ESPP as follows (in thousands):

|                            | Year Ended December 31, |                 |                 | Period from July 13,<br>2005 (Inception)<br>Through December 31,<br>2012 |
|----------------------------|-------------------------|-----------------|-----------------|--|
|                            | 2012                    | 2011            | 2010            |  |
| Research and development   | \$ 998                  | \$ 785          | \$ 810          | \$ 3,377   |
| General and administrative | 1,152                   | 1,048           | 614             | 3,119  |
| <b>Total</b>               | <b>\$ 2,150</b>         | <b>\$ 1,833</b> | <b>\$ 1,424</b> | <b>\$ 6,496</b>  |





# Table of Contents

## AcelRx Pharmaceuticals, Inc. (A Development Stage Company) Notes to Financial Statements

The following table summarizes option activity under the 2011 Plan and 2006 Plan:

|  | Number<br>of Stock<br>Options<br>Outstanding | Weighted-<br>Average<br>Exercise<br>Price | Weighted-<br>Average<br>Remaining<br>Contractual<br>Life<br>(Years) | Aggregate<br>Intrinsic<br>Value<br>(in thousands) |
|--|--|---|---|---|
| January 1, 2007  |  | \$  |   |   |
| Granted  | 290,625                                      | 1.20                                      |   |   |
| Forfeited  | (1,250)                                      | 1.20                                      |   |   |
| December 31, 2007  | 289,375                                      | 1.20                                      |   |   |
| Granted  | 196,875                                      | 4.00                                      |   |   |
| December 31, 2008  | 486,250                                      | 2.36                                      |   |   |
| Granted  | 231,875                                      | 5.52                                      |   |   |
| Forfeited  | (30,885)                                     | 2.56                                      |   |   |
| Exercised  | (21,614)                                     | 1.20                                      |   |   |
| December 31, 2009  | 665,626                                      | 3.48                                      |   |   |
| Granted  | 1,441,610                                    | 2.72                                      |   |   |
| Forfeited  | (87,484)                                     | 5.52                                      |   |   |
| Exercised  | (10,955)                                     | 1.89                                      |   |   |
| December 31, 2010  | 2,008,797                                    | \$ 2.91                                   |   |   |
| Granted  | 514,958                                      | 3.48                                      |   |   |
| Forfeited  | (58,022)                                     | 3.32                                      |   |   |
| Exercised  | (69,765)                                     | 1.20                                      |   |   |
| December 31, 2011  | 2,395,968                                    | \$ 3.08                                   |   |   |
| Granted  | 1,213,391                                    | 3.36                                      |   |   |
| Forfeited  | (165,781)                                    | 3.23                                      |   |   |
| Exercised  | (43,767)                                     | 2.32                                      |   |   |
| December 31, 2012  | 3,399,811                                    | \$ 3.18                                   | 7.9   | 4,006   |
| Vested and exercisable options December 31, 2012   | 1,799,264                                    | \$ 3.01                                   | 7.0   | \$ 2,529  |
| Vested and expected to vest December 31, 2012  | 3,286,003                                    | \$ 3.17                                   | 7.9   | \$ 3,903  |
| As of December 31, 2012, there were 725,719 shares available for future grant under the 2011 Plan. In January 2013, an additional 1,482,201 shares were authorized for issuance under the 2011 Incentive Plan. |  |   |   |   |

## Edgar Filing: ACELRX PHARMACEUTICALS INC - Form 10-K

Additional information regarding the Company's stock options outstanding and vested and exercisable as of December 31, 2012 is summarized below:

| Exercise Prices | Number of<br>Stock Options<br>Outstanding | Options Outstanding  |  | Options Vested and Exercisable        |  |
|-----------------|---|--|--|---------------------------------------|--|
|                 |   | Weighted-Average<br>Remaining<br>Contractual Life<br>(Years) | Weighted-Average<br>Exercise<br>Price per<br>Share | Shares Subject<br>to Stock<br>Options | Weighted-Average<br>Exercise<br>Price per<br>Share |
| \$1.20-\$2.55   | 203,776                                   | 5.0  | \$ 1.23  | 202,212                               | \$ 1.23  |
| \$2.56-\$4.00   | 2,879,785                                 | 8.2  | \$ 3.08  | 1,355,178                             | \$ 2.85  |
| \$4.22-\$5.52   | 316,250                                   | 7.1  | \$ 5.32  | 241,874                               | \$ 5.40  |
|                 | 3,399,811                                 | 7.9  | \$ 3.18  | 1,799,264                             | \$ 3.01  |

