ACELRX PHARMACEUTICALS INC
Form 10-K
March 30, 2011
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS PURSUANT TO SECTIONS 13 OR 15(d)

OF THE SECURITIES EXCHANGE ACT OF 1934

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the fiscal year ended December 31, 2010

or

¨ **TRANSITION REPORTS 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.)

575 Chesapeake 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 ¨ No þ

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. 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 February 11, 2011, based upon the closing price of $4.55 as reported on the NASDAQ Global Market, was approximately $20,285,038. Excludes 14,913,500 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. The registrant has elected to use February 11, 2011 as the calculation date, which was the initial trading date of the registrant s common stock on the NASDAQ Global Market, since on June 30, 2010 (the last business day of the registrant s second fiscal quarter), the registrant was a privately-held concern.

As of March 29, 2011, the number of outstanding shares of the registrant s common stock was 19,371,750.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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ACELRX PHARMACEUTICALS, INC.

2010 ANNUAL REPORT ON FORM 10-K

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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 to complete the third ARX-01 Phase 3 clinical trial required to file our new drug application, or NDA, with the U.S. Food and Drug Administration, or FDA, for ARX-01;
- 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 specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. We were founded to solve the problems associated with post-operative intravenous patient-controlled analgesia, or IV PCA. Although widely used, IV PCA has been shown to cause harm to patients following surgery because of the side effects of morphine, the invasive IV route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps. We are preparing to initiate two Phase 3 clinical trials for our lead product candidate, the Sufentanil NanoTab PCA System, or ARX-01. The system is designed to address these problems by utilizing:

- sufentanil, a high therapeutic index opioid;
- NanoTabs, our proprietary, non-invasive sublingual dosage form; and
- our novel handheld PCA device that enables simple patient-controlled delivery of NanoTabs in the hospital setting and eliminates the risk of programming errors.

We have completed Phase 2 clinical development for two additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, for the treatment of cancer breakthrough pain, or BTP, and the Sufentanil/Triazolam NanoTab, or ARX-03, designed to provide mild sedation, anxiety reduction and pain relief for patients undergoing painful procedures in a physician s office.

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.

The Market Opportunity for Our Product Candidates

ARX-01 Acute Post-Operative Pain

According to the 2010 Decision Resources Acute Pain report, the 2018 post-operative pain market is projected to be $6.5 billion for the United States, Europe and Japan. Opioids are the most efficacious analgesics available to control acute pain and are estimated to represent 74% of the overall post-operative pain market in the United States. Despite the broad array of pain products available, the need for adequate pain relief continues to be a significant issue. According to a report published in 2008 by Datamonitor, 75% of patients reported inadequate pain relief after surgery.

In the post-operative environment, the most common method for the treatment of acute pain is through IV PCA, in which patients self-dose by pushing a button to administer morphine via a programmable intravenous pump. Despite the common use of IV PCA, there are many deficiencies associated with this treatment that create a significant unmet medical need, including:

- *Drug-Related Side Effects*. Morphine, the most commonly used opioid for post-operative pain control, can produce many side effects, such as excessive somnolence, delirium, oxygen desaturation and respiratory depression. Morphine has active metabolites, the compounds that are produced when the body breaks down, or metabolizes, morphine, which amplify these side effects.
- *Complications Associated with IV Delivery*. IV PCA poses infection risk and creates opportunities for analgesic gaps due to dislodged catheters. Peripheral venous catheters have been associated with a 7% to 9% incidence of phlebitis and a 0.2% to 0.4% incidence of bacteremia. Catheter tubing tethering the patient to the PCA pump also hinders early post-operative mobility that can

lead to increased post-operative complications.

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Medication Delivery Errors. The complexity associated with ordering, dispensing, preparing, programming and administering the IV PCA pump results in many analgesia related errors. Human factors, such as programming the PCA pump, or administering the wrong dose, are among the most common and serious type of 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 a national medication error-reporting program, or 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 Manufacturer and User Facility Device Experience, or 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. Recently, the risks associated with the use of infusion pumps, such as those used in IV PCA, have been the subject of scrutiny by the FDA, resulting in a new initiative to address the safety problems associated with infusion pumps and the underreporting of errors. 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.

ARX-01 is designed to avoid many of the limitations of IV PCA by delivering sufentanil, a high therapeutic index opioid, using our proprietary NanoTab sublingual tablet via non-invasive, pre-programmed, handheld PCA device. We have completed three Phase 2 studies with ARX-01 and had an End of Phase 2 meeting with the FDA which defined the required scope and scale for Phase 3 studies, certain formulation requirements, non-clinical and regulatory requirements. We believe ARX-01 has the opportunity to become the new standard of care for post-operative patient-controlled analgesia.

ARX-02 Cancer Breakthrough Pain

Breakthrough pain is a common component of chronic pain and is characterized by its rapid onset, intensity and relatively short duration, which breaks through the analgesic effect of chronic pain medication. According to data published in 2006, more than 700,000 cancer patients in the United States experienced breakthrough pain. Fentanyl-based products are the only medications indicated to treat cancer breakthrough pain and account for less than 20,000 prescriptions per month. We believe this demonstrates a need for additional and improved cancer breakthrough pain medications. Data from the 2010 Decision Resources Acute Pain report indicates that the worldwide breakthrough pain market will grow to $2.9 billion by 2018.

Currently available fentanyl-based cancer breakthrough pain products have limited ability to provide effective and focused pain relief because their average half-lives extend to 6 to 14 hours, which is significantly longer than the average 15 to 60 minute duration of a cancer breakthrough pain episode. Oral transmucosal fentanyl, unlike sufentanil, is extensively absorbed through the gastrointestinal, or GI, tract in addition to the oral mucosal tissue, leading to erratic and delayed timing to peak plasma levels, ranging from 20 to 240 minutes. This can result in a dangerous phenomenon, known as dose-stacking, which occurs when a repeat dose is administered before the peak effect of the previous dose, and can lead to significant side effects, such as respiratory depression.

In addition to the medical limitations of currently approved opioids, the abuse of opioid pain medications is a significant medical and social problem. According to the 2010 National Survey on Drug Use and Health, during 2009 approximately 5.2 million people in the United States used prescription pain relievers for nonmedical purposes, an increase from the estimated 4.7 million in 2005. We believe none of the currently approved cancer breakthrough pain products have effective abuse-deterrent features to address these problems.

ARX-02 is designed to avoid many of the limitations of currently available cancer breakthrough pain medications by combining the rapid onset and appropriate offset of sufentanil with abuse-deterrent packaging. We have completed a Phase 2 study with ARX-02 and had an End of Phase 2 meeting with the FDA that defined the required criteria for Phase 3 studies.

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ARX-03 Mild Sedation and Pain Relief for Procedures in a Physician s Office

Each year in the United States, more than 100 million procedures take place in a physician s office. A substantial subset of these procedures are painful and anxiety inducing, including many interventional radiology procedures, diagnostic procedures such as breast and prostate biopsies, cosmetic procedures such as liposuction and dermal abrasions, and therapeutic procedures such as vasectomies. Ninety-six percent of men report moderate pain immediately after prostate biopsy, with only 4% of patients reporting no pain during the biopsy. In addition, 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.

Intravenous sedation requires specialized monitoring, resuscitative equipment and appropriately trained staff for effective management of patients. As a result, many practitioners have stopped providing any sedation or analgesic medications to their patients prior to or during short duration procedures, and instead rely solely on local anesthetic injections, which are often insufficient in providing effective pain relief and anxiety reduction.

We are developing ARX-03 as a non-invasive method to produce sedation, anxiety reduction and pain relief in patients undergoing painful procedures in a physician s office. ARX-03 is designed to eliminate the need for specialized personnel and requires only minimal monitoring equipment. We have completed a Phase 2 study with ARX-03, and have preliminary guidance as to a clinical development path for this product as a result of completion of an End of Phase 2 meeting with the FDA.

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 studies 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 despite its potency, sufentanil can be developed to provide an effective and relatively safe solution for the treatment of 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

Although the analgesic efficacy of sufentanil has been well established, its use has been limited due to its short duration of action when delivered intravenously. 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. In addition, its pharmacokinetic, or PK, profile when delivered sublingually avoids the high peak plasma levels and short duration of action of IV administration.

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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 three products under development. These studies demonstrated desirable and consistent PK parameters, including:

- relatively high bioavailability via the oral mucosa and very low 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.

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 below, 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.

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.

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None of our product candidates have been approved by the FDA. We have not generated any revenue from the sale of any of our product candidates.

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	Acute post-operative pain	Three Phase 2 clinical trials and End of Phase 2 meeting successfully completed
			Two efficacy trials and one open label safety trial planned in Phase 3; the first efficacy trial and the open label safety trial are anticipated to begin in the second half of 2011
ARX-02	Sufentanil NanoTab BTP Management System	Cancer breakthrough pain	Phase 2 clinical trial and End of Phase 2 meeting successfully completed
			One efficacy trial and two open label safety trials planned in Phase 3
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
			Two efficacy trials planned in Phase 3

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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 ARX-01

The post-operative pain market in the United States, Europe and Japan is growing steadily and is expected to reach $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 Decision Resources Acute Pain report projects that in 2013, 24.6 million in-patient procedures performed in the United States, Europe and Japan will require post-operative treatment of pain, growing at a rate of approximately 1% per annum.

Market research among surgeons and anesthesiologists has identified a consistent positive response to the attributes of ARX-01 and indicates an interest in using ARX-01 in 85% of their eligible patients. Additionally, physicians expressed interest in using ARX-01 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 ARX-01, with 91% of those interviewed indicating likely adoption to formulary.

How ARX-01 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 manufacturers to address safety problems.

ARX-01 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.

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We believe that ARX-01 will provide a favorable safety, efficacy and tolerability profile, enabling ARX-01 to become the new standard of care for patient-controlled analgesia. Further, we believe use of ARX-01 will result in increased patient satisfaction and reduced overall healthcare costs.

ARX-01 Description

ARX-01 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 Sufentanil NanoTab PCA System, ARX-01, consists of three components:

- sufentanil, a high therapeutic index opioid;
- NanoTabs, our proprietary, non-invasive sublingual dosage form; and
- our novel handheld PCA device that enables simple patient-controlled delivery of NanoTabs in the hospital setting and eliminates the risk of programming errors.

ARX-01 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 handheld PCA device consists of a stack of 40 sufentanil 15 mcg NanoTabs (approximately a two-day supply) in a disposable radio frequency identification and bar-coded cartridge (see Figure 1); a disposable dispenser tip (see Figure 2); and a reusable, rechargeable handheld controller (see Figure 3).

Figure 1, Cartridge with NanoTab Tablets *Figure 2, Dispenser Tip* *Figure 3, Controller*

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.

Our novel handheld PCA device has the following safety features:

- 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;

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

fully automated inventory record of NanoTabs usage.

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To set up the handheld PCA device, the nurse or healthcare professional turns on the controller and follows the simple step by-step instructions 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 ARX-01, 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.

During our Phase 2 clinical study, 100% of patients reported that they could handle the system easily and that user instructions were clear.

Sufentanil NanoTab PCA System ARX-01 Clinical Program

Summary

We have completed three successful Phase 2 clinical trials of sufentanil NanoTabs in the post-operative setting. These studies demonstrated analgesic efficacy, a low adverse event profile and excellent device functionality. We held an End of Phase 2 meeting with the FDA at the end of 2009. The FDA stated that the demonstration of efficacy versus placebo in two Phase 3 studies with a total safety database of at least 600 patients exposed to the active drug, should suffice to support an NDA. We are designing our Phase 3 trials based on the feedback from the FDA.

Planned Phase 3 Clinical Trials for ARX-01

We plan to conduct two Phase 3 trials to evaluate the efficacy of ARX-01. In addition, we plan to conduct one Phase 3 open-label active comparator study that will provide both incremental safety and marketing data. Manufacturing scale up activities and Phase 3 clinical trial planning are ongoing to enable initiation and patient enrollment in our first Phase 3 efficacy trial in the second half of 2011. We expect to start the Phase 3 active comparator study in early 2012. We expect to receive the top-line data from these two trials in the first half of 2012. Contingent on our ability to secure additional funding, we plan to begin a second Phase 3 efficacy study in the second half of 2012 and submit an NDA in 2013 if the results from these studies are positive.

Our first Phase 3 clinical study on ARX-01 will be a placebo-controlled trial for a minimum of 48 hours and, as needed, up to 72 hours in adult patients undergoing open abdominal surgery. The objective is to compare the efficacy of ARX-01 to placebo for the management of acute post-operative pain. Approximately 165 patients will be randomly assigned to treatment with sufentanil or placebo. The primary endpoint will be the summed pain intensity difference over the first 48 hours of the study period, or SPID-48. This value is obtained for each patient by subtracting all pain intensity scores after drug dosing from the patient s baseline score prior to dosing, and then adding these pain intensity differences together to obtain that patient s SPID score.

