

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**AMENDMENT NO. 4
TO
FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

ACELRX PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)

41-2193603
(I.R.S. Employer
Identification Number)

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)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration number of the earlier effective registration statement for the same offering.

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.

Large accelerated filer

Accelerated filer

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

Smaller reporting company

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the Securities and Exchange Commission declares our registration statement effective. This prospectus is not an offer to sell these securities and is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated January 31, 2011

5,770,000 Shares

ACELRX PHARMACEUTICALS, INC.



Common Stock

\$ per share

- AcelRx Pharmaceuticals, Inc. is offering 5,770,000 shares.
- We anticipate that the initial public offering price will be between \$12.00 and \$14.00 per share.
- This is our initial public offering and no public market currently exists for our shares.
- Proposed trading symbol: NASDAQ Global Market—ACRX.

This investment involves risk. See "[Risk Factors](#)" beginning on page 13.

	<u>Per Share</u>	<u>Total</u>
Public offering price	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to AcelRx Pharmaceuticals, Inc.	\$	\$

The underwriters have a 30-day option to purchase up to 865,500 additional shares of common stock from us to cover over-allotments, if any.

Neither the Securities and Exchange Commission nor any state securities commission has approved of anyone's investment in these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Piper Jaffray

Canaccord Genuity

Cowen and Company

JMP Securities

The date of this prospectus is , 2011



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

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You should rely only on the information contained in this prospectus or any related free writing prospectus we may authorize to be delivered to you. We have not, and the underwriters have not, authorized anyone to provide you with information different from, or in addition to, that contained in this prospectus or any related free writing prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and are seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus or any related free writing prospectus is accurate only as of its date, regardless of its time of delivery, or of any sale of the common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

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Until and including [redacted], 2011 (25 days after the date of this prospectus), all dealers that buy, sell or trade our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside of the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

Unless the context indicates otherwise, as used in this prospectus, the terms “AcelRx,” “AcelRx Pharmaceuticals,” “we,” “us” and “our” refer to AcelRx Pharmaceuticals, Inc. The name “ACELRX” is our trademark. We have a trademark application pending for the term, “NANOTAB” and for our tagline, “ACCELERATE, INNOVATE, ALLEVIATE” in Class 5, in the United States. This prospectus also contains trademarks and trade names that are the property of their respective owners.

PROSPECTUS SUMMARY

The items in the following summary are described in more detail later in this prospectus. This summary provides an overview of selected information and does not contain all the information you should consider. Before you decide to invest in our common stock, you should read the entire prospectus carefully, including the “Risk Factors” and the financial statements and related notes included in this prospectus.

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 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.

Sufentanil NanoTabs

All of our product candidates utilize sufentanil in our proprietary, non-invasive NanoTab sublingual dosage form.

Sufentanil has many pharmacological advantages over other opioids. Sufentanil has a high therapeutic index, or the ratio of the toxic dose to the therapeutic dose of a drug, which is used as a measure of the relative safety of a drug for a particular treatment. Published studies demonstrate that sufentanil produces less respiratory depressive effects relative to its analgesic effects compared to other opioids, which correlates well with preclinical studies demonstrating sufentanil’s high therapeutic index. The molecular attributes of sufentanil allow rapid cell membrane penetration and onset of action, which we believe make sufentanil an attractive opioid for the treatment of both acute and breakthrough pain. Although the analgesic efficacy and tolerability of sufentanil has been well established, its use has been limited due to a short duration of action when delivered intravenously and low gastrointestinal uptake when delivered orally.

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 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 through the oral tissues directly into the bloodstream, and consistent pharmacokinetics.

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

We have established and continue to build proprietary positions for our product candidates in the United States and internationally. We seek patent protection for compositions of matter related to NanoTabs, our formulations, our devices, the combination of our drugs and devices, and methods of treatment using these compositions. We have filed patent applications in the United States and internationally and have one issued patent in Europe. Our issued European patent, though granted, may be opposed by third parties during a nine-month opposition period that ends on April 21, 2011. If issued, we expect our patents will expire between 2027 and 2030.

Our Product Candidates

The following table summarizes key information about our existing product candidates. We currently hold worldwide commercialization rights to all of our product candidates.

<u>Product Candidate</u>	<u>Description</u>	<u>Target Indication</u>	<u>Development Status</u>
ARX-01	Sufentanil NanoTab PCA System	Acute post-operative pain	<ul style="list-style-type: none">• 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 is anticipated to begin in the second half of 2011
ARX-02	Sufentanil NanoTab BTP Management System	Cancer breakthrough pain	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Phase 2 clinical trial and End of Phase 2 meeting successfully completed• Two efficacy trials planned in Phase 3

The Market Opportunity for Our Product Candidates

Acute Post-Operative Pain

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.

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 phlebitis and bacteremia. Catheter tubing tethering the patient to the PCA pump also hinders early post-operative mobility that can lead to increased post-operative complications.
- *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.

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 published data, 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.

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 swallowed and absorbed extensively through the gastrointestinal tract in addition to the oral mucosal tissue, leading to erratic and delayed timing to peak plasma levels, ranging from 20 to 240 minutes. In addition, we believe none of the currently approved cancer breakthrough pain products have effective deterrent features to address the problem of abuse and misuse of pain medication.

Mild Sedation for Painful 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. Many practitioners do not

provide 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 to provide effective pain relief and do not address patient anxiety.

ARX-01—Sufentanil NanoTab PCA System

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 a non-invasive, pre-programmed, handheld PCA device.

Sufentanil 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 has relatively high bioavailability, with lower peak drug levels and a longer duration of action compared to IV delivery. Our novel handheld PCA device enables simple patient-controlled delivery of NanoTabs in the hospital setting. ARX-01 has the potential to address many of the key disadvantages of IV PCA by:

- reducing the incidence of drug related side effects;
- eliminating the risk of IV PCA related infections, reducing analgesic gaps and enhancing mobility; and
- eliminating the risk of programming errors.

We believe that 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.

We have completed three successful Phase 2 clinical trials of sufentanil NanoTabs in 212 patients in the post-operative setting and have completed an End of Phase 2 meeting with the FDA. Our Phase 2 studies for ARX-01 demonstrated analgesic efficacy, a low adverse event profile and excellent device functionality. Across all studies, the average time interval between doses was approximately 80 minutes, which compares favorably to typical redosing intervals for IV PCA, which have an average period between dosing of 20 to 40 minutes. 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 a new drug application, or NDA, for the treatment of acute post-operative pain.

We plan to conduct two Phase 3 trials to evaluate the efficacy of ARX-01 and one Phase 3 open-label active comparator study. Manufacturing scale up activities and Phase 3 clinical trial planning are ongoing to enable initiation and patient enrollment in our first Phase 3 trial in the second half of 2011. We expect to receive top-line data from this trial in the first half of 2012 and expect to complete all studies by the end of 2012, with a potential NDA submission in 2013 if the results from these studies are positive.

ARX-02—Sufentanil NanoTab BTP Management System

ARX-02 is a potential new treatment option for cancer patients who suffer from breakthrough pain. 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. The ARX-02 system consists of a magazine containing 30 single dose applicators. Each single dose applicator includes a sufentanil NanoTab that a patient can self-administer under their tongue for rapid transmucosal absorption.