F-25

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

The weighted average grant-date fair value of options granted during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, was \$2.25, \$2.45, \$2.72 and \$2.18 per share. As of December 31, 2012, total stock-based compensation expense related to unvested options to be recognized in future periods was \$3.1 million which is expected to be recognized over a weighted-average period of 2.7 years. The grant date fair value of shares vested during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, was \$1.3 million, \$1.1 million, \$1.1 million and \$3.8 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012 was \$85,000, \$204,000, \$3,000 and \$354,000, respectively.

The Company used the following assumptions to calculate the fair value of each employee stock option:

|                          | Year Ended December 31, |           |           | Period from July 13,<br>2005 (Inception)<br>Through December 31,<br>2012 |
|--------------------------|-------------------------|-----------|-----------|--|
|                          | 2012                    | 2011      | 2010      |  |
| Expected term (in years) | 5.75-6.25               | 5.75-6.25 | 5.75-6.25 | 5.75-6.25  |
| Risk-free interest rate  | 0.6%-1.74%              | 1.1%-2.5% | 1.6%-4.6% | 0.6%-4.6%  |
| Expected volatility      | 80%                     | 79%       | 75%       | 70%-80%  |
| Expected dividend rate   | 0%                      | 0%        | 0%        | 0%   |

*Restricted Stock Units*

In March 2011, the Company granted 343,815 Restricted Stock Units, or RSUs, to employees and directors under the 2011 Plan at a grant date fair value of \$3.45. The fair value of the RSUs was determined on the date of grant based on the market price of the Company's common stock. RSUs are recognized as expense ratably over the vesting period and the Company's RSUs generally vest over three years as follows: 25% on the 6 month anniversary of the vesting commencement date, 25% on the 12 month anniversary of the vesting commencement date, 25% on the 24 month anniversary of the vesting commencement date and 25% on the 36 month anniversary of the vesting commencement date, so long as the RSU recipient continues to provide services to the Company. As of December 31, 2012, there were 161,096 RSUs outstanding. During 2012, 10,816 RSUs were forfeited and 78,341 common shares were issued upon settlement of vested RSUs. The expense related to RSUs during the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012 was \$315,000, \$492,000, \$0 and \$807,000, respectively.

**11. Net Loss per Share of Common Stock**

The following table sets forth the computation of the Company's basic and diluted net loss per share of common stock during the years ended December 31, 2012, 2011 and 2010 (in thousands, except for share and per share amounts):

|  | Year Ended December 31, |             |             |
|--|-------------------------|-------------|-------------|
|  | 2012                    | 2011        | 2010        |
| Net loss   | \$ (33,363)             | \$ (20,101) | \$ (14,344) |
| Shares used in computing net loss per share of common stock, basic and diluted | 22,124,637              | 17,344,727  | 656,650     |
| Net loss per share of common stock, basic and diluted                          | \$ (1.51)               | \$ (1.16)   | \$ (21.84)  |

F-26

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net loss per share of common stock for the periods presented because including them would have been antidilutive:

|   | Year Ended December 31, |           |           |
|---|-------------------------|-----------|-----------|
|   | 2012                    | 2011      | 2010      |
| Convertible preferred stock                         |                         |           | 7,151,802 |
| Stock options to purchase common stock              | 3,399,811               | 2,395,968 | 2,008,797 |
| Restricted Stock Units                              | 161,096                 | 257,868   |           |
| Convertible preferred stock warrants <sup>(1)</sup> |                         |           | 230,764   |
| Common stock warrants                               | 3,136,300               | 506,197   |           |

- <sup>(1)</sup> Upon execution of the IPO, the 230,764 then outstanding convertible preferred stock warrants were converted to 231,689 common stock warrants and remain outstanding as of December 31, 2012.