Our second Phase 3 study will be an active comparator study of ARX-01 versus morphine IV PCA in patients undergoing orthopedic or abdominal surgery. Approximately 390 patients will be randomly assigned to treatment with Sufentanil NanoTab PCA System or morphine IV PCA. The primary endpoint will be the demonstration of

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statistical non- inferiority between the two groups for global patient satisfaction over the course of the study by patient reporting on a 4-point rating scale of poor, fair, good and excellent. Important secondary endpoints for comparison to IV PCA morphine will be drop-out due to inadequate analgesia, level of sedation, ease of care for patients and nurses, reporting of analgesic gaps and interdosing intervals.

Contingent on our ability to secure additional funding, our third Phase 3 clinical study will be a placebo-controlled trial in patients who are undergoing a total hip or knee replacement under general or spinal anesthesia. The objective is to compare the efficacy of the Sufentanil NanoTab PCA System to placebo for the management of acute post-operative pain. Approximately 484 patients will be randomly assigned to treatment with sufentanil or placebo. The primary endpoint also will be the SPID-48.

The ARX-01 Phase 3 device will be an upgraded version of the Phase 2 device, with enhanced features, including a color graphical user interface screen, security features to allow only the patient to use the device and prevent unauthorized access to the drug and improved industrial design for hospital use. The design of the Phase 3 device is at an advanced engineering prototype stage where several standalone prototypes have been built to conduct testing. Many of the subsystems within the device have not yet been integrated or tested to the specifications of the Phase 3 device design.

ARX-01: Sufentanil NanoTab PCA System Phase 2 Studies

We completed three Phase 2 studies in support of sufentanil NanoTabs. Across all studies, 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 serious adverse events, or SAEs, were reported that were considered to be related to the study 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.

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

In the first Phase 2 study, we conducted a randomized, double-blind, placebo-controlled, multicenter Phase 2 clinical study to evaluate the efficacy, safety and tolerability of sublingual sufentanil NanoTabs in patients undergoing elective unilateral knee replacement. The study 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 study 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 study duration, or SPID-12.

The study 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. A p-value is a probability with a value ranging from 0 to 1, which indicates the likelihood that a clinical study is different between treatment and control groups. P-values below 0.05 are typically referred to as statistically significant. 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 study there were statistically significant differences in SPID 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 study. The five SAEs reported were all considered unrelated to study drug and occurred after the end of study drug dosing.

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The following figure shows the Summed Pain Intensity Difference over the 12-Hour Study Period for the placebo, 5 mcg, 10 mcg and 15 mcg groups.

* Intent-to-Treat Population: The intent-to-treat, or ITT, population includes all randomized patients regardless of whether they received or adhered to the allocated treatment group. ITT analysis provides unbiased comparisons among the treatment groups and is the primary statistical analysis used by the FDA.

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Phase 2 Clinical Results in Major Abdominal Surgery (ARX-C-005)

Our second Phase 2 study tested sufentanil NanoTabs 10 mcg, 15 mcg, or placebo in patients undergoing major abdominal surgery. In all other respects this study was similar in design to our first study. 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 study 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 study. There were no SAEs reported during the study drug treatment period. The following figure shows the SPID-12 for the placebo, 10 mcg and 15 mcg groups.

Phase 2 Clinical Results for ARX-01 in Open-Label Device Functionality Study in Unilateral Knee Replacement (ARX-C-004)

We conducted an open-label functionality, safety and efficacy study of the ARX-01 NanoTab delivery system in patients undergoing elective unilateral knee replacement surgery. The study 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 study without any Sufentanil NanoTab PCA System failures. The study also collected patient feedback on the design characteristics of the PCA System.

Patients self-administered sufentanil NanoTabs repeatedly over the 12-hour study using the ARX-01 Sufentanil NanoTab PCA 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 was 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 study drug treatment period.

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Summary of Phase 2 Adverse Events

Overall the AE profile for the three Phase 2 studies suggests that ARX-01 is well-tolerated compared to typical AE rates seen with post-operative opioids. Published data indicates a much higher rate of somnolence (approximately 50%) and oxygen desaturation (approximately 10%) during standard IV PCA use compared to results obtained in our Phase 2 studies. The high therapeutic index of sufentanil (26,716) in animal studies suggests that opioid-induced sedation and oxygen desaturation does not occur with sufentanil until doses much higher than required for analgesia are administered. We believe our Phase 2 AE data confirm the high safety index of sufentanil. The table below summarizes the investigator s rating of probably or possibly related AEs based on sufentanil NanoTab dosage strength.

Adverse Events	Placebo N=54	Sufentanil NanoTab (5 mcg) N=24	Sufentanil NanoTab (10 mcg) N=55	Sufentanil NanoTab (15 mcg) N=79
Nausea	17(31%)	7(29%)	22(40%)	23(29%)
Vomiting	3(6%)	2(8%)	6(11%)	9(11%)
Itching	0(0%)	1(4%)	4(8%)	6(8%)
Somnolence	1(2%)	1(4%)	0(0%)	2(3%)
Oxygen desaturation	0(0%)	0(0%)	1(2%)	1(1%)
Respiratory depression	1(2%)	0(0%)	2(4%)	0(0%)

ARX-02 Sufentanil NanoTab BTP Management System

Market Opportunity for ARX-02

According to published data, in 2006 more than 700,000 cancer patients in the United States experienced 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.

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.

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. Given the positive reaction to the product profile and the potential benefits of ARX-02 compared to currently available products, we believe that ARX-02 represents a significant commercial opportunity.

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;

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- 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 studies; 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.

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 single dose applicator includes a sufentanil NanoTab that a patient can self-administer to their 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

Summary

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 study 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.

Planned Phase 3 Clinical Trials for ARX-02

We plan to conduct one Phase 3 efficacy study for ARX-02 for the management of cancer breakthrough pain in adult patients, who are already taking opioids for their underlying persistent cancer pain. In addition, we plan to conduct two open-label studies to demonstrate long term safety, which will include the use of the MSD.

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The first planned Phase 3 clinical study for ARX-02 is a multi-center, randomized, double-blind, placebo-controlled crossover study for the evaluation of the safety and efficacy of the Sufentanil NanoTab BTP Management System in the treatment of cancer breakthrough pain. We plan to screen 170 patients in order to titrate approximately 140 patients, of which 110 patients will be randomized, such that at least 100 patients will generate primary efficacy data for analysis. The planned study consists of a screening visit, an open-label titration phase of up to three weeks to establish a dose of sufentanil (20, 30, 40, 60, 80 or 100 mcg) at home or in a hospice setting, that provides adequate relief of cancer breakthrough pain with tolerable side effects. This will be followed by a randomized, double-blind treatment phase of up to three weeks. Patients will be randomized to one of six sequences, each including nine doses of which six are active and three are placebo. Patients will use an electronic diary to record primary and secondary efficacy outcomes including pain intensity, pain relief, and global evaluation of treatment. The primary endpoint is the time-weighted summed pain intensity difference over 30 minutes, SPID-30, following treatment.

Patients who complete our Phase 3 efficacy trial will be allowed to participate in an open-label extension study to continue evaluating the safety of ARX-02 for up to one year. During each month while participating in the study, patients will present to the clinical site for visits to assess their medical status and proper use of study medication. The primary objective is to determine the long-term safety of sufentanil NanoTabs in patients with cancer breakthrough pain.

The dispensing device that was used in the Phase 2 study for ARX-02 was a simple, mechanical single dose applicator, or SDA, designed for a single use. The design for Phase 3 device contains both mechanical and electronic components and is intended to be a multiple use device with a magazine containing smaller SDAs than those used in Phase 2. The magazine is loaded into a multiple SDA dispenser, or MSD, which will include software to electronically track removal of each SDA from the MSD. Several industrial models have been developed that depict the size and form factor of the smaller SDA and the MSD.

We also plan to conduct an additional open-label study to ensure there is adequate data for analysis of drug safety and device functionality. We plan to screen approximately 470 patients in order to titrate approximately 370 patients, such that at least 300 patients will enroll in this study. Patients will use the MSD that will contain a magazine holding 30 SDAs. Each SDA will contain a single sufentanil NanoTab. The MSD will electronically track removal of each SDA from the MSD in order to record dosing history in the outpatient setting. This study will be up to three-months in duration and will utilize the same titration scheme as in the Phase 3 efficacy study. After patients achieve an efficacious and tolerable dose, they will use the MSDs to dispense the SDAs throughout the 3-month study.

Phase 2 Clinical Results for ARX-02

We have completed a Phase 2 study of the analgesic efficacy of the sufentanil NanoTab in adult cancer patients who are opioid tolerant and suffering from breakthrough pain events. This study was a prospective, multicenter, randomized, placebo-controlled multicenter, crossover study for the evaluation of the safety, efficacy and tolerability of the Sufentanil NanoTab BTP Management System in the treatment of cancer breakthrough pain.

Patients were screened and, if qualified for the study, would titrate to an effective dose of sufentanil that provided adequate relief of cancer breakthrough pain without producing intolerable side effects. Patients self-administered a single sufentanil NanoTab using a single-dose applicator, starting with a 20 mcg dose, followed by titration with 30, 40, 60 and 80 mcg sufentanil NanoTabs. The primary objective during the titration phase was to assess the safety and efficacy of ARX-02. The primary endpoint during the randomized, double-blind phase was to assess the efficacy of ARX-02 compared to placebo in the management of cancer breakthrough pain as determined by SPID-30.

Once a dosage strength that alleviated pain without producing intolerable side effects was identified, the patient was randomized to that dosage strength in the double-blind phase of the study. Patients were randomized to receive 10 doses, of which seven were active and three were placebo. Efficacy was assessed by patient data

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recorded and scored in an electronic diary, including pain intensity, pain relief, and global medication performance assessment just prior to and after taking each of the ten doses of study drug in the double-blind phase of the study. Forty-two patients were enrolled and received titration study medication. Eighty-four percent of patients with a mean age of 53.5 years (range 25 to 73 years) were randomized to the double-blind treatment period. Thirty-three patients completed the study.

The primary endpoint of time-weighted SPID-30 for sufentanil NanoTab-treated episodes was greater than placebo-treated episodes ($p<0.001$) as shown in the figure below.

* Modified Intent-to-Treat Population: The modified intent-to-treat population is a subset of the ITT population and included all randomized patients who took at least one active dose and one placebo dose, and had pre-treatment and at least one post-treatment pain intensity score for each of these episodes.

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).

Patient Global Medication Performance Assessment, or GMPA, at 60 minutes after each dose of study medication showed 59 (27.4%) and 37 (17.2%) of the sufentanil-treated episodes were rated as very good or excellent on the GMPA, respectively, compared with seven (7.5%) and nine (9.7%) in the placebo-treated episodes. There was a statistically significant difference for GMPA measurements between the sufentanil-treated episodes and the placebo-treated episodes ($p<0.001$).

Three patients reported an SAE; however, all SAEs were considered unrelated to study drug. The most common AEs were nervous system disorders, general disorders, and gastrointestinal disorders. The most common nervous system disorder was dysgeusia, or altered sense of taste (four patients, 9.5%). The most common gastrointestinal disorder was dry mouth (three patients, 7.1%). The most common AEs were nervous system disorders, general disorders, and gastrointestinal disorders. The most common nervous system disorder was headache (two patients, 5.9%). The most common gastrointestinal disorder was nausea (three patients, 8.8%). There was no statistical difference between sufentanil and placebo treatments for any AE.

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There were a few statistically significant mean changes and no clinically significant changes from baseline in hematology and chemistry variables. During the safety monitoring period at the site, there were no statistically significant changes from baseline in heart rate or respiratory rate, and no clinically significant changes in oxygen saturation.

ARX-03 Sufentanil/Triazolam NanoTabs

The Market Opportunity for ARX-03

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

Each year in the United States, more than 100 million procedures take place in a physician s office that are known to be anxiety-inducing and painful. These procedures 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, causing unnecessary 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

Summary

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. We held End of Phase 2 meeting with the FDA in May 2010 to discuss the Phase 3 clinical program and requirements for NDA filing. Two four-arm factorial Phase 3 studies will be required with a minimum of 700 patients exposed to active drug.

Planned Phase 3 Clinical Trials for ARX-03

We plan to conduct two Phase 3 efficacy studies in a range of painful procedures, such as prostate biopsy, breast biopsy, vasectomy and low-volume abdominal liposuction. In each study, approximately 720 patients will be randomized to treatment with one of the following: sufentanil/triazolam 15 mcg/200 mcg NanoTab, sufentanil 15 mcg NanoTab, triazolam 200 mcg NanoTab, or placebo NanoTab. We intend to evaluate the time-weighted summed Richmond Agitation-Sedation Scale, or RASS, score over the 4-hour study period, or SRS-4, compared to placebo as the primary efficacy endpoint. RASS is a ten-point scale to evaluate agitated behavior where unarousable is graded as -5 and combative is graded as a +4 and a score of 0 is alert and calm. Secondary endpoints are intended to include comparisons of SRS-4 among active comparator arms, patient report of procedural anxiety and pain intensity using an 11-point Numerical Rating Scale, or NRS, patient and physician global assessments of satisfaction with study drug, and time to a modified Aldrete score of 8 (readiness for discharge measurement).