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 and have completed an End of Phase 2 meeting with the FDA. Our Phase 2 study for ARX-02 demonstrated analgesic efficacy versus placebo and a low adverse event profile. 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 the active drug, with at least 100 patients treated for a minimum of three months, may support an indication for the treatment of breakthrough pain in cancer patients with underlying chronic pain.

Based on the availability of additional financial resources subsequent to this offering, we plan to conduct one Phase 3 efficacy study for ARX-02 and two open-label studies to demonstrate long term safety.

ARX-03—Sufentanil/Triazolam NanoTab

ARX-03 is a single, fixed-dose sublingual product candidate designed to provide non-invasive sedation, anxiety reduction and pain relief for patients prior to a painful procedure 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 successful Phase 2 clinical trial of ARX-03 demonstrating rapid onset of mild sedation and reduction in anxiety in 15 to 30 minutes. We 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.

Further development of ARX-03 will depend on the identification of a partner to support this effort.

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 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.

We plan to advance ARX-01 into Phase 3 trials, to submit an NDA and, if approved, to commercialize ARX-01 ourselves in the United States. Based on the availability of additional 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.

Risks Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary, beginning on page 13. You should read these risks before you invest in our common stock. We may be unable, for many reasons, including those that are beyond our control, to implement our business strategy. In particular, our risks include:

- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- We have never generated any revenue and may never be profitable.
- We depend substantially on the success of our product candidate ARX-01, which is still under clinical development and may not receive regulatory approval or be successfully commercialized.

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- 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.
- 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.
- 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.
- Our designs for the device components of our product candidates for Phase 3 clinical trials may not be fully functional or commercially viable.
- 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.
- We have numerous pending patent applications, but no issued patents in the United States, and the degree of future protection for our proprietary rights is uncertain.

Corporate Information

We were originally incorporated as SuRx Pharmaceuticals, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006. Our principal executive offices are located at 575 Chesapeake Drive, Redwood City, California 94063, and our telephone number is (650) 216-3500. Our website address is www.acelrx.com. The information contained in or that can be accessed through our website is not part of this prospectus.

THE OFFERING

Common stock offered	5,770,000 shares
Over-allotment option	We have granted the underwriters an option for a period of 30 days to purchase up to 865,500 additional shares of common stock.
Common stock outstanding after the offering	16,134,660 shares
Use of proceeds	We intend to use the net proceeds from this offering of approximately \$67.7 million (assuming an initial public offering price of \$13.00 per share, which is the mid-point of the price range set forth on the cover page of this prospectus) to fund Phase 3 development of ARX-01, and for working capital and other general corporate purposes. See “Use of Proceeds” on page 39.
Proposed NASDAQ Global Market symbol	ACRX
Risk factors	You should read the “Risk Factors” section of, and all of the other information set forth in, this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.

The number of shares of common stock outstanding immediately after this offering is based on 10,364,660 shares of common stock outstanding as of September 30, 2010. This number excludes:

- 1,892,860 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2010 under our 2006 Stock Plan having a weighted average exercise price at September 30, 2010 of \$1.88 per share (or \$2.76 per share assuming that the December 2010 stock option modification described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” had occurred as of September 30, 2010);
- 167,630 shares of common stock reserved for future issuance under our 2006 Stock Plan as of September 30, 2010, which share reserve will become available for issuance under our 2011 Equity Incentive Plan upon the execution and delivery of the underwriting agreement for this offering;
- 231,678 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2010 having a weighted average exercise price of \$3.94 per share, which warrants are expected to remain outstanding upon completion of this offering;
- 1,875,000 shares of common stock (which will include the shares then reserved for issuance under our 2006 Stock Plan at the time of the execution and delivery of the underwriting agreement for this offering) reserved for future issuance under our 2011 Equity Incentive Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan; and

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- 250,000 shares of common stock reserved for future issuance under our 2011 Employee Stock Purchase Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan.

Unless otherwise indicated, all information in this prospectus assumes or gives effect to:

- a 1-for-4 reverse stock split of our common stock and preferred stock that became effective on January 28, 2011;
- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
- the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010 that we issued in connection with a bridge loan financing in September 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus;
- the automatic conversion of our remaining warrants to purchase convertible preferred stock, which warrants are expected to remain outstanding upon completion of this offering, into warrants to purchase an aggregate of 231,678 shares of common stock upon completion of this offering;
- the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011;
- the filing of our amended and restated certificate of incorporation, which will occur immediately prior to the completion of this offering; and
- no exercise of the underwriters' over-allotment option.

Because the number of shares that will be issued upon exercise of the 2010 warrants and conversion of the 2010 notes depends upon the actual initial public offering price per share in this offering and, in the case of the 2010 notes, the closing date of this offering, the actual number of shares issuable upon such exercise and conversion will likely differ from the respective number of shares set forth above.

A \$1.00 increase in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would decrease the number of shares of our common stock issued on conversion of the 2010 notes (and therefore the number of shares to be outstanding after this offering) by 55,799 shares, assuming that the closing date of this offering (and therefore the conversion date of the 2010 notes) is January 31, 2011. A \$1.00 decrease in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase the number of shares of our common stock issued on conversion of the 2010 notes (and therefore the number of shares to be outstanding after this offering) by 65,099 shares, assuming that the closing date of this offering (and therefore the conversion date of the 2010 notes) is January 31, 2011. To the extent the closing date of this offering occurs after January 31, 2011,

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the 2010 notes will continue to accrue interest at a rate of 4.0% per annum and additional shares of our common stock will be issued upon conversion of this additional accrued interest. Likewise, if the closing date occurs prior to January 31, 2011, fewer shares will be issued upon conversion of the 2010 notes.

A \$1.00 increase in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase the number of shares of our common stock issued upon the net exercise of the 2010 warrants (and therefore the number of shares to be outstanding after this offering) by 10,989 shares. A \$1.00 decrease in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would decrease the number of shares of our common stock issued upon the net exercise of the 2010 warrants (and therefore the number of shares to be outstanding after this offering) by 12,821 shares.

SUMMARY FINANCIAL DATA

The following table summarizes our financial data. We have derived the following summary statement of operations data for the years ended December 31, 2007, 2008 and 2009 from our audited financial statements included elsewhere in this prospectus. The summary statement of operations data for the nine months ended September 30, 2009 and 2010 and the balance sheet data as of September 30, 2010 have been derived from our unaudited interim financial statements included elsewhere in this prospectus. The unaudited interim financial results have been prepared on the same basis as the audited financial statements and reflect all adjustments necessary to fairly reflect our financial position as of September 30, 2010 and results of operations for the nine months ended September 30, 2009 and 2010. Our historical results are not necessarily indicative of the results that may be expected in the future. The following summary financial data should be read in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,			Nine Months Ended September 30,	
	2007	2008	2009	2009	2010
	(Unaudited)				
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Operating Expenses:					
Research and development	\$ 8,209	\$ 18,325	\$ 15,502	\$ 13,180	\$ 6,309
General and administrative	2,082	2,365	3,529	2,510	3,033
Total operating expenses	10,291	20,690	19,031	15,690	9,342
Loss from operations	(10,291)	(20,690)	(19,031)	(15,690)	(9,342)
Interest income	687	484	33	37	2
Interest expense	(25)	(404)	(1,242)	(965)	(656)
Other income (expense), net	(1)	(52)	121	196	(825)
Loss before provision for income taxes	(9,630)	(20,662)	(20,119)	(16,422)	(10,821)
Provision for income taxes	—	—	—	—	—
Net loss	\$ (9,630)	\$ (20,662)	\$ (20,119)	\$ (16,422)	\$ (10,821)
Net loss per share of common stock, basic and diluted	\$ (26.45)	\$ (43.69)	\$ (34.93)	\$ (29.09)	\$ (16.63)
Shares used in computing net loss per share of common stock, basic and diluted	364,039	472,914	576,021	564,571	650,774
Pro forma net loss per share of common stock, basic and diluted (unaudited) ⁽¹⁾			\$ (3.51)		\$ (1.09)
Shares used in computing pro forma net loss per share of common stock, basic and diluted (unaudited) ⁽¹⁾			5,746,372		9,204,999