**12. Accounts Payable and Accrued Liabilities**

Accounts payable and accrued liabilities consist of the following (in thousands):

|   | December 31,    |                 |
|---|-----------------|-----------------|
|   | 2012            | 2011            |
| Accounts payable                                      | \$ 2,235        | \$ 1,530        |
| Accrued compensation and employee benefits            | 1,613           | 1,302           |
| Accrued research and development expenses             | 2,371           | 497             |
| Professional fees                                     | 361             | 180             |
| Interest Payable                                      | 119             | 116             |
| Other   | 189             | 416             |
| <b>Total accounts payable and accrued liabilities</b> | <b>\$ 6,888</b> | <b>\$ 4,041</b> |

**13. 401(k) Plan**

The Company sponsors a 401(k) plan that stipulates that eligible employees can elect to contribute to the 401(k) plan, subject to certain limitations. Pursuant to the 401(k) plan, the Company makes a discretionary safe harbor contribution equal to 3% of the related compensation. Eligible employees are 100% vested in this safe harbor contribution regardless of whether they make salary deferrals into the 401(k) plan. Company contributions were \$120,000, \$107,000, \$106,000, and \$592,000 for the years ended December 31, 2012, 2011, 2010 and the period from July 13, 2005 (inception) through December 31, 2012, respectively.

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements****14. Income Taxes**

The Company did not record a provision for income taxes during the years ended December 31, 2012, 2011 and 2010. Net deferred tax assets as of December 31, 2012 and 2011 consist of the following (in thousands):

|                                 | December 31,<br>2012 | December 31,<br>2011 |
|---------------------------------|----------------------|----------------------|
| Deferred tax assets:            |                      |                      |
| Accruals and other              | \$ 802               | \$ 623               |
| Research credits                | 2,050                | 1,936                |
| Net operating loss carryforward | 35,730               | 32,646               |
| Section 59(e) R&D expenditures  | 8,572                |                      |
| Total deferred tax assets       | 47,154               | 35,205               |
| Valuation allowance             | \$ (47,154)          | (35,205)             |
| Net deferred tax assets         | \$                   | \$                   |

Reconciliations of the statutory federal income tax to the Company's effective tax during the years ended December 31, 2012, 2011 and 2010 are as follows (in thousands):

|                                      | 2012        | 2011       | 2010       |
|--------------------------------------|-------------|------------|------------|
| Tax at statutory federal rate        | \$ (11,343) | \$ (6,834) | \$ (4,877) |
| State tax net of federal benefit     | (1,953)     | (1,104)    | (757)      |
| Other                                | 1,347       | 161        | 853        |
| Change in valuation allowance        | 11,949      | 7,777      | 4,781      |
| Provision (benefit) for income taxes | \$          | \$         | \$         |

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is more likely than not. Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$11.9 million, \$7.8 million and \$4.8 million during the years ended December 31, 2012, 2011 and 2010, respectively. The amount of the valuation allowance for deferred tax assets associated with excess tax deduction from stock based compensation arrangement that is allocated to contributed capital if the future tax benefits are subsequently recognized is \$0.

As of December 31, 2012, 2011 and 2010, the Company had federal net operating loss carryforwards of \$89.7 million, \$82.2 million and \$63.8 million, which begin to expire in 2025. As of December 31, 2012, 2011, and 2010, the Company had state net operating loss carryforwards of \$89.7 million, \$80.6 million and \$63.7 million, which begin to expire in 2015.

As of December 31, 2012, 2011 and 2010, the Company had federal research credit carryovers of \$1.3 million, \$1.3 million and \$1.1 million which begin to expire in 2026. As of December 31, 2012, 2011 and 2010, the Company had state research credit carryovers of \$1.1 million, \$0.9

million and \$0.7 million, which will carryforward indefinitely.