There was no dispensing device used in the ARX-03 Phase 2 studies. Tablets were placed in the patients sublingual space through the use of forceps. The design for Phase 3 device for ARX-03 consists of a simple mechanical dispenser or SDA. We have produced several working prototypes.

Phase 1 and Phase 2 Clinical Results for ARX-03

We completed an initial dose finding study for three different strengths of sublingual Sufentanil/Triazolam NanoTabs (10 mcg/100 mcg, 10 mcg/200 mcg and 15 mcg/200 mcg) in 24 subjects. The onset of sedation was approximately 40% faster with the sufentanil 15 mcg/triazolam 200 mcg NanoTab treatment compared to the sufentanil 10 mcg/triazolam 200 mcg NanoTab treatment in younger subjects. There were minimal differences between treatments for time to maximum sedation and for total duration of sedation, leading us to select the sufentanil 15 mcg/triazolam 200 mcg NanoTab dosage strength to study further in a Phase 2 trial.

We completed a Phase 2 study of analgesic and anxiety reducing efficacy of the sufentanil/triazolam NanoTab in patients undergoing an elective abdominal liposuction procedure. The study was a prospective, randomized, double-blind, placebo-controlled single center study in adult patients. Patients were randomly assigned to treatment with the sufentanil 15 mcg/triazolam 200 mcg NanoTab or placebo. Forty-one patients were randomized and 40 patients received study drug and underwent the procedure and completed the 4-hour study period. The mean age for all randomized patients was 36.7 years (range 19 to 55 years). The primary endpoint was the SRS-4 and the sufentanil/triazolam NanoTab demonstrated superiority over placebo ($p<0.001$). The sufentanil/triazolam NanoTab was more effective than placebo in reducing anxiety as measured by the secondary endpoint, the NRS anxiety scale. A significant difference ($p<0.05$) in anxiety score between the sufentanil/triazolam NanoTab and placebo was seen at 15 minutes, the first time point measured after study drug dosing.

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The sufentanil/triazolam NanoTab did not show a statistical difference from placebo in providing analgesia as measured by the NRS pain intensity scale (p=0.311). The summed pain intensity score was lower for the sufentanil/triazolam NanoTab compared to placebo for all time points; however, the difference was not significant with the small number of patients.

There was a statistically significant difference between the sufentanil/triazolam NanoTab treatment group and placebo (p<0.001) in the proportion of patients for which the physician rated the treatment very good or excellent on the global assessment of effectiveness and tolerability. There was also a statistically significant difference between the sufentanil/triazolam NanoTab treatment group and placebo (p=0.028) for the proportion of patients who rated the treatment very good or excellent on the global assessment of effectiveness and tolerability. All patients in both the sufentanil/triazolam NanoTab treatment group and the placebo group were ready for discharge immediately following the procedure.

There were no SAEs reported during treatment or 12 hours after dosing. The most frequent AE was nervous system disorders, which were observed in two patients (9.5%) in the sufentanil/triazolam NanoTab treatment group and in two patients (10.5%) in the placebo group. Dizziness was also reported by two patients (9.5%) in the sufentanil/triazolam NanoTab treatment group and one patient (5.3%) in the placebo group. There were no significant differences between the treatment groups for any AEs. All events were mild or moderate in severity. There were no clinically significant changes in vital signs or oxygen saturation during the study.

Other potential applications for our NanoTab technology

We believe that as a platform technology, the NanoTab, either as a stand alone dosage form or in conjunction with various forms of dispensing mechanisms, has the potential to enable other product candidates utilizing sufentanil or 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. We believe our pending patent filings and issued European patent will broadly protect NanoTab compositions and their use in oral transmucosal delivery of compounds other than sufentanil.

One such opportunity is in the treatment of acute pain in medically supervised settings. According to the American Hospital Association, there were 127 million emergency room, or ER, visits and 17 million hospital-based outpatient surgeries in the United States in 2009. In addition, according to the Ambulatory Surgery Center Association, over 22 million procedures were conducted in ambulatory surgery centers in the United States in 2008. Typically, patients requiring pain relief in these settings have most commonly been treated with either opioids or anti-inflammatory agents in either injectable or oral form. Injectable medications require invasive IV or intramuscular, or IM, administration. In many cases, patients do not have readily available IV access, such as upon admission to the ER, ambulatory care environments or in the field during civilian and military patient transport. IM injections are painful and present an increased risk of infection. The oral route does not offer a rapid or consistent onset of action, which limits the ability to provide effective pain relief.

We believe there is significant opportunity for a single-dose, rapid-acting, non-invasive analgesic to treat acute pain in these medically supervised settings. We believe that providing non-invasive, sublingual delivery of higher doses (20-30 mcg) of the high therapeutic index opioid sufentanil, utilizing our proprietary NanoTab technology, delivered with a SDA by a health care professional could address this need. If we are able to secure additional financial resources beyond our IPO, we plan to commence clinical development of this product concept for the treatment of moderate-to-severe acute pain in a medically supervised setting.

Our Strategy

Our strategy is to develop and commercialize a portfolio of sufentanil NanoTab-based products in specialty markets. We have designed and are developing product candidates which have clearly defined clinical development programs, target large commercial market opportunities and require modest commercial

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organizations in the United States. We selectively utilize third party contractors in order to maximize the capital efficiency of our development and commercialization efforts. We plan to enter into partnerships to market our product candidates outside the United States.

Our lead program, ARX-01, is focused on the management of post-operative pain in the hospital setting. Our second program, ARX-02, is focused on the management of cancer breakthrough pain. Both of these product candidates have completed Phase 2 development. We intend to advance ARX-01 into two Phase 3 trials, and contingent on our ability to secure additional funding, we plan to complete the third ARX-01 Phase 3 clinical trial, submit an NDA and, if approved, to commercialize ARX-01 ourselves in the United States. Based on the availability of financial resources, we plan to advance ARX-02 into Phase 3 trials, submit an NDA and, if approved, commercialize ARX-02 ourselves or with a partner in the United States. Further development of ARX-03 will depend on the identification of a partner to support this effort.

Our specific strategy with respect to ARX-01 is to:

- complete one Phase 3 efficacy study and one Phase 3 active comparator study following our IPO, and contingent on the availability of additional funding, complete the third Phase 3 study and seek regulatory approval in the United States and other countries;
- establish at least one commercial relationship in North America for the manufacturing of the components of the Sufentanil NanoTab PCA system;
- build a targeted hospital-directed sales force in the United States; and
- partner with third parties for commercialization outside of the United States.

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 ARX-01 to the United States market as we move towards NDA submission and approval. We foresee two stages of commercial execution to support successful introduction of ARX-01 in the United States:

In parallel with our Phase 3 clinical studies, we plan to:

- highlight the clinical and health economic data identifying the limitations of IV PCA in use today;
- increase awareness of the development of ARX-01 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 ARX-01 effectively at the time of commercial launch;
- establish advisory boards with anesthesiologists, surgeons and nurses to provide us with input on appropriate commercial positioning for ARX-01 for each of these key audiences; and

design a post-approval clinical development program, including potential head-to-head superiority studies with IV PCA.

Following FDA approval, we plan to:

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

establish ARX-01 on hospital formularies through deployment of an experienced team to describe the clinical and pharmacoeconomic benefits of ARX-01 in comparison to IV PCA;

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conduct post-approval clinical program for ARX-01;

establish ARX-01 as the product of choice for traditional post-operative PCA; and

expand the market through deployment of ARX-01 for 24 hour stay patients, where IV PCA is not used today.

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 Item 1A. 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 December 31, 2010, we held 15 pending United States utility patent applications, and 39 foreign national patent applications covering various aspects of our product candidates. We also hold a European Patent, EP2114383, granted on July 21, 2010, validated and translated in Switzerland, Germany, Denmark, Spain, France, the United Kingdom, Italy, the Netherlands, Portugal and Sweden, with an expiration date of December 28, 2027, excluding any additional term for patent term adjustments. We also hold three pending Patent Cooperation Treaty applications that have not yet been nationally filed.

We seek patent protection for both compositions of matter, as well as methods of treatment related to our ARX-01, ARX-02 and ARX-03 product candidates. We are pursuing composition of matter claims for our ARX-01, ARX-02 and ARX-03 NanoTabs and formulations, our ARX-01 PCA devices, the combination of drugs and our ARX-01 PCA devices, our ARX-02 and ARX-03 SDAs, as well as to methods of treatment using such drug and device compositions.

Issued European Patent No. EP2114383 includes composition of matter claims directed to ARX-01, ARX-02 and ARX-03 NanoTabs for oral transmucosal delivery of sufentanil, alone and in combination with key features of the ARX-01 PCA device, the ARX-02 and ARX-03 SDAs, and use of the claimed compositions in the treatment of pain.

We have filed for patent coverage in the United States, Europe, 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.

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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. Our ACELRX mark has also been registered in the European Community and Canada, and is pending in India. We have filed for trademark protection in the United States for the NanoTab mark, which we use in connection with our pharmaceutical product candidates, and the ACCELERATE, INNOVATE, ALLEVIATE tagline.

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, reliability, convenience of dosing, price and reimbursement.

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 ARX-01

We are developing ARX-01, the Sufentanil NanoTab PCA System, for the management of acute post-operative pain in adult patients during hospitalization. We believe that ARX-01 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 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. MOD is a unit that is locked onto an IV pole within the patient s reach and allows patients to access their oral pain medication. Other products under development for the treatment of post-operative pain that we are aware of include:

Fentanyl iontophoretic transdermal system, IONSYS, originally developed by ALZA Corporation and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson subsidiaries.

IONSYS received NDA approval in May 2006 in the United States; however, the product was never launched. IONSYS was approved in Europe but the Marketing Authorization was suspended by the EMA in November 2008. IONSYS is currently under development by Incline Therapeutics, Inc.

Rylomine, an intranasal morphine product developed by Javelin Pharmaceuticals, Inc., and currently in Phase 3 trials in the United States and in Phase 2 in Europe.

There are a number of non-opioid drugs in development that are delivered either systemically or locally for the treatment of acute post-operative pain. These drugs are usually evaluated for their ability to treat milder types of pain (for example, the day following laparoscopic surgery) or to decrease, but not replace, the need for post-

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operative opioids. Therefore, we do not believe that these product candidates will compete with ARX-01 because they will not be utilized commercially as the sole method of treating acute post-operative pain immediately following surgery, which is the role of ARX-01.

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. We expect that ARX-02, if approved, may compete with these commercial products listed in the table below.

Product Name	Company	Formulation	Commercial Market
ACTIQ	Cephalon, Inc.	Oral fentanyl transmucosal lozenge	United States
FENTORA/ EFFENTORA	Cephalon, Inc.	Fentanyl buccal tablet	United States and European Union
Onsolis	Meda Pharmaceuticals Inc. / BioDelivery Sciences International, Inc.	Fentanyl buccal soluble film	United States
Abstral	ProStrakan Group plc	Sublingual fentanyl tablet	United States and European Union
Instanyl	Nycomed International Management GmbH	Fentanyl nasal spray	European Union
PecFent	Archimedes Pharma Limited	Fentanyl nasal spray	European Union
Fentanyl Citrate (Oral Transmucosal)	Teva Pharmaceuticals USA	Oral fentanyl transmucosal lozenge	United States

Additionally, we are aware of the following products in late stage development for cancer breakthrough pain:

Fentanyl TAIFUN, an inhaled fentanyl product developed by Akela Pharma, Inc., and currently in Phase 3 clinical trials.

Fentanyl SL Spray, a fentanyl sublingual spray developed by Insys Therapeutics, Inc., and currently in Phase 3 clinical trials.

If approved, these product candidates could compete directly with ARX-02.

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.

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Pharmaceutical Manufacturing and Supply

We currently rely on contract manufacturers to produce sufentanil and sufentanil/triazolam NanoTabs for our clinical studies under 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 drug product manufacturers that could satisfy our clinical study requirements but this would require a significant delay in setting up the facility and moving equipment. Additionally, should a supplier or a manufacturer on whom we rely to produce a product candidate provide us with a faulty product or such product is later recalled, we would likely experience significant delays and material additional costs.

Device Manufacturing and Supply

The ARX-01 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 ARX-01 system. FDA regulations require that materials be produced under cGMPs 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; 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 the ARX-02 system. 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; filling, packaging and labeling of SDAs.

Government Regulation And Product Approval

Government authorities in the United States at the federal, state and local level, and 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 new drug application, or NDA, process before they may legally be marketed in the United States.

United States Drug Development Process

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 compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, 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 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 studies and formulation studies according to Good Laboratory Practices regulations;

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submission to the FDA of an IND which must become effective before human clinical studies may begin;

performance of adequate and well-controlled human clinical studies 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; and

FDA review and approval of the NDA; and

payment of user and facility fees.

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.