⁽¹⁾See Note 11 of the audited financial statements included elsewhere in this prospectus for a discussion regarding the calculations for the net loss per share and the pro forma net loss per share and the shares used in these calculations.

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	As of September 30, 2010		
	<u>Actual</u>	<u>Pro Forma</u> (Unaudited) (in thousands)	<u>Pro Forma as</u> <u>Adjusted</u>
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	\$8,082	\$ 8,082	\$ 75,816
Working capital (deficit)	(1,894)	2,709	70,443
Total assets	9,786	9,786	77,520
Total debt, including convertible notes	10,985	6,382	6,382
Convertible preferred stock warrant liability	2,219	—	—
Convertible preferred stock	55,941	—	—
Total stockholders' equity (deficit)	(60,986)	2,253	69,987

The pro forma column in the balance sheet data above gives effect to the following transactions and adjustments as if they had occurred as of September 30, 2010:

- (1) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
- (2) the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010 that we issued in connection with a bridge loan financing in September 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus;
- (3) the automatic conversion of our remaining warrants to purchase convertible preferred stock, which warrants are expected to remain outstanding upon the completion of this offering, into warrants to purchase an aggregate of 231,678 shares of common stock upon completion of this offering;
- (4) the reclassification of the liability associated with the warrants to purchase convertible preferred stock to additional paid-in capital; and
- (5) the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes, or the 2010 notes, into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011, and the reclassification of the convertible note liability to common stock and additional paid-in capital in connection with the conversion.

The pro forma as adjusted column in the balance sheet data above gives further effect to the sale of 5,770,000 shares of common stock in this offering at an assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, as if the sale of the shares in this offering had occurred as of September 30, 2010.

Because the number of shares of common stock that will be issued upon exercise of the 2010 warrants and conversion of the 2010 notes depends upon the actual initial public offering price per share in this

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offering and, in the case of the 2010 notes, the closing date of this offering, the actual number of shares issuable upon such exercise and conversion will likely differ from the respective number of shares set forth above. See “Prospectus Summary – The Offering.”

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash, cash equivalents and short-term investments, working capital, total assets and total stockholders’ equity (deficit) by \$5.4 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of 1.0 million shares in the number of shares of common stock offered by us would increase (decrease) each of cash, cash equivalents and short-term investments, working capital, total assets and total stockholders’ equity (deficit) by approximately \$12.1 million, assuming that the assumed initial public offering price, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering.

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 prospectus. We believe the risks described below are the risks that are material to us as of the date of this prospectus. 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 \$9.6 million, \$20.7 million, \$20.1 million and \$10.8 million for fiscal years 2007, 2008, 2009 and for the nine months ended September 30, 2010, respectively. As of September 30, 2010, we had an accumulated deficit of \$65.0 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations exclusively 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 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 September 30, 2010, we had negative working capital of approximately \$1.9 million, and our audit report in our 2009 financial statements contains an explanatory paragraph stating that our recurring losses from operations and cash used in operating activities raise substantial doubt about our ability to continue as a going concern. If we are unable to successfully complete this offering, we will need to seek alternative financing or operational plans to continue as a going concern. Even if the offering is successful, we will need to raise additional funds to support our operations, and such funding may not be available to us on acceptable terms, or at all.

We estimate that the net proceeds from this offering will be approximately \$67.7 million, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and offering expenses payable by us. We expect that the net proceeds from this offering and our existing cash and cash equivalents, together with interest, will be sufficient to fund our current operations at least through the end 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 may need to raise additional funds or otherwise obtain partnering if we choose to initiate clinical trials for our product candidates other than ARX-01. In any event, we will require 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;

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- 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.

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, which will have a material adverse effect on our business, operating results and prospects.

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

Pursuant to the loan agreement with Pinnacle Ventures L.L.C., or Pinnacle, we granted to Pinnacle a first priority security interest in substantially all of our assets, with the exception of our intellectual property, where the security interest is limited to proceeds of intellectual property. As of September 30, 2010, we had \$6.4 million of outstanding debt under the Pinnacle loan agreement. Under the terms of this agreement, we are required to make monthly payments of approximately \$442,000 on the first day of each month through November 1, 2011, the maturity date of the loan, with an additional final interest payment of \$600,000 due on November 1, 2011. The loan carries an 8.5% annual interest rate. If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, if we breach the agreement or become insolvent, Pinnacle could elect to declare all amounts outstanding, together with accrued and unpaid interest and penalty, to be immediately due and payable. Even if we were able to prepay the full amount in cash, any such repayment could leave us with little or no working capital for our business. If we are unable to repay those amounts, Pinnacle will have a first claim on our assets pledged under the loan agreement. If Pinnacle should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the loan agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

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 plan to initiate Phase 3 clinical trials for ARX-01 in the second half of 2011. 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.

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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.

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 plan to initiate our first Phase 3 clinical trial of ARX-01 in the second half of 2011. 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;
- 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

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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;
- 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.

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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 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

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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 approval 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.

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;

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- 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 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.

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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.

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.

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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 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;

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- 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 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.

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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.

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.;

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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.

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

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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.

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

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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 "Management" on page 98 of this prospectus, 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 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

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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.

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

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

The patent positions of pharmaceutical companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. The pharmaceutical patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. 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.

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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 these 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, 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.

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Risks Related to this Offering and Ownership of Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

Prior to this offering, there has not been a public market for our common stock. An active trading market for our common stock may not develop following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares will be determined by negotiations between us and representatives of the underwriters and may not be indicative of prices that will prevail in the trading market.

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;
- 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.

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

Our executive officers, directors, 5% stockholders and their affiliates beneficially own approximately 98% of our voting stock and, upon completion of this offering, that same group will beneficially own approximately 62% of our outstanding voting stock. Therefore, even after this offering these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be 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 will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. 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 Global Market have imposed various requirements on public companies. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to 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 will be 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 are not currently required to comply with Section 404 of the Sarbanes-Oxley Act and are therefore not required to make an assessment of the effectiveness of our internal control over financial reporting. Further, our independent registered public accounting firm has not been engaged to express, nor have they expressed, an opinion on the effectiveness of our internal control over financial reporting.

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. For the year ending December 31, 2011, pursuant to Section 404 of the Sarbanes-Oxley Act, our management will be required to deliver a report that assesses the effectiveness of our internal control over financial reporting. In addition, our independent registered public accounting firm will also be required to deliver an attestation report on the operating 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.