F-28

**Table of Contents****AcelRx Pharmaceuticals, Inc.****(A Development Stage Company)****Notes to Financial Statements**

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 credits, to offset its post-change income may be limited. Based on an analysis performed by the Company as of December 31, 2012, it was determined that one ownership change has occurred since inception of the Company. This ownership change occurred in 2006 at the time of the Series A financing and, as a result of the change, \$1.4 million in federal and state net operating loss carryforwards will expire unutilized. In addition, \$26,000 in federal and state research and development credits will expire unutilized.

***Uncertain Tax Positions***

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2012, 2011 and 2010 is as follows (in thousands):

|  | <b>Year Ended December 31,</b> |             |             |
|--|--------------------------------|-------------|-------------|
|  | <b>2012</b>                    | <b>2011</b> | <b>2010</b> |
| Unrecognized benefit beginning of period     | \$ 748                         | \$ 603      | \$ 495      |
| Gross decreases prior period tax positions   | (17)                           |             |             |
| Gross increases current period tax positions | 79                             | 145         | 108         |
| Unrecognized benefit end of period           | \$ 810                         | \$ 748      | \$ 603      |

The entire amount of the unrecognized tax benefits would not impact the Company's effective tax rate if recognized.

Accrued interest and penalties related to unrecognized tax benefits are classified as income tax expense and were immaterial. The Company files income tax returns in the United States and in California. The tax years 2006 through 2012 remain open in both jurisdictions. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions.

**15. Unaudited Quarterly Financial Data** (in thousands, except per share amounts)

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2012. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per share data.

|  | <b>2012</b> |            |            |             | <b>2011</b> |            |            |            |
|--|-------------|------------|------------|-------------|-------------|------------|------------|------------|
|  | <b>Q1</b>   | <b>Q2</b>  | <b>Q3</b>  | <b>Q4</b>   | <b>Q1</b>   | <b>Q2</b>  | <b>Q3</b>  | <b>Q4</b>  |
| Revenues                               | \$ 329      | \$ 224     | \$ 166     | \$ 1,675    | \$ 329      | \$ 40      | \$ 408     | \$ 624     |
| Operating Expenses                     | \$ 6,875    | \$ 7,170   | \$ 8,358   | \$ 9,704    | \$ 3,535    | \$ 4,659   | \$ 5,813   | \$ 6,417   |
| Net loss                               | \$ (7,065)  | \$ (7,194) | \$ (8,582) | \$ (10,522) | \$ (3,204)  | \$ (4,763) | \$ (5,761) | \$ (6,373) |
| Net loss per share (basic and diluted) | \$ (0.36)   | \$ (0.35)  | \$ (0.38)  | \$ (0.41)   | \$ (0.30)   | \$ (0.25)  | \$ (0.30)  | \$ (0.33)  |