Once a pharmaceutical product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, formulation and stability, as well as animal studies to assess its potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, to the FDA as part of the IND. The sponsor will also include a protocol detailing, among other things, the objectives of the initial clinical study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the initial clinical study lends itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical study on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance.

All clinical studies must be conducted under the supervision of one or more qualified investigators in accordance with protection of human subjects at 21 CFR Part 50 and GCP guidances. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board, or IRB, must review and approve the plan for any clinical study before it commences at an institution. An IRB considers, among other things, whether the risks to individuals participating in the studies are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the information regarding the clinical study and the consent form that must be provided to each clinical study subject or his or her legal representative and must monitor the clinical study until completed.

Each new clinical protocol and any amendments to the protocol must be submitted to the IND for FDA review, and to the IRBs for approval. Protocols detail, among other things, the objectives of the clinical study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Human clinical studies 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 studies 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.

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Phase 3. Clinical studies are undertaken to further evaluate dosage, clinical safety and efficacy in an expanded patient population at geographically dispersed clinical study sites. These studies 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 studies 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. Phase 1, Phase 2 and Phase 3 testing of our product candidates may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical study 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 IRB can suspend or terminate approval of a clinical study at its institution if the clinical study 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 studies, companies usually complete additional animal studies 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.

Our product candidates ARX-01, ARX-02 and ARX-03 are regulated under IND s and in the case of ARX-01, all device related information is filed under the Chemistry, Manufacturing and Controls Section, or CMC, of an IND.

United States Review and Approval Processes

The results of product development, preclinical studies and clinical studies, 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 of 2003, or PREA, which was reauthorized under the Food and Drug Administration Amendments Act of 2007, 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 FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, an NDA must be re-submitted with the additional information. The re-submitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product s identity, strength, quality and purity. Before approving an NDA the FDA will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA to an advisory committee for review, evaluation and recommendation as to whether the application should be approved and under what conditions.

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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 studies are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional preclinical or clinical studies. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, we may either resubmit the NDA addressing all of the deficiencies identified in the letter, or withdraw the application.

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 studies designed to further assess a drug product s safety and effectiveness after the NDA.

Marketing Exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain competing applications containing the same active ingredient as our products, if approved. The FDCA provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug such as for our product candidates. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Three-year exclusivity will not delay the submission or approval of a full NDA.

Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, under the Best Pharmaceutical for Children Act, if applied for and granted, provides an additional six months to an existing exclusivity or statutory delay in approval resulting from a patent certification. This six-month exclusivity, which runs from the end of other exclusivity protection or patent delay, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued Written Request. The current pediatric exclusivity provision was reauthorized in September 2007. At present, we do not plan to apply for pediatric exclusivity.

We intend to submit 505(b)(2) NDA applications for each of our product candidates and if approved, we would be granted three years of marketing exclusivity. We expect that our patents, if issued and not successfully challenged, will expire between 2027 and 2030.

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

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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 ARX-01 the device component must comply with 21 CFR 820.

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 studies, 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.

In addition, from time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, in September 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-market authority, including the authority to require post-market studies and clinical studies, labeling changes based on new safety information and compliance with REMS, approved by the FDA. In determining whether a REMS is necessary, the FDA must consider the size of the population likely to use the drug or biological product, the seriousness of the disease or condition to be treated, the expected benefit of the product, the duration of treatment, the seriousness of known or potential adverse events for the product and whether the product is a new molecular entity.

All three of our products in clinical development contain sufentanil, an opioid that is designated Schedule II by the DEA. As a result, all three products will be subjected to a REMS. In the case of ARX-02 for cancer breakthrough pain which will be outpatient use, this is likely to be the most comprehensive REMS. The FDA may require that a REMS include some or all of the following elements, such as medication guide, communication plan, elements to assure safe use, implementation system and timetable for submission and assessments or other measures.

In addition to new legislation that may be enacted, the FDA regulations and policies are often revised or reinterpreted by the agency in ways that may significantly affect our business and our product candidates. It is impossible to predict whether further legislative or FDA regulation or policy changes will be enacted or implemented and what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical studies and commercial sales and distribution of our products to the extent we choose to sell any products outside of the United States. Whether or not we obtain FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of foreign countries before we can commence clinical studies or

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marketing of the product in those countries. The approval process varies 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 studies, product licensing, pricing and reimbursement vary greatly from country to country.

In the European Union, our product candidates are subject to extensive regulatory requirements, which provide, among other things, that no medicinal product may be placed on the market of a European Union member state unless a marketing authorization has been issued by the European Medicines Agency or a national competent authority. European Union member states require both regulatory clearance by the national competent authority and a favorable ethics committee opinion prior to the commencement of a clinical study.

Controlled Substances Regulations

Sufentanil, a Schedule II controlled substance, is the active pharmaceutical ingredient in the ARX-01, ARX-02 and ARX-03 NanoTab product candidates. Triazolam, a Schedule IV controlled substance, is also an active pharmaceutical ingredient in ARX-03. Controlled substances are governed by the Drug Enforcement Administration 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. Our current supply chain is also subject to the regulations of Health Canada s Drug Strategy and Controlled Substances Programme, and specifically, the Office of Controlled Substances.

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.

Pharmaceutical Pricing and Reimbursement

Sales of pharmaceutical products depend significantly on the availability of third party reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. We anticipate third-party payors will provide reimbursement for our products. However, these third -party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. The product candidates that we develop may not be considered cost-effective. It is time consuming and expensive for us to seek reimbursement from third party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

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. Our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. 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. Recently, several pharmaceutical and other health care companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been

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prosecuted for causing false claims to be submitted because of the company s marketing of the product for unapproved, and thus non-reimbursable, uses. 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 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. Among the provisions of the PPACA of greatest importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, beginning in 2011;

- new requirements to report certain financial arrangements with physicians and others, including reporting any transfer of value made or distributed to prescribers and other healthcare providers and reporting any investment interests held by physicians and their immediate family members during each calendar year beginning in 2012, with reporting starting in 2013;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and

- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending beginning by January 1, 2011.

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 $8.2 million, $15.5 million and $18.3 million during the years ended December 31, 2010, 2009 and 2008. We plan to increase our research and development expenses for the foreseeable future as we seek to complete the development of ARX-01 and subsequently advance the development of ARX-02 and ARX-03.

Employees

As of December 31, 2010, we employed 19 full-time employees. Eleven of our employees were engaged in research and development activities and eight were engaged in support administration, including business development, finance, information systems, facilities and human resources. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

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Item 1A. Risk Factors

Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this Form 10-K. 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. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

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 ARX-01. We have two additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, and the Sufentanil/Triazolam NanoTab, or ARX-03. We have incurred significant net losses in each year since our inception in July 2005, including net losses of approximately $14.3 million, $20.1 million and $20.7 million during the years ended December 31, 2010, 2009 and 2008. As of December 31, 2010, we had an accumulated deficit of $68.6 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. 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.

We expect to continue to incur substantial and increased expenses as we expand our research and development activities and advance our clinical programs. We also expect an increase in our expenses associated with preparing for the potential commercialization of ARX-01 and creating additional infrastructure to support operations as a public company. 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 revenue and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development, obtain the necessary regulatory approvals and commercialize our product candidates. 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 ARX-01, initially for the treatment of post-operative pain in the hospital setting;
- obtaining regulatory approval for ARX-01;
- launching and commercializing ARX-01, including building a hospital-directed sales force and collaborating with third parties; and
- completing the clinical development, obtaining regulatory approval, launching and commercializing ARX-02 and ARX-03, which will require additional funding.

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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, 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 FDA to perform studies 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 which 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.

If we fail to obtain additional financing, we would be forced to delay, reduce or eliminate our product development programs.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our clinical programs. As of December 31, 2010, we had negative working capital of approximately $7.6 million. Although we raised $35.6 million in net proceeds in our initial public offering, or IPO, 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.

We believe that our current cash and cash equivalents, including the net proceeds of $35.6 million from our IPO in February 2011, and the interest earned thereon, will be sufficient to fund our current operations through the second quarter of 2012. However, changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. For example, our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expected. We will need to raise additional funding or otherwise enter into collaborations to complete the third ARX-01 Phase 3 clinical trial required to file our NDA and, if we choose, to initiate clinical trials for our product candidates other than ARX-01. In any event, we will require substantial additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Raising funds in the current economic environment, when the capital markets have been affected by the global recession, may present additional challenges.

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

- significantly delay, scale back or discontinue the development or commercialization of our product candidates;
- seek corporate partners for ARX-01 at an earlier stage than otherwise would be desirable or on terms that are 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.

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If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, including completing the third ARX-01 Phase 3 clinical trial required to file our NDA, which will have a material adverse effect on our business, operating results and prospects.

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, 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.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of our product candidate, ARX-01, 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 ARX-01, which has completed Phase 2 clinical trials for the treatment of post-operative pain. We expect to initiate one of the three planned Phase 3 clinical trials for ARX-01 in the second half of 2011 with a second Phase 3 initiating in early 2012. Contingent on our ability to secure additional funding, we plan to begin a third Phase 3 clinical trial in the second half of 2012. We intend to use these trials as a basis to submit an NDA for ARX-01. There is no guarantee that our Phase 3 clinical trials will be completed, or if completed, will be successful.

Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing ARX-01, generating revenues and achieving profitability. If any of these events occur, we may be forced to abandon our development efforts for ARX-01, 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 for our product candidates in Phase 2 clinical studies may not be repeated in Phase 3.

We have completed Phase 2 clinical studies and participated in an End of Phase 2 meeting for each of our three product candidates. However, we have never conducted a Phase 3 clinical trial. 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 Phase 3 clinical trials. Negative or inconclusive results of a Phase 3 clinical study could cause the FDA to require that we repeat it or conduct additional clinical studies. Furthermore, while we 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.

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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 may experience delays in clinical trials of our product candidates. We expect to initiate one of the three planned Phase 3 clinical trials of ARX-01 in the second half of 2011 with a second Phase 3 study being initiated in early 2012. Our 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 can be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial, including the inability to secure additional funding to complete the third ARX-01 Phase 3 clinical trial required to file our NDA;
- delays in pharmacokinetic studies required prior to Phase 3 initiation;
- 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;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If initiation or completion of the Phase 3 trials are delayed for our product candidates 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 study sites or regulatory authorities to interrupt, delay or halt clinical studies and could result in the denial of regulatory approval. Phase 2 clinical studies conducted by us with our product candidates have generated some AEs, but no serious adverse events, or SAEs. For example, in ARX-01 clinical studies completed to date, 11% of the patients experienced vomiting and 8% experienced itching for 10 mcg and 15 mcg treated groups, as compared to the placebo treated subjects, of which 6% experienced vomiting and none experienced itching. If SAEs are observed in any of our clinical studies, our ability to obtain regulatory approval for our product candidates may be adversely impacted.

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 a form of a modified Risk Evaluation and Mitigation Strategy, or REMS;

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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 studies;

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 ARX-01 product candidate because it is a drug/device combination.

ARX-01 is a drug/device combination. We have filed an IND for ARX-01. Based on our discussions with the FDA, we believe that ARX-01 will be reviewed as a combination product, with both drug and device components submitted in the IND, and both components will eventually be part of an NDA. There are very few examples of the FDA approval process for drug/device combination products such as ARX-01. As a result, we may experience delays in regulatory approval for ARX-01 due to uncertainties in the approval process, in particular as it relates to device approval under an NDA.

After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize ARX-01 and we cannot, therefore, predict the timing of any future revenue from ARX-01.

We cannot commercialize ARX-01 until the appropriate regulatory authorities, such as the FDA, 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 ARX-01. Additional delays may result if ARX-01 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 studies and the review process.

Even if we obtain regulatory approval for ARX-01 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 studies or post-market surveillance. For example, the labeling ultimately approved for ARX-01 and our other product candidates will likely include restrictions on use due to the opiate nature of sufentanil. ARX-01 and our other product candidates will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we, or a regulatory

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agency discovers 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 ARX-01 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. 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 studies 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.

ARX-01 and our other product candidates will require Risk Evaluation and Mitigation Strategies.

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and require the adoption of REMS. Our product candidates will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. While we have received information from the FDA regarding certain aspects of the required REMS for ARX-01, we cannot predict the specific REMS to be required as part of the FDA s approval of ARX-01. Depending on the extent of the REMS requirements, our costs to commercialize ARX-01 may increase significantly. ARX-02 and ARX-03, if approved, will also require REMS programs that may 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.

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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 risks to which we would not be subject if we manufactured the pharmaceutical, device and drug cartridge aspects of our product candidates ourselves, 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 study 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, Covidien plc and Johnson Matthey plc. For each product candidate, only one of the two suppliers will be qualified as a vendor with the FDA. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. The alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies 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 a 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

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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, is flammable, which necessitates 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 facility to manufacture our sufentanil NanoTabs and have not identified a back up 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 increase product and regulatory approval costs or delay 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 the drug substance or excipients that comprise the sufentanil or sufentanil/triazolam NanoTab products. 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.