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If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing common stock in this offering will pay a price per share that substantially exceeds the pro forma book value (deficit) per share of our tangible assets after subtracting our liabilities. As a result, investors purchasing common stock in this offering will incur immediate dilution of \$8.66 per share, based on an assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and our pro forma net tangible book value (deficit) as of September 30, 2010. Further, based on these assumptions, investors purchasing common stock in this offering will contribute approximately 53% of the total amount invested by stockholders since our inception, but will own only approximately 36% of the shares of common stock outstanding. For information on how the foregoing amounts were calculated, see “Dilution.”

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of September 30, 2010, options to purchase 1,892,860 shares of our common stock at a weighted average exercise price at September 30, 2010 of \$1.88 per share (or \$2.76 per share assuming that the December 2010 stock option modification described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” had occurred as of September 30, 2010) and warrants exercisable for up to 231,678 shares of our common stock, that are expected to remain outstanding after completion of this offering at a weighted average exercise price of approximately \$3.94 per share, were outstanding. The exercise of any of these options or warrants would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

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.

Substantially all of our existing stockholders are subject to lock-up agreements with the underwriters of this offering that restrict the stockholders’ ability to transfer shares of our common stock for at least 180 days from the date of this prospectus. The lock-up agreements limit the number of shares of common stock that may be sold immediately following the public offering. Subject to certain limitations, approximately 10,364,660 shares will become eligible for sale upon expiration of the lock-up period, as calculated and described in more detail in the section entitled “Shares Eligible for Future Sale”. 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 these 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 180-day 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, adopted by our board of directors in January 2011, or the 2011 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 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 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.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

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 believe that, with our initial public offering, our most recent private placement and other transactions that have occurred over the past three years, we may have triggered an "ownership change" limitation. We may also 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.

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

We have never declared or paid any cash 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.

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 the 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements under “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business” and elsewhere in this prospectus contain forward-looking statements. In some cases, you can identify forward-looking statements by the following words: “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, 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;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our use of the proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- our ability to obtain and maintain intellectual property protection for our product candidates.

In addition, you should refer to the “Risk Factors” section of this prospectus for a discussion of 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 prospectus 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

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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. 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.

USE OF PROCEEDS

We estimate that our net proceeds from the sale of the common stock that we are offering will be approximately \$67.7 million, assuming an initial public offering price of \$13.00 per share, which is the mid-point of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' over-allotment option to purchase additional shares in this offering is exercised in full, we estimate that our net proceeds will be approximately \$78.2 million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each \$1.00 increase (decrease) in the assumed initial public offering price of \$13.00 per share would increase (decrease) the net proceeds to us from this offering by approximately \$5.4 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately \$12.1 million, assuming that the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

We currently expect to use the net proceeds from this offering as follows:

- approximately \$43.1 million of these net proceeds to fund our Phase 3 development of ARX-01; and
- the remainder to fund working capital needs and other general corporate purposes.

The costs and timing of drug development and marketing approval, particularly conducting clinical trials, are highly uncertain, are subject to substantial risks and can often change. Accordingly, we may change the allocation of use of these proceeds as a result of contingencies such as the progress and results of our clinical trials and other development activities, the establishment of collaborations, our manufacturing requirements and regulatory or competitive developments.

Pending their use, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the United States government.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and our capitalization as of September 30, 2010:

- on an actual basis;
- on a pro forma basis to give effect to the following transactions and adjustments as if they had occurred as of September 30, 2010:
 - (1) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
 - (2) the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010 that we issued in connection with a bridge loan financing in September 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus;
 - (3) the automatic conversion of our remaining warrants to purchase convertible preferred stock, which warrants are expected to remain outstanding upon the completion of this offering, into warrants to purchase an aggregate of 231,678 shares of common stock upon completion of this offering;
 - (4) the reclassification of the liability associated with the warrants to purchase convertible preferred stock to additional paid-in capital; and
 - (5) the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes, or the 2010 notes, into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011, and the reclassification of the convertible note liability to common stock and additional paid-in capital in connection with the conversion; and
- on a pro forma as adjusted basis to give further effect to the sale of 5,770,000 shares of common stock in this offering at an assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, as if the sale of the shares in this offering had occurred as of September 30, 2010.

Because the number of shares of common stock that will be issued upon exercise of the 2010 warrants and conversion of the 2010 notes depends upon the actual initial public offering price per share in this offering and, in the case of the 2010 notes, the closing date of this offering, the actual number of shares issued upon such exercise and conversion will likely differ from the respective number of shares set forth above. See “Prospectus Summary – The Offering.”

You should read this table in conjunction with the sections titled “Selected Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes included elsewhere in this prospectus. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial public offering price and other terms of this offering determined at pricing.

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	September 30, 2010		
	Actual	Pro Forma	Pro Forma as Adjusted
	(in thousands, except share and per share data) (Unaudited)		
Cash, cash equivalents and short-term investments	\$ 8,082	\$ 8,082	\$ 75,816
Long-term debt, including current portion	6,382	6,382	6,382
Convertible notes	4,603	—	—
Call option liability	476	—	—
Convertible preferred stock warrant liability	2,219	—	—
Convertible preferred stock, \$0.001 par value: 46,736,125 shares authorized, 7,151,802 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	55,941	—	—
Stockholders' equity (deficit):			
Preferred stock, \$0.001 par value: no shares authorized, issued or outstanding, actual and pro forma; 10,000,000 shares authorized, no shares issued and outstanding, pro forma as adjusted	—	—	—
Common stock, \$0.001 par value: 71,000,000 shares authorized, 674,353 shares issued and outstanding, actual; 71,000,000 shares authorized, 10,364,660 shares issued and outstanding, pro forma; 100,000,000 shares authorized, 16,134,660 shares issued and outstanding, pro forma as adjusted	1	10	16
Additional paid-in capital	4,053	67,283	135,011
Deficit accumulated during the development stage	(65,040)	(65,040)	(65,040)
Total stockholders' equity (deficit)	(60,986)	2,253	69,987
Total capitalization	\$ 8,635	\$ 8,635	\$ 76,369

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase (decrease) each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately \$5.4 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1.0 million shares in the number of shares offered by us would increase (decrease) each of cash, cash equivalents and short-term investments, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately \$12.1 million, assuming that the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial public offering price and other terms of this offering determined at pricing.

The outstanding share information in the table above excludes:

- 1,892,860 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2010 under our 2006 Stock Plan having a weighted average exercise price at September 30, 2010 of \$1.88 per share (or \$2.76 per share assuming that the December 2010 stock option modification described under "Management's Discussion and

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Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” had occurred as of September 30, 2010);

- 167,630 shares of common stock reserved for future issuance under our 2006 Stock Plan as of September 30, 2010, which share reserve will become available for issuance under our 2011 Equity Incentive Plan upon the execution and delivery of the underwriting agreement for this offering;
- 231,678 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2010 having a weighted average exercise price of \$3.94 per share, which warrants are expected to remain outstanding upon completion of this offering;
- 1,875,000 shares of common stock (which will include the shares then reserved for issuance under our 2006 Stock Plan at the time of the execution and delivery of the underwriting agreement for this offering) reserved for future issuance under our 2011 Equity Incentive Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan; and
- 250,000 shares of common stock reserved for future issuance under our 2011 Employee Stock Purchase Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan.