**Table of Contents**

**EXHIBIT INDEX**

| <b>Exhibit Number</b> | <b>Description of the Document</b>  |
|-----------------------|---|
| 3.1                   | Amended and Restated Certificate of Incorporation of the Registrant, currently in effect. <sup>(1)</sup>  |
| 3.2                   | Amended and Restated Bylaws of the Registrant, currently in effect. <sup>(2)</sup>  |
| 4.1                   | Reference is made to Exhibits 3.1 through 3.2.  |
| 4.2                   | Specimen Common Stock Certificate of the Registrant. <sup>(3)</sup>   |
| 4.3                   | Second Amended and Restated Investors Rights Agreement, among the Registrant and certain of its security holders, dated as of November 23, 2009. <sup>(4)</sup>                             |
| 4.4                   | Warrant to Purchase Stock of the Registrant, issued to Wells Fargo Bank, N.A., dated March 15, 2007. <sup>(5)</sup>   |
| 4.5                   | Warrant to Purchase Preferred Stock of the Registrant, issued to Pinnacle Ventures II Equity Holdings, L.L.C., dated September 16, 2008. <sup>(6)</sup>                                     |
| 4.6                   | Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology II, L.P., dated as of June 29, 2011. <sup>(7)</sup>   |
| 4.7                   | Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology Growth Capital, dated as of June 29, 2011. <sup>(8)</sup>   |
| 4.8                   | Form of Warrant issued to certain purchasers pursuant to the Securities Purchase Agreement dated May 29, 2012, between the Registrant and the purchasers identified therein. <sup>(9)</sup> |
| 10.1+                 | Form of Indemnification Agreement between the Registrant and each of its directors and executive officers. <sup>(10)</sup>  |
| 10.2+                 | 2006 Stock Plan, as amended. <sup>(11)</sup>  |
| 10.3+                 | Forms of Notice of Grant of Stock Option, Stock Option Agreement and Stock Option Exercise Notice under 2006 Stock Plan. <sup>(12)</sup>  |
| 10.4+                 | 2011 Equity Incentive Plan. <sup>(13)</sup>   |
| 10.5+                 | Forms of Stock Option Grant Notice, Notice of Exercise and Option Agreement under 2011 Equity Incentive Plan. <sup>(14)</sup>   |
| 10.6+                 | Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under 2011 Equity Incentive Plan. <sup>(15)</sup>   |
| 10.7+                 | 2011 Employee Stock Purchase Plan. <sup>(16)</sup>  |
| 10.8                  | Lease Agreement, between Metropolitan Life Insurance Company and Registrant, dated January 2, 2007. <sup>(17)</sup>   |
| 10.9                  | Lease between Metropolitan Life Insurance Company and the Registrant, dated December 15, 2011. <sup>(18)</sup>  |
| 10.10                 | Loan and Security Agreement between Registrant and Pinnacle Ventures, L.L.C., as agent for the Lenders (as defined therein) and the Lenders, dated September 16, 2008. <sup>(19)</sup>      |
| 10.11                 | Note and Warrant Purchase Agreement between Registrant and the Purchasers defined therein, dated September 14, 2010, as amended. <sup>(20)</sup>  |
| 10.12                 | Loan and Security Agreement among the Registrant, Hercules Technology II, L.P. and Hercules Technology Growth Capital, dated as of June 29, 2011. <sup>(21)</sup>                           |
| 10.13                 | Award/Contract with the U.S. Army Medical Research and Material Command, dated May 26, 2011. <sup>(22)</sup>  |

## Table of Contents

| Exhibit Number | Description of the Document  |
|----------------|--|
| 10.15+         | Amended and Restated Offer Letter between the Registrant and Larry Hamel, dated December 31, 2010. <sup>(23)</sup>   |
| 10.16+         | Amended and Restated Offer Letter between the Registrant and Badri (Anil) Dasu, dated December 30, 2010. <sup>(24)</sup>   |
| 10.17+         | Amended and Restated Offer Letter between the Registrant and Pamela Palmer, dated December 29, 2010. <sup>(25)</sup>   |
| 10.18+         | Amended and Restated Offer Letter between the Registrant and Richard King, dated December 31, 2010. <sup>(26)</sup>  |
| 10.19+         | Amended and Restated Offer Letter between the Registrant and James Welch, dated December 29, 2010. <sup>(27)</sup>   |
| 10.21+         | Non-Employee Director Compensation Policy. <sup>(28)</sup>   |
| 10.22+         | Summary of 2011 Cash Bonus Plan. <sup>(29)</sup>   |
| 10.23+         | Summary of 2012 Cash Bonus Plan. <sup>(30)</sup>   |
| 10.24          | Securities Purchase Agreement dated May 29, 2012, between the Registrant and the purchasers identified therein. <sup>(31)</sup>  |
| 10.25          | At Market Issuance Sales Agreement, dated August 31, 2012, by and between the Registrant and MLV & Co. LLC. <sup>(32)</sup>  |
| 23.1           | Consent of Independent Registered Public Accounting Firm.  |
| 24.1           | Power of Attorney (included in signature page).  |
| 31.1           | Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.                        |
| 31.2           | Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.                        |
| 32.1           | Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.* |
| 101.INS        | XBRL Instance Document   |
| 101.SCH        | XBRL Taxonomy Extension Schema Document  |
| 101.CAL        | XBRL Taxonomy Extension Calculation Linkbase Document  |
| 101.DEF        | XBRL Taxonomy Extension Definition Linkbase Document   |
| 101.LAB        | XBRL Taxonomy Extension Label Linkbase Document  |
| 101.PRE        | XBRL Taxonomy Extension Presentation Linkbase Document   |

+ Indicates management contract or compensatory plan.