Our designs for the device components of our product candidates for Phase 3 clinical trials may not be fully functional or commercially viable.

The ARX-01 device we plan to use in Phase 3 clinical trials and commercially, or Phase 3 device, has more features than the device used in Phase 2, including additional software and functionality. Although we have conducted multiple human factor and usability studies, the design of the ARX-01 Phase 3 device is still under development. We plan to complete an additional user testing study prior to release of the device for Phase 3 clinical trials. However, we cannot predict if the Phase 3 device will be fully functional or acceptable for commercial use. If we need to modify the Phase 3 device after the completion of the Phase 3 studies, we may incur higher costs and experience delay in regulatory approval and commercialization of ARX-01. Furthermore, if the changes to the device are substantial, we may need to conduct further clinical studies in order to have the commercial device approved by the FDA.

The dispensing components of ARX-02 and ARX-03 are still under development. We cannot be certain that the dispensing components of ARX-02 and ARX-03 will be fully functional or acceptable for commercial use or that we will be able to effectively scale up the manufacturing process. Failure to do so may delay or prevent regulatory approval or commercialization of ARX-02 and ARX-03.

We have no experience manufacturing the ARX-01 Phase 3 device on a clinical or commercial scale and do not own or operate a manufacturing facility.

We have relied on contract manufacturers, component fabricators and secondary service providers to produce ARX-01 devices for Phase 2 clinical trials. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the ARX-01 device to third parties and intend to continue to do so. We may encounter unanticipated problems in the scale-up and automation process that will result in delays in the manufacturing of the ARX-01 cartridge, dispenser or controller.

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We do not currently have any agreements with third party manufacturers for the manufacture of the Phase 3 device. We may not be able to enter into agreements for commercial supply of ARX-01 with third party manufacturers, or may be unable to do so on acceptable terms.

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 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 studies, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We rely on clinical research organizations, or CROs, and 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 ARX-01 and our other product candidates, as well as the execution of nonclinical studies. We control only certain aspects of our CROs activities. Nevertheless, we are responsible for ensuring that each of our studies 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.

Since our drug products are controlled substances, all of our contract manufacturing organizations, or CMOs, and CROs must follow proper DEA rules and procedures or comparable rules and procedures in other countries. Failure to properly follow these rules and procedures could result in DEA action, up to and including losing their license to work with controlled substances. This would result in a major delay in our clinical studies and/or NDA submission.

We and our CROs are required to comply with the FDA s current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. Upon inspection, the FDA may determine that our Phase 3 clinical trials do not comply with cGCPs. In addition, our Phase 3 clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of ARX-01. 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 studies, 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

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approval for, or successfully commercialize ARX-01, or our other product candidates. As a result, our financial results and the commercial prospects for ARX-01 and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Commercialization of Our Product Candidates

The commercial success of ARX-01 and our other product candidates will depend upon the acceptance of these products by the medical community, including physicians, patients and health care payors.

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;
- 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 ARX-01;
- availability of alternative treatments;
- 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 ARX-01 is approved, but does not achieve an adequate level of acceptance by physicians, patients and health care payors, we may not generate sufficient revenue from ARX-01 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 ARX-01 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

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regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to negotiate a strategic partnership or obtain additional financial resources for ARX-02 or ARX-03, we may be forced to curtail the development of ARX-02 or ARX-03, delay potential commercialization, reduce the scope of our sales or marketing activities or undertake development or commercialization activities at our own expense. In addition, without a partnership, we will bear all the risk related to the development of ARX-02 or ARX-03. 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 or ARX-03 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 ARX-01 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 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 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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The primary competition for ARX-01 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 ARX-01 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.; and Rylomine, an intranasal morphine product developed by Javelin Pharmaceuticals, Inc.

Our potential competitors for ARX-02 include products approved in the United States for cancer breakthrough pain, including: ACTIQ and FENTORA, currently manufactured by Cephalon Inc.; Onsolis, currently manufactured by BioDelivery Sciences International, Inc.; and Abstral, currently manufactured by ProStrakan Group plc; 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: PecFent, currently manufactured by Archimedes Pharma Limited; Fentanyl TAIFUN, currently manufactured by Akela Pharma, Inc.; and SL Spray, currently manufactured by Insys Therapeutics, Inc.

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 ARX-01 and ARX-02, respectively, non-competitive or obsolete. These and other risks may materially adversely affect our ability to attain or sustain profitable operations.

Hospital formulary approval and reimbursement may not be available for ARX-01 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 ARX-01, or any future product candidates that we develop, 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 ARX-01, or any future 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 ARX-01, or any future product candidates that we develop.

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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 ARX-01. The potential 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 the sale of ARX-01 and any other products that we develop, 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. At present, our contract manufacturers have applied for a quota on our behalf which allocates a sufficient quantity of sufentanil to meet our planned clinical and pre-clinical needs during 2011. In future years, we may need greater amounts of sufentanil to sustain and complete our Phase 3 development program for ARX-01, and we will need significantly greater amounts of sufentanil to implement our commercialization plans if the FDA approves ARX-01. 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 as we anticipate could delay or stop the clinical development or commercial sale of ARX-01. This could have a material adverse effect on our business, results of operations, financial condition and prospects.

In addition, we purchase sufentanil in the United States and ship it to our third party manufacturer, Patheon Inc. in Toronto, Canada, where much of our clinical trial manufacturing has been completed to date. Shipping across international borders is a bureaucratic process that takes a minimum of three months and requires permits to export drug out of the United States and import NanoTabs into the United States. If we fail to comply with applicable regulatory requirements or fail to submit permit applications in a timely manner, the government could refuse to permit sufentanil to be exported from or imported into the United States. Our failure to comply with these requirements could result in increased costs, delayed shipments, the loss of DEA registration for one of our suppliers, significant restrictions on ARX-01, civil penalties or criminal prosecution and delays in conducting our clinical trials.

Drug Enforcement Administration regulations require that sufentanil be manufactured in the United States if sufentanil-based products are to be marketed in the United States, and there is no guarantee that we will secure a commercial supply agreement with a manufacturer based in the United States.

A substantial portion of our clinical trial manufacturing to date has been completed at Patheon Inc. in Toronto, Canada. However, we cannot rely on the Patheon facility located in Toronto for commercial manufacturing of sufentanil because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States.

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We have identified potential commercial manufacturers for ARX-01 in the United States. However, we do not yet have a commercial supply contract in place. If we cannot establish a supply contract on commercially reasonable terms, or if facility modifications, equipment manufacture or modification do not meet expected deadlines, we may not be able to successfully commercialize our product candidates.

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 NDA and before approval of ARX-01 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 cannot successfully produce material that conforms to our specifications and 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 ARX-01. These challenges may have a material adverse impact on our business, results of operations, financial condition and prospects.

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

Our headquarters is located in the San Francisco Bay Area, near known earthquake fault zones and is vulnerable to significant damage from earthquakes. We are also vulnerable to other types of natural disasters and other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

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

We are highly dependent on principal members of our executive team listed under Item 10. Directors, Executive Officers and Corporate Governance Executive Officers of the Registrant appearing elsewhere in this Form 10-K, 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 studies 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, 2010, we had 19 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

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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 ARX-01 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 studies 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 study participants;

costs due to related litigation;

distraction of management s attention from our primary business;

substantial monetary awards to patients or other claimants;

the inability to commercialize our product candidates; and

decreased demand for our product candidates, if approved for commercial sale.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Risks Related to Our Intellectual Property

We have numerous pending patent applications in the United States, but no issued patents. Our only patent, which is issued in Europe, is currently in the opposition period. If our pending patent applications fail to issue or if our issued European patent is successfully opposed, our business will be adversely affected.

Our commercial success will depend in part on obtaining and maintaining patent protection for our product candidates, as well as successfully defending our current and future patents against third party challenges. To protect our proprietary technology, we rely on patents as well as other

intellectual property protections, including trade secrets, nondisclosure agreements and confidentiality provisions.

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In addition, there can be no assurance that our pending patent applications will result in issued patents. As of December 31, 2010, we are the owner of record and are pursuing 15 U.S. non-provisional patent applications, three pending international Patent Cooperation Treaty applications and 39 foreign national and ten European regional counterpart patent 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.

Our European patent, though granted, may be opposed by third parties during a nine-month opposition period that ends on April 21, 2011. If a third party opposes our European patent, we will need to spend considerable time and resources to defend our granted patent claims. European opposition proceedings may fail and, even if successful, may result in substantial costs and distract our management.

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.

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

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

As we enter our 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

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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. 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.

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 to remind us to pay periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees, and we employ an outside firm, McDonnell Boehnen Hulbert Berghoff LLP, or MBHB, in Chicago, Illinois, to pay these fees. The United States Patent and Trademark Office, or the USPTO,

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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. We employ MBHB and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If this occurs, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

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

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

We have registered our ACELRX mark in 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 has also been registered in the European Community and in Canada, and is pending in India. We have filed a trademark application for our NANOTAB mark and our tagline, ACCELERATE, INNOVATE, ALLEVIATE in Class 5, 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 IPO in February 2011, there was no public market for our common stock. An active public trading market may not 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 to complete the third ARX-01 Phase 3 clinical trial required to file our NDA;

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

failure to successfully develop and commercialize our product candidates;

changes in laws or regulations applicable to our products;

inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;

adverse regulatory decisions;

introduction of new products, services or technologies by our competitors;

failure to meet or exceed financial projections we provide to the public;

failure to meet or exceed the estimates and projections of the investment community;

the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

sales of our common stock by us or our stockholders in the future; and

trading volume of our common stock.

In addition, the stock market in general, and the NASDAQ Global Market 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 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 78% of our outstanding voting stock as of March 1, 2011. 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 Securities and Exchange Commission, or SEC, and the NASDAQ Stock Market have imposed various

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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. In addition, our independent registered public accounting firm will also be required to deliver an attestation report on the effectiveness of our internal control over financial reporting beginning with the year ending December 31, 2012, unless 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 investors. If we or our independent registered public accounting firm identify and report a material weakness, it could adversely affect our stock price.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. As of March 1, 2011, we had 19,371,750 shares of common stock outstanding.

Substantially all of our stockholders that held stock prior to our IPO are subject to lock-up agreements with the underwriters of our IPO that restrict the stockholders ability to transfer shares of our common stock until at least August 10, 2011. The lock-up agreements limit the number of shares of common stock that may be sold until the expiration of the lock-up period. Upon the expiration of the lock-up period, approximately 16,171,750 of the shares outstanding as of March 1, 2011 will become 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. The remaining 3,200,000 shares of common stock outstanding as of March 1, 2011 are freely tradable without restriction or further registration. In addition, shares issued or issuable upon exercise of options and warrants vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by our existing stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 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.

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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, 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. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

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

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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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

Not applicable**.**

Item 2. Properties

We lease approximately 11,305 square feet of space for our headquarters in Redwood City, California under an agreement that expires on April 8, 2012. We believe that our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

We are not a party to any litigation and do not have contingent reserves established for any litigation liabilities.

Item 4. [Removed and Reserved]

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PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

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. On March 29, 2011, the closing price of our common stock as reported on the NASDAQ Global Market was $3.54 per share.

Holders of Record

As of March 1, 2011, there were approximately 38 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future.

Recent Sales of Unregistered Securities

In January 2010, we issued 19,275 shares of our Series C convertible preferred stock to two purchasers at approximately $3.94 per share, for approximately $76,000. Upon completion of our IPO, these shares of Series C convertible preferred stock converted into 19,275 shares of our common stock.

In September 2010, in connection with a bridge loan financing, we granted warrants to purchase an aggregate of $2.0 million of our preferred stock to eight purchasers. In connection with our IPO, these warrants became warrants to purchase 507,245 shares of our Series C convertible preferred stock at an exercise price of approximately $3.94 per share. These warrants were net exercised for an aggregate of 107,246 shares of our Series C convertible preferred stock, which shares automatically converted into 107,246 shares of our common stock immediately prior to our IPO. In September 2010, in connection with a bridge loan financing, we issued convertible promissory notes to eight purchasers for an aggregate principal amount of $8.0 million. Upon completion of our IPO, the outstanding principal and accrued interest under these convertible promissory notes converted into 2,034,438 shares of our common stock at a conversion price equal to $4.00 per share.

The issuances of securities described above were exempt from registration under the Securities Act of 1933, as amended, or the Securities Act, in reliance on Section 4(2) of the Securities Act, and Regulation D promulgated thereunder, as transactions by an issuer not involving any public offering. The purchasers of the securities in these transactions represented that they were accredited investors and that they were acquiring the securities for investment only and not with a view toward the public sale or distribution thereof. Such purchasers received written disclosures that the securities had not been registered under the Securities Act, and that any resale must be made pursuant to a registration statement or an available exemption from registration. All purchasers either received adequate financial statement or non-financial statement information about us or had adequate access, through their relationship with us, to financial statement or non-financial statement information about us. The sale of these securities was made without general solicitation or advertising.