DILUTION

If you invest in our common stock, you will experience immediate and substantial dilution to the extent of the difference between the initial public offering price of our common stock and the pro forma as adjusted net tangible book value (deficit) per share of our common stock immediately after the offering.

Our historical net tangible book value (deficit) per share is determined by dividing our total tangible assets, less total liabilities and convertible preferred stock, by the actual number of outstanding shares of our common stock. The historical net tangible book value (deficit) of our common stock as of September 30, 2010 was \$(61.0) million, or \$(90.44) per share. The pro forma net tangible book value (deficit) of our common stock as of September 30, 2010 was \$2.3 million, or \$0.22 per share. The pro forma net tangible book value (deficit) per share gives effect to:

- (1) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
- (2) the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010 that we issued in connection with a bridge loan financing in September 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus;
- (3) the automatic conversion of our remaining warrants to purchase convertible preferred stock, which warrants are expected to remain outstanding upon the completion of this offering, into warrants to purchase an aggregate of 231,678 shares of common stock upon completion of this offering;
- (4) the reclassification of the liability associated with the warrants to purchase convertible preferred stock to additional paid-in capital; and
- (5) the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes, or the 2010 notes, into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011, and the reclassification of the convertible note liability to common stock and additional paid-in capital in connection with the conversion.

Because the number of shares of common stock that will be issued upon exercise of the 2010 warrants and conversion of the 2010 notes depends upon the actual initial public offering price per share in this offering and, in the case of the 2010 notes, the closing date of this offering, the actual number of shares issuable upon such exercise and conversion will likely differ from the respective number of shares set forth above. See “Prospectus Summary – The Offering.”

The pro forma as adjusted net tangible book value (deficit) of our common stock as of September 30, 2010 was \$70.0 million, or \$4.34 per share. The pro forma as adjusted net tangible book value (deficit) gives effect to (1) the sale of 5,770,000 shares of common stock in this offering at an assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, and (2) the pro forma transactions and other adjustments described in the second preceding paragraph. The difference between the initial public offering price and the pro forma as adjusted net tangible book value (deficit) per share represents an immediate dilution of \$8.66 per share to new investors purchasing common stock in this offering.

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The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share	<u>\$ 13.00</u>
Historical net tangible book value (deficit) per share as of September 30, 2010	<u>\$(90.44)</u>
Pro forma increase in net tangible book value (deficit) per share attributable to the pro forma transactions and other adjustments described in the preceding second paragraph	<u>90.65</u>
Pro forma net tangible book value (deficit) per share before this offering	0.22
Pro forma increase in net tangible book value (deficit) per share attributable to investors participating in this offering	<u>4.12</u>
Pro forma as adjusted net tangible book value (deficit) per share after this offering	<u>4.34</u>
Dilution per share to new investors purchasing common stock in this offering	<u>\$ 8.66</u>

Each \$1.00 increase (decrease) in the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase (decrease) our pro forma as adjusted net tangible book value (deficit) by approximately \$5.4 million, or approximately \$0.33 per share, and the dilution per share to new investors purchasing common stock in this offering by approximately \$0.67 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of 1.0 million shares in the number of shares offered by us would increase our pro forma as adjusted net tangible book value (deficit) by approximately \$12.1 million, or \$0.45 per share, and the dilution per share to new investors purchasing common stock in this offering would be \$8.21 per share, assuming that the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a decrease of 1.0 million shares in the number of shares offered by us would decrease our pro forma as adjusted net tangible book value (deficit) by approximately \$12.1 million, or \$0.51 per share, and the dilution per share to new investors purchasing common stock in this offering would be \$9.17 per share, assuming that the assumed initial public offering price remains the same, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial public offering price and other terms of this offering determined at pricing.

If the underwriters' over-allotment option to purchase additional shares from us is exercised in full, and assuming the initial public offering price is \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, the pro forma as adjusted net tangible book value (deficit) per share after this offering would be \$4.73 per share, the increase in pro forma as adjusted net tangible book value (deficit) per share to existing stockholders would be \$0.39 per share and the dilution to new investors purchasing shares in this offering would be \$8.27 per share.

The table below summarizes as of September 30, 2010, on the pro forma as adjusted basis described above, the number of shares of our common stock we issued and sold, the total consideration we received and the average price per share (1) paid to us by existing stockholders; (2) to be paid by new investors purchasing our common stock in this offering at the assumed initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by

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us; and (3) the average price per share paid by existing stockholders and by new investors who purchase shares of common stock in this offering.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	10,364,660	64%	\$ 67,283	47%	\$ 6.49
New investors	5,770,000	36	75,010	53	13.00
Totals	16,134,660	100%	\$142,293	100%	\$ 8.82

The number of shares of common stock outstanding immediately after this offering is based on 10,364,660 shares of common stock outstanding as of September 30, 2010, after giving effect to the pro forma transactions described in the second preceding paragraph. This number excludes:

- 1,892,860 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2010 under our 2006 Stock Plan having a weighted average exercise price at September 30, 2010 of \$1.88 per share (or \$2.76 per share assuming that the December 2010 stock option modification described under “Management’s Discussion and Analysis of Financial Condition and Results of Operations – Critical Accounting Policies and Estimates – Stock-Based Compensation” had occurred as of September 30, 2010);
- 167,630 shares of common stock reserved for future issuance under our 2006 Stock Plan as of September 30, 2010, which share reserve will become available for issuance under our 2011 Equity Incentive Plan upon the execution and delivery of the underwriting agreement for this offering;
- 231,678 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2010 having a weighted average exercise price of \$3.94 per share, which warrants are expected to remain outstanding upon completion of this offering;
- 1,875,000 shares of common stock (which will include the shares then reserved for issuance under our 2006 Stock Plan at the time of the execution and delivery of the underwriting agreement for this offering) reserved for future issuance under our 2011 Equity Incentive Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan; and
- 250,000 shares of common stock reserved for future issuance under our 2011 Employee Stock Purchase Plan, which will become effective immediately upon the execution and delivery of the underwriting agreement for this offering, as well as any future increases in the number of shares of common stock reserved for issuance under this plan.

If the underwriters’ over-allotment option is exercised in full, the pro forma as adjusted number of shares held by the existing stockholders after this offering would be 10,364,660, or 61% of the pro forma as adjusted total number of shares of our common stock outstanding after this offering, and the number of shares held by new investors would increase to 6,635,500, or 39% of the pro forma as adjusted total number of shares of our common stock outstanding after this offering.

Effective upon the closing of this offering, an aggregate of up to 2,125,000 shares of our common stock will be reserved for future issuance under our equity benefit plans, and the number of reserved shares will also be subject to automatic annual increases in accordance with the terms of the plans. To the extent that new options are issued under our equity benefit plans or we issue additional shares of common stock in the future, there will be further dilution to investors purchasing common stock in this offering.

