ACELRX PHARMACEUTICALS INC
Form 10-K
March 12, 2013
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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)

Delaware	41-2193603
(State or other jurisdiction of incorporation or organization)	(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:

Title of Each Class	Name of Each Exchange on Which Registered
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 þ

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 þ

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 þ 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 þ 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. þ

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):

Large accelerated filer ¨ Accelerated filer ¨

Non-accelerated filer ¨ (Do not check if a smaller reporting company) Smaller reporting company þ

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2) Yes ¨ No þ

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.

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ACELRX PHARMACEUTICALS, INC.

2012 ANNUAL REPORT ON FORM 10-K

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

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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, co of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Form 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.

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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

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

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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.

Opioid	Therapeutic Index
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.

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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.

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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.

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Our Product Candidates

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

Product Candidate	Description	Target Indication	Development Status
ARX-01	Sufentanil NanoTab PCA System	Moderate-to-severe acute post-operative pain	Three Phase 3 clinical trials were initiated in 2012 as follows:
			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.
			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.
			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.
ARX-02	Sufentanil NanoTab BTP Management System	Cancer breakthrough pain	Phase 2 clinical trial and End of Phase 2 meeting successfully completed.
			Future development contingent upon identification of corporate partnership resources.
ARX-03	Sufentanil/Triazolam NanoTab	Mild sedation for painful procedures in a physician s office	Phase 2 clinical trial and End of Phase 2 meeting successfully completed.
			Future development contingent upon identification of corporate partnership resources.
ARX-04	Sufentanil Single-Dose NanoTab	Moderate-to-severe acute pain	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.

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ARX-01 Sufentanil NanoTab PCA 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.

The Market Opportunity for the NanoTab System

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.

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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.

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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

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.

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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.

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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

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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.

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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.

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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 s 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.

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ARX-02 Sufentanil NanoTab BTP Management 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.

The Market Opportunity for ARX-02

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;

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.

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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.

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ARX-03 Sufentanil/Triazolam NanoTab

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.

The Market Opportunity for ARX-03

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

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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

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.

The Market Opportunity for ARX-04

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.

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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.

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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;

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;

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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.

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.

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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

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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.

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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

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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.

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.

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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.

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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

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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.

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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.

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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;

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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.

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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

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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

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.

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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

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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,

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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.

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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

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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.

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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

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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.

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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

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.

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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.

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.

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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/analgesic products that would present competition to ARX-03. In the future, there may be products developed or approved for this market which could directly compete with ARX-03.

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

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

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

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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.

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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.

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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.

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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.

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As we enter our target markets, it is possible that competitors or other third parties will claim that our products and/or processes infringe their intellectual property rights. These third parties may have obtained and may in the future obtain patents covering products or processes that are similar to, or may include compositions or methods that encompass our technology, allowing them to claim that the use of our technologies infringes these patents.

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

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

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

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

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

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The United States Patent Office has developed new and untested regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, 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.

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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

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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;

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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.

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.

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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

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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.

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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

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.

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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.

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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

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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.

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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	2011	2010	2009	2008	2012
	(in thousands, except share and per share data)					
Statements of Operations Data:						
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	

	As of December 31,				
	2012	2011	2010	2009	2008
			(in thousands)		
Balance Sheet Data:					
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)

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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.

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.

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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.

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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.

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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.

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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.

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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;

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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/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2012	2011	2010	2012 vs. 2011	2011 vs. 2010	2012 vs. 2011	2011 vs. 2010
Research and development expenses	$ 24,908	$ 13,624	$ 8,193	$ 11,284	$ 5,431	83%	66%

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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,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2012	2011	2010	2012 vs. 2011	2011 vs. 2010	2012 vs. 2011	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,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2012	2011	2010	2012 vs. 2011	2011 vs. 2010	2012 vs. 2011	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.

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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,						
	2012	2011	2010	Increase/ (Decrease) 2012 vs. 2011	Increase/ (Decrease) 2011 vs. 2010	Percentage Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2011 vs. 2010
Interest and Other income (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.

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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.

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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;

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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):

		Payment by Period			
Contractual Obligations:	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Operating Lease[1]	$ 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	

(1) 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

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

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Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Not applicable.

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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.

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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 AcelRx Pharmaceuticals internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act):

1. AcelRx Pharmaceuticals management is responsible for establishing and maintaining adequate internal control over financial reporting.

2. AcelRx 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 AcelRx Pharmaceuticals internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of AcelRx 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 AcelRx Pharmaceuticals internal control over financial reporting as of December 31, 2012 and has concluded that such internal control over financial reporting was effective.

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

Item 9B. Other Information

None.

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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

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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., Genocea 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.

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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:

Name	Age	Position
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

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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*. 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.

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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.acelrx.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 ($)	Bonus ($)	Stock Awards ($)[1]	Option Awards ($)[2]	Non-Equity Incentive Plan Compensation ($)[3]	Total ($)
Richard A. King	2012	426,006			616,203	170,400	1,212,609
President and Chief Executive Officer	2011	411,600		425,927	279,955	100,842	1,218,324
James H. Welch	2012	299,000			170,561	95,232	564,793
Chief Financial Officer	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
Chief Medical Officer	2011	385,000		233,199	243,000	89,513	950,712
Lawrence G. Hamel	2012	292,800			120,600	95,160	508,560
Chief Development Officer	2011	283,000		58,302	75,330	70,892	487,524
Badri Dasu	2012	278,000			120,600	93,964	492,564
Chief Engineering Officer	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.

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(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.

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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:

Named Executive Officer	Target Bonus (as a percentage of FY 2011 Base Salary)
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 be 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.

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

Name	Target Award	Actual Award
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:

Named Executive Officer	Target Bonus (as a percentage of FY 2011 Base Salary)
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 be 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:

Name	Target Award	Actual Award
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

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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

	Option Awards				Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)[1]	Market Value of Shares or Units of Stock That Have Not Vested ($)[2]
Richard A. King		262,214[3]	3.39	02/13/2022		
	50,403	64,805[4]	3.45	03/02/2021		
	28,538[5]		2.56[6]	06/15/2020		
	285,381	142,690[7]	2.56[6]	06/15/2020		
					61,729	262,966
James H. Welch		72,579[3]	3.39	02/07/2022		
	10,937	14,063[4]	3.45	03/02/2021		
	70,312	54,688[8]	5.32	11/04/2020		
Pamela P. Palmer, M.D., Ph.D.		231,911[3]	3.39	02/07/2022		
	43,749	56,251[4]	3.45	03/02/2021		
	250,000		2.56[6]	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[3]	3.39	02/07/2022		
	13,562	17,438[4]	3.45	03/02/2021		
	62,500		2.56[6]	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		