During the twelve months ended December 31, 2010, we granted options in unregistered transactions to purchase an aggregate of 1,441,610 shares of common stock at a weighted average exercise price of $2.72 per share to our employees. The issuances of these securities were exempt from registration under Rule 701 promulgated under the Securities Act as transactions pursuant to a compensatory benefit plan or a written contract relating to compensation.

The share and per share information above gives effect to a 1-for-4 reverse stock split of our common stock and preferred stock that became effective on January 28, 2011.

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Use of Proceeds

On February 10, 2011, our registration statement on Form S-1 (File No. 333-170594) was declared effective for our IPO, pursuant to which we sold 8,000,000 shares of common stock at a public offering price of $5.00 per share for an aggregate offering price of $40.0 million. Piper Jaffray & Co. acted as sole book-running manager and Cowen and Company, LLC, Canaccord Genuity Inc., and JMP Securities LLC acted as co-managers for the offering.

As a result of the IPO, we received net proceeds of $35.6 million, after deducting underwriting discounts and commissions and other offering expenses totaling $4.4 million. None of the expenses associated with the IPO were paid to directors, officers or persons owning ten percent or more of our common stock or to their associates, or to our affiliates.

$27.8 million of the net proceeds are expected to be used to fund two of our three planned ARX-01 Phase 3 clinical trials, with the balance to be used for general corporate purposes. As of March 1, 2011, the net offering proceeds have been invested in high credit quality U.S. government agency obligations and commercial paper. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b) on February 11, 2011.

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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 statements of operations data for the period from July 13, 2005 (inception) through December 31, 2010 and for the years ended December 31, 2008, 2009 and 2010, and the balance sheet data at December 31, 2009 and 2010, are derived from our audited financial statements included elsewhere in this Form 10-K. The statements of operations data for the years ended December 31, 2006 and 2007, and the balance sheet data at December 31, 2006, 2007 and 2008 are derived from our audited financial statements that are not included in this Form 10-K. Historical results are not indicative of the results to be expected in the future.

	Year Ended December 31,					Period from July 13, 2005 (Inception) Through December 31,
	2010	2009	2008	2007	2006	2010
	(in thousands, except share and per share data)					
Statements of Operations Data:						
Operating Expenses:						
Research and development	$ 8,193	$ 15,502	$ 18,325	$ 8,209	$ 3,533	$ 53,797
General and administrative	3,993	3,529	2,365	2,082	520	12,494
Total operating expenses	12,186	19,031	20,690	10,291	4,053	66,291
Loss from operations	(12,186)	(19,031)	(20,690)	(10,291)	(4,053)	(66,291)
Interest income	4	33	484	687	347	1,556
Interest expense	(1,397)	(1,242)	(404)	(25)	(62)	(3,130)
Other income (expense), net	(765)	121	(52)	(1)		(698)
Net loss	$ (14,344)	$ (20,119)	$ (20,662)	$ (9,630)	$ (3,768)	$ (68,563)
Net loss per share of common stock, basic and diluted	$ (21.84)	$ (34.93)	$ (43.69)	$ (26.45)	$ (36.90)	
Shares used in computing net loss per share of common stock, basic and diluted	656,650	576,021	472,914	364,039	102,102	

	As of December 31,				
	2010	2009	2008	2007	2006
			(in thousands)		
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 3,682	$ 12,546	$ 20,207	$ 7,699	$ 17,098
Working capital (deficit)	(7,632)	6,931	16,450	6,959	16,537
Total assets	6,830	14,491	22,679	10,038	18,193
Total debt, including convertible notes	12,009	9,734	12,334	525	
Convertible preferred stock warrant liability	2,529	169	240		
Convertible preferred stock	55,941	55,871	41,156	21,016	21,016
Total stockholders (deficit)	(68,563)	(52,994)	(33,335)	(13,189)	(3,715)

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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 specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. We were founded to solve the problems associated with post-operative intravenous patient-controlled analgesia, or IV PCA. Although widely used, IV PCA has been shown to cause harm to patients following surgery because of the side effects of morphine, the invasive IV route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps. We are preparing to initiate two Phase 3 clinical trials for our lead product candidate, the Sufentanil NanoTab PCA System, or ARX-01. The system is designed to address these problems by utilizing:

- sufentanil, a high therapeutic index opioid;
- NanoTabs, our proprietary, non-invasive sublingual dosage form; and
- our novel handheld PCA device that enables simple patient-controlled delivery of NanoTabs in the hospital setting and eliminates the risk of programming errors.

We have completed Phase 2 clinical development for two additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, for the treatment of cancer breakthrough pain, or BTP, and the Sufentanil/Triazolam NanoTab, or ARX-03, designed to provide mild sedation, anxiety reduction and pain relief for patients undergoing painful procedures in a physician s office.

We are a development stage company with a limited operating history. We have funded our operations through December 31, 2010 primarily from the private placement of convertible preferred stock and proceeds received from our debt financings. From inception through December 31, 2010, we have received net proceeds of $54.9 million from the sale of convertible preferred stock and $21.6 million from proceeds of our debt financings. As of December 31, 2010, we had $13.2 million of debt outstanding, of which $5.2 million related to our loan and security agreement and $8.0 million, which does not include the debt discount of $1.2 million, related to our convertible note agreement. In February 2011, we completed our IPO, pursuant to which we sold 8,000,000 shares of our common stock at a public offering price of $5.00 per share for an aggregate offering price of $40.0 million. As a result of the offering, we received net proceeds of $35.6 million, after underwriting discounts, commissions and offering expenses of $4.4 million. In addition, the outstanding principal amount of $8.0 million and accrued interest under the convertible notes issued in connection with our convertible note agreement automatically converted into shares of our common stock in connection with our IPO.

Since our inception in July 2005, we have not generated any revenue from the sale of our products and do not anticipate generating any revenues for the foreseeable future. We have incurred losses and generated negative cash flows from operations since inception. Our net losses were $14.3 million, $20.1 million and $20.7 million during the years ended December 31, 2010, 2009 and 2008. As of December 31, 2010, we had an accumulated deficit of $68.6 million. Substantially all of our operating losses resulted from costs incurred in connection with our development programs and from general and administrative costs associated with our operations. As of December 31, 2010, our principal sources of liquidity were our cash, cash equivalents and short-term investments, which totaled $3.7 million.

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We expect to incur significant and increasing expenses over the next several years, principally to develop ARX-01, including completion of the first two Phase 3 clinical trials, as well as to further increase our spending to manufacture, sell and market our product candidates. Contingent on our ability to secure additional funding, we plan to complete the third ARX-01 Phase 3 clinical trial required to submit an NDA. In addition, based on the availability of additional financial resources, we plan to advance ARX-02 into Phase 3 trials, submit an NDA and commercialize it ourselves or with a partner in the United States. Further development of ARX-03 will depend on the identification of a partner to support this effort. Furthermore, as a result of our IPO in February 2011, we expect to incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses and negative cash flows for the foreseeable future.

Financial Overview

Revenue

To date, we have not generated any 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.

Research and Development Expenses

The majority of our operating expenses to date have been for research and development activities related to ARX-01, ARX-02 and ARX-03. Research and development expenses consist of:

- expenses incurred under agreements with contract research organizations, or CROs, and clinical trial sites;
- employee and consultant-related expenses, which include salaries, benefits and stock-based compensation;
- 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.

Conducting research and development is central to our business model. 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 plan to increase our research and development expenses for the foreseeable future as we seek to complete development of ARX-01, and subsequently advance the development of ARX-02 and ARX-03.

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Prior to January 1, 2009, we did not track our research and development costs including personnel and personnel-related costs on a project-by-project basis. Our development resources are shared among all of our programs. Since January 1, 2009, we have tracked external development expenses on a program-by-program basis. 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, 2010 and 2009 (in thousands):

	Year Ended December 31,	
	2010	2009
ARX-01	$ 1,289	$ 5,343
ARX-02	507	2,721
ARX-03	1,555	1,426
Overhead	4,842	6,012
Total research and development expenses	$ 8,193	$ 15,502

Due to the inherently unpredictable nature of product development, we are unable to estimate the costs we will incur in the continued development of ARX-01, ARX-02 and ARX-03. Development timelines, the probability of success and development costs can differ materially from expectations. While we are currently focused on advancing ARX-01, 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. We expect our research and development expenses to substantially increase as we commence two of our planned ARX-01 Phase 3 clinical trials, and subject to additional funding, our third Phase 3 clinical trial required to file our NDA.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and stock-based compensation for personnel in administration, finance and business development. Other significant expenses include legal expenses to pursue patent protection of our intellectual property, allocated facility costs and professional fees for general legal and consulting services. We expect general and administrative expenses 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.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and short-term investments.

Interest Expense

Interest expense consists primarily of interest accrued or paid on our loan and security agreement and our convertible notes.

Other Income (Expense), net

Other income (expense), net consisted primarily of the change in the fair value of our warrants to purchase convertible preferred stock. Our outstanding 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 in February

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2011, all of our warrants to purchase convertible preferred stock were 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.

Provision for Income Taxes

Since inception, we have incurred net losses and have not recorded any U.S. federal or state income tax provisions as these losses have been offset by valuation allowances.

Reduction in Work Force

On December 7, 2009, we announced a workforce reduction of approximately 44%, or 14 employees, a majority of whom were employed in product development and related support functions. This decision was made based on the challenging economic conditions and a decline in forecasted research and development activities expected during the year ending December 31, 2010.

As a result of this workforce reduction, we recorded a charge of $119,000 related to employee severance and other benefits which was included as operating expenses in the statement of operations during the year ended December 31, 2009. As of December 31, 2009, we had paid $30,000 for these employee severance and other termination benefits and had accrued the remaining $89,000 on the balance sheet. During the year ended December 31, 2010, we paid the remaining $89,000.

Critical Accounting Policies and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States which requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, costs and expenses and related disclosures. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. In many instances, we could have reasonably used different accounting estimates, and in other instances, changes in the accounting estimates are reasonably likely to occur from period-to-period. Accordingly, actual results could differ significantly from the estimates made by our management. To the extent that there are material differences between these estimates and actual results, our future financial statement presentation, financial condition, results of operations and cash flows will be affected. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management s judgments and estimates.

Stock-Based Compensation

We recognize compensation costs related to stock options and shares of restricted stock granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value and the resulting stock-based compensation expense using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

The fair value of the stock-based awards granted to our employees was estimated on the grant dates using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2010	**2009**	**2008**
Expected volatility	75%	73%	74%
Expected term (in years)	5.75-6.25	6.25	6.25
Risk-free interest rate	1.6%-4.6%	3.0%	3.5%
Expected dividend yield	0%	0%	0%

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The Black-Scholes model requires the use of highly subjective and complex assumptions which determine the fair value of share-based awards, including the option s expected term and the price volatility of the underlying stock. These assumptions include:

Expected Term. The expected term represents the period that our share-based awards are expected to be outstanding and was primarily determined using the simplified method in accordance with guidance provided by the SEC. For option grants considered to be plain vanilla, the simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the awards. For awards that are not considered plain vanilla, the expected term is based on the historical option exercise behavior of our employees and post-vesting cancellations.

Expected Volatility. The expected 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. When making the selections of our industry peer companies to be used in the volatility calculation, we considered the size, operational and economic similarities to our principal business operations.

Expected Dividend. The expected dividend was assumed to be zero as we have never paid dividends and have no current plans to do so.

Risk-Free Interest Rate. The risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero coupon U.S. Treasury notes with maturities approximately equal to each award s expected term.

In addition to assumptions used in the Black-Scholes option-pricing model, we must also estimate a forfeiture rate to calculate the stock-based compensation for our awards. Our forfeiture rate is based on an analysis of our actual forfeitures. We will continue to evaluate the appropriateness of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover and other factors. Quarterly changes in the estimated forfeiture rate can have a significant impact on our stock-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. If a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in the financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in the financial statements.

We will continue to use judgment in evaluating the expected term, expected volatility and forfeiture rate related to our own stock-based compensation on a prospective basis. As we continue to accumulate additional data related to our common stock, we may have refinements to the estimates of our expected volatility, expected terms and forfeiture rates, which could materially impact our future stock-based compensation expense.

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. Prior to our IPO, 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. Our board of directors is comprised of a majority of non-employee directors with significant experience in the pharmaceutical and biotechnology industries. We believe that our board of directors had the relevant experience and expertise to determine a fair value of our common stock on each respective grant date. Given the absence of a public trading market of our common stock prior to our IPO in February 2011, and in accordance with the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, our board of directors exercised reasonable judgment and considered numerous objective and subjective factors to determine the best estimate of the fair value of our common stock including:

- contemporaneous and retrospective valuations performed by unrelated third party specialists;
- prices for our convertible preferred stock sold to outside investors in arm s-length transactions;

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rights, preferences and privileges of our convertible preferred stock relative to those of our common stock;

actual operating and financial performance;

hiring of key personnel and the experience of our management;

status of research and development efforts, including the clinical results for ARX-01, ARX-02 and ARX-03;

risks inherent in the development of our products and services;

likelihood of achieving a liquidity event, such as an initial public offering or a sale of our company given prevailing market conditions and the nature and history of our business;

market value of a comparable group of privately held pharmaceutical and biotechnology companies that are in a similar state of development to ours;

illiquidity of stock-based awards involving securities in a private company;

industry information such as market size and growth; and

macroeconomic conditions.