SELECTED FINANCIAL DATA

We derived the selected statements of operations data for the years ended December 31, 2007, 2008 and 2009 and the balance sheet data as of December 31, 2008 and 2009 from our audited financial statements included elsewhere in this prospectus. The summary statement of operations data for the nine months ended September 30, 2009 and 2010 and the balance sheet data as of September 30, 2010 have been derived from our unaudited financial statements included elsewhere in this prospectus. We derived the selected statements of operations data for the period from July 13, 2005 (inception) through December 31, 2005 and the year ended December 31, 2006 and the balance sheet data as of December 31, 2005, 2006 and 2007 from our audited financial statements which are not included in this prospectus. Our historical results are not necessarily indicative of the results that may be expected in the future. You should read the following selected financial data below in conjunction with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes included elsewhere in this prospectus. The selected financial data in this section is not intended to replace the financial statements and is qualified in its entirety by the financial statements and related notes included in this prospectus.

	Period from July 13, 2005 (Inception) Through December 31, 2005	Year Ended December 31,				Nine Months Ended September 30,	
		2006	2007	2008	2009	2009	2010
(Unaudited)							
(in thousands, except share and per share data)							
Statement of Operations Data:							
Operating Expenses:							
Research and development	\$ 35	\$ 3,533	\$ 8,209	\$ 18,325	\$ 15,502	\$ 13,180	\$ 6,309
General and administrative	5	520	2,082	2,365	3,529	2,510	3,033
Total operating expenses	40	4,053	10,291	20,690	19,031	15,690	9,342
Loss from operations	(40)	(4,053)	(10,291)	(20,690)	(19,031)	(15,690)	(9,342)
Interest income	—	347	687	484	33	37	2
Interest expense	—	(62)	(25)	(404)	(1,242)	(965)	(656)
Other income (expense), net	—	—	(1)	(52)	121	196	(825)
Loss before provision for income taxes	(40)	(3,768)	(9,630)	(20,662)	(20,119)	(16,422)	(10,821)
Provision for income taxes	—	—	—	—	—	—	—
Net loss	(40)	\$ (3,768)	\$ (9,630)	\$ (20,662)	\$ (20,119)	\$ (16,422)	\$ (10,821)
Net loss per share of common stock, basic and diluted	\$ 0.00	\$ (36.90)	\$ (26.45)	\$ (43.69)	\$ (34.93)	\$ (29.09)	\$ (16.63)
Shares used in computing net loss per share of common stock, basic and diluted	—	102,102	364,039	472,914	576,021	564,571	650,774
Pro forma net loss per share of common stock, basic and diluted (unaudited) ⁽¹⁾				\$ (3.51)			\$ (1.09)
Shares used in computing pro forma net loss per share of common stock, basic and diluted (unaudited) ⁽¹⁾				5,746,372			9,204,999

⁽¹⁾See Note 11 of the audited financial statements included elsewhere in this prospectus for discussion regarding the calculations for the net loss per share and the pro forma net loss per share and the shares used in these calculations.

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	As of December 31,					September 30,
	2005	2006	2007	2008	2009	2010
						(Unaudited)
				(in thousands)		
Balance Sheet Data:						
Cash, cash equivalents and short-term investments	\$—	\$ 17,098	\$ 7,699	\$ 20,207	\$ 12,546	\$ 8,082
Working capital (deficit)	(40)	16,537	6,959	16,450	6,931	(1,894)
Total assets	—	18,193	10,038	22,679	14,491	9,786
Total debt, including convertible notes	—	—	525	12,334	9,734	10,985
Convertible preferred stock warrant liability	—	—	—	240	169	2,219
Convertible preferred stock	—	21,016	21,016	41,156	55,871	55,941
Total stockholders' deficit	(40)	(3,715)	(13,189)	(33,335)	(52,994)	(60,986)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and the related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results could differ materially from those discussed below. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section entitled "Risk Factors" included elsewhere in this prospectus.

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 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 to date primarily from the private placement of convertible preferred stock and proceeds received from our debt financings. From inception through September 30, 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 September 30, 2010, we had \$14.4 million of debt outstanding, of which \$6.4 million relates to our loan and security agreement and \$8.0 million, which does not include the debt discount of \$3.4 million, relates to our convertible note agreement.

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 \$20.1 million and \$10.8 million for the year ended December 31, 2009 and the nine months ended September 30, 2010. As of September 30, 2010, we had an accumulated deficit of \$65.0 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 September 30, 2010, our principal sources of liquidity are our cash, cash equivalents and short-term investments, which totaled \$8.1 million.

We expect to incur increasing expenses over the next several years, principally to develop ARX-01, as well as to further increase our spending to manufacture, sell and market our product candidates. Based on the availability of additional financial resources, subsequent to this offering, 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.

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Furthermore, upon closing of this offering, 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 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.

Prior to January 1, 2009, we did not track our internal research and development costs or our 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 for the year ended December 31, 2009 and the nine months ended September 30, 2010:

	Year Ended December 31, 2009	(in thousands)	Nine Months Ended September 30, 2010
ARX-01	\$ 5,343		\$ 505
ARX-02	2,721		517
ARX-03	1,426		1,538
Overhead	6,012		3,749
Total Research & Development Expenses	<u>\$ 15,502</u>		<u>\$ 6,309</u>

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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 to incur increased research and development expenses as we commence our Phase 3 clinical program including the clinical trials necessary to obtain regulatory approval for ARX-01.

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 as we begin operating as a public company and 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 consists primarily of the change in the fair value of our warrants to purchase convertible preferred stock. Our outstanding warrants to purchase convertible preferred stock are classified as liabilities and, as such, are remeasured to fair value at each balance sheet date with the corresponding gain or loss from the adjustment recorded as other income (expense), net. We will continue to record adjustments to the fair value of the warrants until they are exercised, converted to warrants to purchase common stock or expire, at which time the warrants will no longer be remeasured at each balance sheet date. Upon the closing of this offering, our outstanding warrants to purchase convertible preferred stock will automatically convert into warrants to purchase common stock.

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 then expected for the year ended December 31, 2010.

As a result of this workforce reduction, we recorded a charge of \$0.1 million related to employee severance and other benefits which was included as operating expenses in the statement of operations for

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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 nine months ended September 30, 2010, we paid the remaining amounts outstanding.

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,			Nine Months Ended September 30,	
	2007	2008	2009	2009	2010
Expected volatility	72%	74%	73%	73%	75%
Expected term (in years)	6.25	6.25	6.25	6.25	5.75 - 6.25
Risk-free interest rate	3.6% - 4.6%	3.5%	3.0%	3.0%	1.6% - 2.4%
Expected dividend yield	0%	0%	0%	0%	0%

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 unrelated 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 have no trading history. 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 principle business operations.

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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 are also required to estimate the fair value of the common stock underlying our stock-based awards when performing the fair value calculations with the Black-Scholes option-pricing model. The fair values of the common stock underlying our stock-based awards were estimated on each grant date by our board of directors, with input from management. 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 has 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, 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;
- 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;

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- 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, the 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 are 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 is adjusted to reflect the risks inherent in our cash flows. The market approach estimates the fair value of a company by applying market multiples of comparable publicly traded companies in our industry or similar lines of business which are 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 exceeds 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 is allocated to the convertible preferred stock to incorporate higher aggregate liquidation preferences. In the IPO scenarios, the equity value is allocated pro rata among the shares of common stock and each series of convertible preferred stock, which causes 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 will be weighted according to the board of directors' estimate of the probability of each scenario.