- (1) Incorporated herein by reference to Exhibit 3.1 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on February 18, 2011.
- (2) Incorporated herein by reference to Exhibit 3.4 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (3) Incorporated herein by reference to Exhibit 4.2 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 31, 2011.
- (4) Incorporated herein by reference to Exhibit 4.3 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.
- (5) Incorporated herein by reference to Exhibit 4.4 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.
- (6) Incorporated herein by reference to Exhibit 4.5 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.

## **Table of Contents**

- (7) Incorporated herein by reference to Exhibit 4.4 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on June 30, 2011.
- (8) Incorporated herein by reference to Exhibit 4.5 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on June 30, 2011.
- (9) Incorporated herein by reference to Exhibit 4.8 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on May 30, 2012.
- (10) Incorporated herein by reference to Exhibit 10.1 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (11) Incorporated herein by reference to Exhibit 10.2 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.
- (12) Incorporated herein by reference to Exhibit 10.3 to the Registrant's annual report on Form 10-K (File No. 001-35068), as filed with the SEC on March 30, 2011.
- (13) Incorporated herein by reference to Exhibit 99.3 to the Registrant's registration statement on Form S-8 (File No. 333-172409), as filed with the SEC on February 24, 2011.
- (14) Incorporated herein by reference to Exhibit 10.5 to the Registrant's annual report on Form 10-K (File No. 001-35068), as filed with the SEC on March 30, 2011.
- (15) Incorporated herein by reference to Exhibit 10.6 to the Registrant's annual report on Form 10-K (File No. 001-35068), as filed with the SEC on March 30, 2011.
- (16) Incorporated herein by reference to Exhibit 99.6 to the Registrant's registration statement on Form S-8 (File No. 333-172409), as filed with the SEC on February 24, 2011.
- (17) Incorporated herein by reference to Exhibit 10.8 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.
- (18) Incorporated herein by reference to Exhibit 10.9 to the Registrant's annual report on Form 10-K (File No. 001-35068), as filed with the SEC on March 23, 2012.
- (19) Incorporated herein by reference to Exhibit 10.9 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on November 12, 2010.
- (20) Incorporated herein by reference to Exhibit 10.10 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 31, 2011.
- (21) Incorporated herein by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on June 30, 2011.
- (22) Incorporated herein by reference to Exhibit 10.3 to the Registrant's quarterly report on Form 10-Q (File No. 001-35068), as filed with the SEC on August 11, 2011.
- (23) Incorporated herein by reference to Exhibit 10.14 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (24) Incorporated herein by reference to Exhibit 10.15 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (25) Incorporated herein by reference to Exhibit 10.16 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (26) Incorporated herein by reference to Exhibit 10.17 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (27) Incorporated herein by reference to Exhibit 10.18 to the Registrant's registration statement on Form S-1, as amended (File No. 333-170594), as filed with the SEC on January 7, 2011.
- (28) Incorporated by reference to the information under Item 11. Executive Compensation Director Compensation Non-Employee Director Compensation of this Annual Report on Form 10-K.
- (29) Incorporated herein by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on May 16, 2011.
- (30) Incorporated by reference to the information under Item 11. Executive Compensation Employment Agreements and Arrangements 2012 Cash Bonus Plan of this Annual Report on Form 10-K.
- (31) Incorporated herein by reference to Exhibit 10.23 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on May 30, 2012.
- (32) Incorporated herein by reference to Exhibit 10.1 to the Registrant's current report on Form 8-K (File No. 001-35068), as filed with the SEC on August 31, 2012.
- \* The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed filed by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.