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.

The fair value of our business was then allocated to each of our classes of stock using either the Option Pricing Method or the Probability Weighted Expected Return Method.

The Option Pricing Method, or OPM, treats common stock and convertible preferred stock as call options on an enterprise value, with exercise prices based on the liquidation preference of the convertible preferred stock. Therefore, the common stock has value only if the funds available for distribution to the stockholders exceed the value of the liquidation preference at the time of a liquidity event such as a merger, sale or initial public offering, assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the stockholders. The common stock is modeled to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the convertible preferred stock is liquidated. The OPM uses the Black-Scholes option-pricing model to price the call option. The OPM is appropriate to use when the range of possible future outcomes is so difficult to predict that forecasts would be highly speculative.

The Probability Weighted Expected Return Method, or PWERM, involves a forward-looking analysis of the possible future outcomes of the enterprise. This method is particularly useful when discrete future outcomes can be predicted at a high confidence level with a probability distribution. Discrete future outcomes considered under the PWERM included non-IPO market based outcomes as well as IPO scenarios. In the non-IPO scenarios, a large portion of the equity value would be allocated to the convertible preferred stock to incorporate higher aggregate liquidation preferences. In the IPO scenarios, the equity value would be allocated pro rata among the shares of common stock and each series of

convertible preferred stock, which would cause the common stock to have a higher relative value per share than under the non-IPO scenario. The fair value of the enterprise determined using the IPO and non-IPO scenarios was weighted according to our board of directors estimate of the probability of each scenario at the time.

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Over time, as certainty developed regarding possible discrete events, including our IPO, the allocation methodology utilized to allocate our enterprise value to our common stock transitioned from the OPM, which was utilized through July 2009, to the PWERM, which had been utilized from July 2009 through December 31, 2010.

Information regarding stock option grants to our employees from January 1, 2009 through December 31, 2010 is summarized as follows:

Grant Date	Number of Options Granted	Exercise Price	Fair Value Per Share of Common Stock	Aggregate Grant Date Fair Value[1]
July 1, 2009	231,875	$ 5.52	$ 5.52	$ 452,000
June 15, 2010	83,125	1.20	2.56	165,000
June 15, 2010	1,233,485	2.56	2.56	2,471,000
November 4, 2010	125,000	5.32	5.32	450,000

(1) Aggregate grant date fair value was determined using the Black-Scholes option pricing model.

The intrinsic value of all outstanding options as of December 31, 2010 was $4.2 million based on the estimated fair value for our common stock of $5.00 per share, the IPO price.

No single event caused the valuation of our common stock to increase or decrease through December 31, 2010. Instead, a combination of the factors described below in each period led to the changes in the fair value of the underlying common stock.

October 2008 to July 2009. After a period of significant volatility in the United States and global capital markets during the third and fourth quarters of 2008, capital market conditions began to stabilize and recover in early 2009. During this time period, we reported our first successful ARX-01 Phase 2 study results in November 2008, in the midst of significant financial market turmoil. We reported positive results for an additional efficacy study for ARX-01 in April 2009 and a device functionality study for ARX-01 in July 2009.

As of December 31, 2008, our board of directors determined a fair value of our common stock to be $5.52 per share. The December 31, 2008 contemporaneous valuation determined the enterprise value using a market approach due to the uncertain nature of the financial projections underlying the income approach and the significant ongoing capital requirements for our business to reach profitability. In applying the OPM to the enterprise value during this period, the expected time to a liquidity event of 3.0 years was based on a reasonable time frame for us to achieve significant milestones in our business strategy and experience a liquidity event. The volatility of 62% was based on the median volatility over the expected time to a liquidity event for our comparable publicly traded companies. The risk-free interest rate of 1.0% was based on the yield on a three-year U.S. Treasury bond corresponding to the expected time to a liquidity event. Based on a lack of a public market for our common stock, a discount of 39% was based upon a protective put analysis using the same assumptions for the term, volatility and risk-free rate. For options granted during this period, our board of directors determined that the fair value of our common stock remained unchanged at $5.52 per share as the positive clinical data results were offset by the deterioration of the financial markets during the period.

December 2009 to June 2010. In late October 2009, we completed a successful ARX-01 End of Phase 2 meeting with the FDA. Between November 2009 and April 2010, the United States economy and capital markets continued to improve. We also reported our first positive Phase 2 data from our ARX-03 program in October 2009. In early 2010, we were successful in hiring a new Chief Executive Officer. During the second quarter of 2010, we received positive Phase 2 data on our ARX-02 program and completed an End of Phase 2 meeting with the FDA for our ARX-03 program. Despite our positive clinical results, the End of Phase 2 meetings with the FDA and the improved conditions of the public markets, there was a limited availability for private capital. In November 2009, we closed our Series C convertible preferred stock financing for approximately $3.94 per share raising a total of $14.7 million in proceeds, which was below the $16.00 per share we received in connection

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with our Series B convertible preferred stock financing in February 2008. During the first quarter of 2010, we continued to focus on private sources of capital, but traditional venture capital investors continued to be highly risk averse and faced significant industry-wide challenges. During the second quarter of 2010, we became focused on establishing a financing strategy that would enable our product candidates to advance into Phase 3 development. Despite the challenges in the private financing, we began to have initial discussions with a small number of banks regarding our prospects for an IPO.

As of December 31, 2009, our board of directors determined a fair value of our common stock to be $1.20 per share. As noted previously, the OPM is preferred when future outcomes are difficult to predict and the PWERM becomes useful when discrete future outcomes become more predictable. During the period between July 2, 2009 and December 30, 2009, when our board of directors did not make valuation determinations or grant any stock-based awards, the range of discrete events, specifically IPO scenarios, became fairly well established; therefore, the PWERM was utilized to estimate the fair value of our common stock during this period. The PWERM allocation method used a risk-adjusted discount rate of 46% based upon an adjusted capital asset pricing model and a lack of marketability discount rate of 30% in the remaining private scenario. The expected outcomes were weighted as follows: (1) 20% towards IPO scenarios occurring during late 2010 and through 2012, valued using the market approach; (2) 20% towards a sale occurring during late 2010 and through 2012, valued using the market approach; (3) 20% towards a recapitalization, valued using the income approach; and (4) 40% to remaining a private operating company, valued using the income approach. For options granted in June 2010, our board of directors originally estimated the fair value of our common stock to be $1.20 per share. However, this fair value, which was used as the exercise price for the stock options granted in June 2010, was subsequently revisited for financial reporting purposes when our board of directors began to analyze the prospects of an IPO. As such, our board of directors subsequently determined a fair value of our common stock for financial reporting purposes to be $2.56 per share. The PWERM allocation method was used with a risk-adjusted discount rate of 39% based upon an adjusted capital asset pricing model and a lack of marketability discount rate of 30% in the remaining private scenario. The slight decrease in the discount rate from the December 31, 2009 valuation was due to changes in industry and market conditions. The expected outcomes were weighted as follows: (1) 32.5% towards IPO scenarios occurring during late 2010 and through 2012, valued using the market approach; (2) 20% towards a sale occurring during late 2010 and through 2012, valued using the market approach; (3) 20% towards a recapitalization, valued using the income approach; and (4) 27.5% to remaining a private operating company, valued using the income approach. The increase in the fair value of our common stock from our December 30, 2009 valuation was primarily attributable to our business developments in 2010 along with our move towards an IPO, including meeting with banks to discuss our IPO prospects. For the stock options we granted in June 2010, we recorded our stock-based compensation utilizing the updated fair value of $2.56 per share because our board of directors determined that there were no events in the period between the option grants on June 15, 2010 and the date of the retrospective valuation on June 30, 2010 that would result in a change to the fair value of the underlying common stock. Most of the stock options granted in June 2010 were subsequently modified in December 2010 as discussed further below.

July 2010 to November 2010. As of September 30, 2010, our board of directors determined a fair value of our common stock to be $5.32 per share. The PWERM allocation method was used with a risk-adjusted discount rate of 33.7% based upon an adjusted capital asset pricing model and a lack of marketability discount rate of 30% in the remaining private scenario. The slight decrease in the discount rate from the June 30, 2010 retrospective valuation was due to changes in industry and market conditions. The expected outcomes were weighted as follows: (1) 57.5% towards IPO scenarios occurring during 2011 and through 2012, valued using the market approach; (2) 20% towards a sale occurring during 2011, valued using the market approach; (3) 12.5% towards a recapitalization, valued using the income approach; and (4) 10% to remaining a private operating company, valued using the income approach. The increase in the fair value of our common stock from our June 2010 valuation was primarily attributable to our progress towards an IPO, including discussions with investment banks regarding our IPO.

Stock option modification in December 2010. In December 2010, our board of directors, out of an abundance of caution, allowed all employees and non-employees to increase the exercise price of stock options granted to them

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on June 15, 2010 in light of the potential risk of adverse tax consequences under Internal Revenue Service Code Section 409A. Under Section 409A, stock options with an exercise price that is less than the fair market value of the stock on the date of grant may be deemed deferred compensation subject to adverse taxation under Section 409A. As described above, when setting the exercise price for the June 15, 2010 stock option grants, our board of directors determined the fair market value of our common stock to be $1.20 per share, which valuation was subsequently revisited for financial reporting purposes, when our board of directors began to analyze the prospects of an IPO, and determined it to be $2.56 per share. We believe that our board of directors determination of the fair market value of our common stock on June 15, 2010 in reliance upon all material facts available to our board of directors on that date, was reasonable. However, given the potential adverse tax consequences to the optionees if the Internal Revenue Service determines that our original determination was grossly unreasonable, our board of directors decided, out of an abundance of caution, to make the offer to amend. Based on the elections made by the optionees, 1,233,485 of the 1,316,610 options granted on June 15, 2010, including vested and unvested options, were amended on December 27, 2010, such that the original exercise prices of $1.20 per share were increased to $2.56 per share. Accordingly, holders of options to purchase an aggregate 83,125 shares of common stock elected to leave their options unchanged. No other terms of the options were modified and there were no incremental stock-based compensation charges as a result of the re-pricing.

Our stock-based compensation expense for awards granted to our employees was as follows:

	Year Ended December 31,		
	2010	2009	2008
	(in thousands)		
Research and development	$ 680	$ 167	$ 66
General and administrative	588	115	60
Total stock-based compensation	$ 1,268	$ 282	$ 126

As of December 31, 2010, 2009 and 2008, we had $2.4 million, $710,000 and $126,000 of unrecognized stock-based compensation expense, net of estimated forfeitures, that is expected to be recognized over a weighted average period of 1.5, 2.7 and 2.3 years. In future periods, our stock-based compensation expense is expected to increase as a result of our existing unrecognized stock-based compensation to be recognized as these awards vest and as we issue additional stock-based awards to attract and retain employees.

Non-Employee Stock-Based Compensation

We account for stock options and shares of restricted stock granted to non-employees based on the estimated fair value of the awards using the Black-Scholes option-pricing model. The measurement of stock-based compensation for awards granted to non-employees is subject to periodic adjustments as the awards vest, and the resulting change in value, if any, is recognized in our statement of operations during the period that the related services are rendered.

Stock-based compensation expense for awards granted to non-employees was $61,000, $30,000 and $71,000 during the years ended December 31, 2010, 2009 and 2008.

There is inherent uncertainty in these estimates and if different assumptions had been used, the fair value of the awards granted to non-employees and the related stock-based compensation expense could have been significantly different.

Liability Associated with 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

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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.

In connection with an equipment financing agreement entered into in March 2007, we issued warrants to purchase 2,500 shares of our Series A convertible preferred stock. The relative fair value of our Series A warrants of $1,000 was recorded on our balance sheet upon issuance as a warrant liability and as a deferred financing cost in other assets. The Series A warrant liability was subsequently remeasured to fair value at each reporting date and, as of December 31, 2010 and 2009, the Series A warrant liability was $13,000 and $2,000. The change in the fair value of the Series A warrants resulted in a charge to other income (expense), net of $11,000 during the year ended December 31, 2010, a benefit to other income (expense), net of $8,000 during the year ended December 31, 2009 and a charge to other income (expense), net of $4,000 during the year ended December 31, 2008.

In connection with a loan and security agreement entered into in September 2008, we issued warrants to purchase 56,250 shares of our Series B convertible preferred stock. At the close of our Series C convertible preferred stock offering in November 2009, these warrants became exercisable for the Series C convertible preferred stock and the number of exercisable shares increased to 228,264. The relative fair value of these warrants of $0.2 million upon issuance was recorded on our balance sheet as a warrant liability and as a deferred financing cost in other assets. The Series C warrant liability related to the loan and security agreement was subsequently remeasured to fair value at each reporting date and, as of December 31, 2010 and 2009 the warrant liability was $1.2 million and $0.2 million. The change in the fair value of the warrants resulted in a charge to other income (expense), net of $1.0 million during the year ended December 31, 2010, a benefit to other income (expense), net of $0.1 million the year ended December 31, 2009 and a charge to other income (expense), net of $.0.1 million during the year ended December 31, 2008.