Over time, as certainty developed regarding possible discrete events, including an 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 has been utilized since July 2009.

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Information regarding stock option grants to our employees since January 1, 2009 is summarized as follows:

<u>Grant Date</u>	<u>Number of Options Granted</u>	<u>Exercise Price</u>	<u>Fair Value Per Share of Common Stock</u>	<u>Aggregate Grant Date Fair Value⁽¹⁾</u>
July 1, 2009	231,875	\$ 5.52	\$ 5.52	\$ 449,000
June 15, 2010	83,125	1.20	2.56	166,000
June 15, 2010	1,233,485	2.56	2.56	2,465,000
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 September 30, 2010 was \$21.0 million based on the estimated fair value for our common stock of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus.

No single event caused the valuation of our common stock to increase or decrease through September 30, 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, the board 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 with our Series B convertible preferred stock financing in February 2008. During the first quarter of 2010, we continued to

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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, the board 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 the 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 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, the board 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.

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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 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, the board 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 the board's determination of the fair market value of our common stock on June 15, 2010 in reliance upon all material facts available to the board 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 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 is as follows:

	Year Ended December 31,			Nine Months Ended September 30,	
	2007	2008	2009	2009	2010
			(in thousands)		(Unaudited)
Research and development	\$ 25	\$ 66	\$ 167	\$ 74	\$ 539
General and administrative	4	60	115	97	444
Total stock-based compensation	\$ 29	\$ 126	\$ 282	\$ 171	\$ 983

As of December 31, 2009 and September 30, 2010, we had \$710,000 and \$2.3 million of unrecognized stock-based compensation expense, net of estimated forfeitures, that is expected to be recognized over a weighted average period of 2.7 and 1.6 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 the related services are rendered.

Stock-based compensation expense for awards granted to non-employees was \$4,000, \$71,000, \$30,000, \$30,000 and \$31,000 during the years ended December 31, 2007, 2008, 2009 and the nine months ended September 30, 2009 and 2010.

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 are classified as liabilities on our balance sheets at fair value because the warrants may conditionally obligate us to redeem the underlying convertible preferred stock at some point in the future. The warrants are subject to remeasurement at each balance sheet date, and any change in fair value is recognized as a component of other income (expense), net, in the statements of operations. We estimated the fair value of these warrants at the respective balance sheet dates using the Black-Scholes option-pricing model. We use 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 expected volatility of the underlying stock. These assumptions are 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 has subsequently been remeasured to fair value at each reporting date and, as of December 31, 2009 and September 30, 2010, the Series A warrant liability was \$2,000 and \$10,000. The change in the fair value of these warrants resulted in a gain of \$8,000 during the year ended December 31, 2009 and a charge of \$8,000 for the nine months ended September 30, 2010 to other income (expense), net.

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 has subsequently been remeasured to fair value at each reporting date and, as of December 31, 2009 and September 30, 2010, the warrant liability was \$0.2 million and \$1.0 million. The change in the fair value of these warrants resulted in a gain of \$0.1 million during the year ended December 31, 2009 and a charge of \$0.8 million during the nine months ended September 30, 2010 to other income (expense), net.

In connection with the issuance of a bridge loan financing in September 2010, we issued convertible notes, or the 2010 notes, and warrants, or the 2010 warrants, that are 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 will 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 upon issuance of 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 September 30, 2010 while applying our estimated probabilities to each scenario value. These scenarios included a potential initial public offering or potential merger or sale at different times during 2011 and 2012 as well as remaining private with estimated future qualifying equity financings. Accordingly, we determined the fair value of the 2010 warrants to be \$1.2 million, which was recorded as a convertible preferred stock warrant liability and a debt discount. There was no change in the fair value of these between the time of issuance on September 14, 2010 and the end of the period on September 30, 2010.

We will continue to record adjustments to the fair value of the warrants to purchase convertible preferred stock until they are exercised, converted into warrants to purchase common stock or expire, at

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which time the warrants will no longer be remeasured at each balance sheet date. At that time, the then-current aggregate fair value of these warrants will be reclassified from liabilities to additional paid-in capital and we will no longer remeasure the liability associated with these warrants to purchase convertible preferred stock to fair value.

Bridge Loan and Beneficial Conversion Features

On September 14, 2010, we entered into a bridge loan financing, in which we issued 2010 notes to certain existing investors for an aggregate purchase price of \$8.0 million. The 2010 notes cannot be prepaid without written consent of the holders of the 2010 notes, accrue interest at a rate of 4.0% per annum and have 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 are automatically convertible (1) into the securities that are sold in our next equity financing prior to September 14, 2011, with total proceeds of not less than \$15.0 million, or qualified financing, at the price at which such securities are sold to other investors in the qualified financing, (2) into securities that are sold in our initial public offering at a conversion price equal to 80% of the initial public offering price or (3) following September 14, 2011, with the consent of the holders of a majority of the principal amount of the 2010 notes still outstanding, into shares of Series C convertible preferred stock at the Series C price of \$3.94 per share. In addition, holders of the 2010 notes have the option to convert the 2010 notes into shares of Series C convertible preferred stock in connection with a liquidation, sale of substantially all of our assets, or merger, if such liquidation, sale of substantially all of our assets, or merger occurs before the qualified financing or initial public offering.

Upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 notes, we will issue an additional \$4.0 million 2010 notes. This additional \$4.0 million was determined to be a call option that has been recorded at its fair value of \$0.5 million as a debt discount that will be amortized to interest expense over the one-year term of the loan. 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 September 30, 2010 while applying estimated probabilities to each scenario value. As of September 30, 2010, these scenarios include a potential initial public offering, merger or sale at different times during 2011 and 2012 as well as remaining private. The call option will be remeasured to its fair value at the end of each reporting period until expired or exercised. During the first quarter of the year ending December 31, 2011, the 2010 notes were amended so that the call option will expire upon the closing of this offering.

Also in connection with the bridge loan financing, we issued the 2010 warrants with a fair value of \$1.2 million, which were recorded as a debt discount that will be amortized to interest expense over the one-year term of the loan.

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.

In addition, we also recognized a beneficial conversion feature related to the 2010 warrants and the call option discussed above in the aggregate amount of \$1.7 million as an additional debt discount that will also be amortized to interest expense over the one-year term of the bridge loan. In addition to these beneficial conversion features, the 2010 notes have contingent beneficial conversion features related to the conversion options following the maturity of the 2010 notes or in connection with a liquidation, sale or merger into Series C convertible preferred stock. The contingent beneficial features were determined on the date of the issuance of the 2010 notes based on the intrinsic value of this feature in the amount of \$2.8 million. This beneficial conversion feature will be recorded if and when the related contingent event occurs.

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

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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, 2008 and 2009, 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, 2007, 2008 or 2009 and we do not expect any significant changes until we are no longer incurring losses.

As of December 31, 2009, we had federal net operating loss carryforwards of \$52.9 million and state net operating loss carryforwards of \$52.8 million. We also had federal and state research credit carryforwards of \$0.9 million and \$0.6 million. 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. Utilization of these net operating losses and credit carryforwards may be subject to an annual limitation due to applicable provisions of the Internal Revenue Section 382 and state and local tax laws if we experience an “ownership change” in the future including, for example, as a result of the shares issued in this offering aggregated with certain other sales of our stock before or after this offering.