In connection with a bridge loan financing in September 2010 (see Bridge Loan below), we issued convertible notes, or the 2010 notes, and warrants, or the 2010 warrants, which 2010 warrants were potentially exercisable into (1) shares of preferred stock sold in the next equity financing with proceeds in excess of $15.0 million with an exercise price equal to the price of the preferred stock sold in such equity financing or (2) shares of our Series C convertible preferred stock at a price $3.94 per share. The aggregate number of shares exercisable under the 2010 warrants was to equal 25% of the principal amount of the corresponding 2010 notes divided by (1) the per share price of the equity securities sold in the next qualified equity financing or (2) the price of the Series C convertible preferred stock of $3.94 per share. In order to determine a fair value for the 2010 warrants issued in the bridge loan, we evaluated multiple potential outcomes using the intrinsic value or Black-Scholes value depending on the scenario and discounted these values back to either September 30, 2010 or December 31, 2010 as appropriate while applying our estimated probabilities to each scenario value. Accordingly, we determined the fair value of the 2010 warrants to be $1.2 million at September 30, 2010, which was recorded as a convertible preferred stock warrant liability and a debt discount. As of December 31, 2010, the related warrant liability was $1.3 million. The change in the fair value of these warrants resulted in a charge of $77,000 to other income (expense), net during the year ended December 31, 2010. The 2010 warrants were net exercised into 107,246 shares of Series C convertible preferred stock in connection with our IPO, which shares were automatically converted to 107,246 shares of common stock immediately prior to our IPO.

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.

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Bridge Loan

On September 14, 2010, we entered into a bridge loan financing, in which we issued the 2010 notes to certain existing investors for an aggregate purchase price of $8.0 million. 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 the 2010 warrants with a fair value of $1.2 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 Liability Associated with 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.

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, 2010, 2009 and 2008, 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, 2010, 2009 or 2008, and we do not expect any significant changes until we are no longer incurring losses.

As of December 31, 2010, 2009 and 2008, we had federal net operating loss carryforwards of $63.8 million, $52.9 million and $33.2 million, and state net operating loss carryforwards of $63.7 million, $52.8 million and $33.2 million. We also had $1.0 million, $0.9 million and $0.5 million of federal research credit carryforwards,

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and $0.7 million, $0.6 million and $0.4 million of state research credit carryforwards as of December 31, 2010, 2009 and 2008. 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 2017. 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, 2010, 2009 and 2008

Revenue

To date, we have not generated any 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.

Research and Development Expenses (in thousands, except percentages)

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2010	2009	2008	2010 vs. 2009	2009 vs. 2008	2010 vs. 2009	2009 vs. 2008
Research and development expenses	$ 8,193	$ 15,502	$ 18,325	$ (7,309)	$ (2,823)	(47)%	(15)%

The $7.3 million decrease during the year ended December 31, 2010 was primarily attributable to a decrease of $4.1 million in development expenses related to our ARX-01 development program which was put on hold due to lack of sufficient funding, and a decrease of $2.2 million in development expenses related to our ARX-02 development program which was completed in early 2010.

The $2.8 million decrease during the year ended December 31, 2009 was primarily attributable to a $1.9 million reduction in clinical development costs for ARX-01 as two Phase 2 studies, which were initiated in the year ended December 31, 2008 and completed later that year and early in the year ended December 31, 2009. This resulted in fewer contract pharmaceutical, engineering and manufacturing costs and lab expenses during the year ended December 31, 2009. The remaining decrease was attributable to a reduction in activity related to contract pharmaceutical, engineering and manufacturing efforts associated with our ARX-02 and ARX-03 development programs during the year ended December 31, 2009.

General and Administrative Expenses (in thousands, except percentages)

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2010	2009	2008	2010 vs. 2009	2009 vs. 2008	2010 vs. 2009	2009 vs. 2008
General and administrative expenses	$ 3,993	$ 3,529	$ 2,365	$ 464	$ 1,164	13%	49%

This $0.5 million increase during the year ended December 31, 2010 was primarily due to an increase in stock option compensation related to the increase in stock option awards granted in 2010, the majority of which were granted to our new Chief Executive Officer, who was hired in May 2010.

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The $1.2 million increase during the year ended December 31, 2009 was attributable to a $0.5 million increase in personnel costs as result of increased headcount, a $0.4 million increase in consulting and professional services related to market research for ARX-01, ARX-02 and ARX-03, and a $0.1 million increase in travel costs related to business development and legal fees to pursue international and domestic patents of our intellectual property during the year ended December 31, 2009.

Interest Income (in thousands, except percentages)

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2010	2009	2008	2010 vs. 2009	2009 vs. 2008	2010 vs. 2009	2009 vs. 2008
Interest income	$ 4	$ 33	$ 484	$ (29)	$ (451)	(88)%	(93)%

The $29,000 decrease during the year ended December 31, 2010 was due to the decrease in our average cash, cash equivalent and short-term investment balances. Our interest income is expected to increase as we invest proceeds from our IPO in high credit quality U.S. government agency obligations and commercial paper.

The $0.5 million decrease during the year ended December 31, 2009 was directly attributable to the $9.5 million decrease in our working capital during the year ended December 31, 2009 as we used the proceeds received from our Series B convertible preferred stock financing and debt financing during the year ended December 31, 2008 to fund operations until we completed our Series C convertible preferred stock financing in November 2009.

Interest Expense (in thousands, except percentages)

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2010	2009	2008	2010 vs. 2009	2009 vs. 2008	2010 vs. 2009	2009 vs. 2008
Interest expense	$ (1,397)	$ (1,242)	$ (404)	$ 155	$ 838	12%	207%

The $0.2 million increase during the year ended December 31, 2010 was primarily attributable to interest related to the $8.0 million in additional debt incurred in September 2010.

The $0.8 million increase during the year ended December 31, 2009 was primarily due to the interest and deferred financing costs we incurred as a result of the $12.0 million in proceeds received from our debt financing in November 2008.

Other Income (Expense), net (in thousands, except percentages)

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2010	2009	2008	2010 vs. 2009	2009 vs. 2008	2010 vs. 2009	2009 vs. 2008
Other income (expense), net	$ (765)	$ 121	$ (52)	$ (886)	$ 173	(732)%	333%

The $0.9 million decrease in other income (expense), net during the year ended December 31, 2010 was primarily attributable to the $1.3 million increase in the fair value of our warrants to purchase convertible preferred stock and the warrants and call option related to our convertible notes issued in 2010, offset by income of $489,000 from the Qualifying Therapeutic Discover Projects grant received in November 2010.

The $0.2 million increase in other income (expense), net during the year ended December 31, 2009 was due to the decrease in the fair value of our warrants to purchase convertible preferred stock combined with realized gains on the sale of investments during the year ended December 31, 2009.

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Liquidity and Capital Resources

We have funded our operations to date primarily with the proceeds from the sale of our securities and the proceeds received from our debt financings. To date, we have not generated any revenue from the sale of our product candidates and do not anticipate generating any revenues for the foreseeable future. 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. As of December 31, 2010, our cash, cash equivalents and short-term investments totaled $3.7 million and we had negative working capital of approximately $7.6 million. In February 2011, we completed our IPO selling 8.0 million shares at $5.00 per share with net proceeds to the company of $35.6 million. We believe that our current cash and cash equivalents, including the net proceeds of $35.6 million from our IPO in February 2011, and the interest earned thereon, will be sufficient to fund our current operations through the second quarter of 2012. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

From inception through December 31, 2010, we have received net proceeds of $54.9 million from the sale of convertible preferred stock and $21.6 million from our debt agreements. As of December 31, 2010, we had $13.2 million of debt outstanding, of which $5.2 million relates to our loan and security agreement and $8.0 million, which does not include the debt discount of $1.2 million, related to the 2010 notes. Subsequent to the end of the year ended December 31, 2010, and in conjunction with our IPO, the outstanding principal and accrued interest under the 2010 notes converted into 2,034,438 shares of common stock.

While we believe that our current cash and cash equivalents, including the net proceeds of $35.6 million from our IPO in February 2011, and the interest earned thereon, will be sufficient to fund our current operations through the second quarter of 2012, we may raise additional funds within this period of time through collaborations, or by undertaking public or private debt or equity financings. Our existing capital resources will not be sufficient to enable us to fund our third Phase 3 trial for ARX-01 and, if we choose, to initiate clinical trials for our product candidates other than ARX-01. We will need to raise substantial additional capital to fund our operations, continue to develop our product candidates and commercialize and market our product candidates.

The sale of additional equity securities could result in additional dilution to our stockholders and those securities may have rights senior to those of our common stock. The incurrence of indebtedness would result in increased debt service obligations and could result in operating and financing covenants that would restrict our operations. We cannot assure you that financing will be available in the amounts we need or on terms acceptable to us, if at all. We currently have no commitments for future external financing.

Cash Flows

The following summary of our cash flows for the periods indicated and has been derived from our financial statements which are included elsewhere in this Form 10-K:

	Year Ended December 31,		
	2010	2009	2008
		(in thousands)	
Net cash used in operating activities	$ (12,225)	$ (19,418)	$ (18,903)
Net cash (used in) provided by investing activities	4,765	8,616	(9,935)
Net cash provided by financing activities	3,365	11,880	31,899

Cash Flows from Operating Activities

Net cash used in operating activities amounted to $12.2 million, $19.4 million and $18.9 million for the years ended December 31, 2010, 2009 and 2008. 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

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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 convertible preferred stock warrant liability.

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 used in operating activities of $19.4 million during the year ended December 31, 2009 reflected a net loss of $20.1 million, partially offset by aggregate non-cash charges of $1.1 million and a net change of $0.4 million in our net operating assets and liabilities. Non-cash charges primarily included $0.5 million of depreciation and amortization, $0.5 million of stock-based compensation and $0.3 million of interest expense relating to our debt, offset by a $0.1 million gain on the revaluation of our convertible preferred stock warrant liability. The net change in our operating assets and liabilities was primarily a result of a $0.4 million decrease in accounts payable and accrued liabilities during the year.

Cash used in operating activities of $18.9 million during the year ended December 31, 2008 reflected a net loss of $20.7 million, partially offset by aggregate non-cash charges of $1.1 million and a net change of $0.7 million in our net operating assets and liabilities. Non-cash charges primarily included $0.4 million of depreciation and amortization, $0.5 million of stock-based compensation, $0.1 million on the revaluation of the convertible preferred stock warrant liability and $0.2 million of interest expense relating to our debt. The net change in our operating assets and liabilities was primarily a result of a $0.7 million increase in our accounts payable and accrued expenses during the year.

Cash Flows from Investing Activities

Our investing activities have consisted primarily of our capital expenditures and purchases and sales of our available-for-sale investments. To date, we have not had significant capital expenditures and we do not have any significant capital expenditures currently planned.

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

During the year ended December 31, 2009, cash provided by investing activities of $8.6 million was primarily a result of $22.6 million in proceeds received from the sale of our investments to fund our working capital needs, partially offset by $13.9 million used for purchases of our investments.

During the year ended December 31, 2008, cash used in investing activities of $9.9 million was primarily a result of $0.5 million in capital expenditures and $14.1 million in purchases of investments using the proceeds we received in our Series B convertible preferred stock financing and the proceeds from a debt financing, partially offset by $4.7 million in proceeds received from sales of our investments.

Cash Flows from Financing Activities

To date, we have financed our operations primarily with the proceeds from the sale of our securities and the proceeds received from our debt financings. As of December 31, 2010, we had outstanding debt of $13.2 million. Subsequent to December 31, 2010, and in conjunction with our IPO, the outstanding principal amount of $8.0 million and accrued interest under the 2010 notes converted into 2,034,438 shares of common stock.

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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.

During the year ended December 31, 2009, cash provided by financing activities of $11.9 million was primarily a result of the receipt of $14.7 million from the sale of our Series C convertible preferred stock in November 2009, partially offset by principal repayments on our long-term debt of $2.9 million.

During the year ended December 31, 2008, cash provided by financing activities of $31.9 million was primarily a result of the receipt of $20.1 million in proceeds from the sale of our Series B convertible preferred stock in February 2008 combined with the receipt of $12.0 million in connection with debt financing.

Contractual Obligations

The following table summarizes our outstanding contractual obligations and commitments as of December 31, 2010 (in thousands):

		Payment by Period			
Contractual Obligations:	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Long-term debt obligations, including current portion[1]	$ 5,465	$ 5,465	$	$	$
Convertible notes[2]	8,097	8,097			
Operating lease agreements[3]	445	348	97		
Total	$ 14,007	$ 13,910	$ 97	$	$