Results of Operations—Comparison of the Nine Months Ended September 30, 2009 and 2010

	Nine Months Ended September 30,		Increase / (Decrease)	% Increase / (Decrease)
	2009	2010		
		(Unaudited) (dollars in thousands)		
Research and development	\$ 13,180	\$ 6,309	\$(6,871)	(52)%
General and administrative	2,510	3,033	523	21 %
Interest income	37	2	(35)	(95)%
Interest expense	(965)	(656)	(309)	(32)%
Other income (expense), net	196	(825)	(1,021)	(521)%

Revenue

We did not generate any revenue during the nine months ended September 30, 2009 or 2010.

Research and Development Expenses

Research and development expenses decreased by \$6.9 million, or 52%, to \$6.3 million during the nine months ended September 30, 2010 from \$13.2 million during the nine months ended September 30, 2009. The \$6.8 million decrease reflects a decrease of \$4.6 million in development expenses related to our ARX-01 development program and a decrease of \$1.8 million in development expenses related to our ARX-02 development program.

General and Administrative Expenses

General and administrative expenses increased by \$0.5 million, or 21%, to \$3.0 million during the nine months ended September 30, 2010 from \$2.5 million during the nine months ended September 30, 2009. This increase was due to \$0.3 million in stock option compensation expense, \$0.1 million in personnel related expense and \$0.1 million in legal expense.

[Table of Contents](#)**Interest Income**

Interest income decreased by \$35,000 to \$2,000 during the nine months ended September 30, 2010 from \$37,000 during the nine months ended September 30, 2009. This decrease was due to a decrease in our average cash, cash equivalent and short-term investment balances during the nine months ended September 30, 2010.

Interest Expense

Interest expense decreased by \$0.3 million to \$0.7 million during the nine months ended September 30, 2010 from \$1.0 million during the nine months ended September 30, 2009. This decrease was primarily attributable to our paying down of our outstanding debt during the related periods without incurring additional debt until the end of the nine months ended September 30, 2010, therefore, maintaining lower average debt balance during the nine months ended September 30, 2010.

Other Income (Expense), net

Other income (expense), net changed by \$1.0 million to an expense of \$0.8 million during the nine months ended September 30, 2010 from income of \$0.2 million during the nine months ended September 30, 2009. The change in other income (expense), net primarily reflects the remeasurement of our convertible preferred stock warrant liabilities.

Results of Operations—Comparison of the Years Ended December 31, 2008 and 2009

	<u>Year Ended December 31,</u>		<u>Increase / (Decrease)</u>	<u>% Increase / (Decrease)</u>
	<u>2008</u>	<u>2009</u>		
	(dollars in thousands)			
Research and development	\$18,325	\$15,502	\$(2,823)	(15)%
General and administrative	2,365	3,529	1,164	49 %
Interest income	484	33	(451)	(93)%
Interest expense	(404)	(1,242)	838	207 %
Other income (expense), net	(52)	121	173	333 %

Revenue

We did not generate any revenue for the years ended December 31, 2008 or 2009.

Research and Development Expenses

Research and development expenses decreased by \$2.8 million, or 15%, to \$15.5 million during the year ended December 31, 2009 from \$18.3 million during the year ended December 31, 2008. This decrease 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

General and administrative expenses increased by \$1.1 million, or 49%, to \$3.5 million during the year ended December 31, 2009 from \$2.4 million during the year ended December 31, 2008. This increase 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

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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

Interest income decreased by \$0.5 million to \$33,000 during the year ended December 31, 2009 from \$0.5 million during the year ended December 31, 2008. This decrease 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

Interest expense increased by \$0.8 million to \$1.2 million during the year ended December 31, 2009 from \$0.4 million during the year ended December 31, 2008. This increase 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

Other income (expense), net changed by \$0.2 million to income of \$0.1 million during the year ended December 31, 2009 from an expense of \$0.1 million during the year ended December 31, 2008. The change in other income (expense), net 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.

Results of Operations—Comparison of the Years Ended December 31, 2007 and 2008

	<u>Year Ended December 31,</u>		<u>Increase / (Decrease)</u>	<u>% Increase / (Decrease)</u>
	<u>2007</u>	<u>2008</u>		
	(dollars in thousands)			
Research and development	\$8,209	\$18,325	\$10,116	123 %
General and administrative	2,082	2,365	283	14 %
Interest income	687	484	(203)	(30)%
Interest expense	(25)	(404)	379	1,516 %
Other income (expense), net	(1)	(52)	(51)	(5,100)%

Revenue

We did not generate any revenue for the years ended December 31, 2007 or 2008.

Research and Development Expenses

Research and development expenses increased by \$10.1 million, or 123%, to \$18.3 million during the year ended December 31, 2008 from \$8.2 million during the year ended December 31, 2007. This increase in research and development costs was directly attributable to an additional \$3.7 million in clinical research costs, \$3.8 million in pharmaceutical, engineering and manufacturing costs, \$1.1 million in increased personnel costs to support our Phase 2 clinical trials for ARX-01 and the commencement and completion of our Phase 1 trial for ARX-03 during the year ended December 31, 2008. In addition, we also incurred costs later in the year ended December 31, 2008 associated with the ARX-02 Phase 2 trial and related development.

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General and Administrative Expenses

General and administrative expenses increased by \$0.3 million, or 14%, to \$2.4 million during the year ended December 31, 2008 from \$2.1 million during the year ended December 31, 2007. This increase was primarily attributable to higher personnel costs including stock-based compensation costs due to increased headcount.

Interest Income

Interest income decreased by \$0.2 million to \$0.5 million during the year ended December 31, 2008 from \$0.7 million during the year ended December 31, 2007. This decrease was primarily attributable to the use of the proceeds from our Series A convertible preferred financing in August 2006, combined with lower yields on our cash equivalents and short-term investments due to adverse market conditions during the year ended December 31, 2008.

Interest Expense

Interest expense increased by \$0.4 million during the year ended December 31, 2008 from \$25,000 during the year ended December 31, 2007. The increase was primarily due to the interest and deferred financing costs related to the proceeds received from the \$12.0 million loan and security agreement in November 2008.

Other Income (Expense), net

Other income (expense), net changed by \$0.1 million during the year ended December 31, 2008 from an expense of \$1,000 during the year ended December 31, 2007. The change is primarily attributable to the increase in the fair value of our convertible preferred stock warrant liability due to the issuance of warrants in conjunction with the loan and security agreement entered into during the year ended December 31, 2008.

Liquidity and Capital Resources

To date, we have funded our operations primarily with proceeds from the sale of convertible preferred stock 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. As of September 30, 2010, our principal sources of liquidity are our cash, cash equivalents and short-term investments, which totaled \$8.1 million. We believe that our available cash, cash equivalents and short-term investments, not including the proceeds we will receive in this offering, will allow us to meet our obligations through at least March 2011. 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 September 30, 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 September 30, 2010, we have \$14.4 million of debt outstanding, of which \$6.4 million relates to our loan and security agreement and \$8.0 million relates to our convertible notes.

Our recurring operating losses and our need for additional sources of capital to fund our ongoing operations raise substantial doubt about our ability to continue as a going concern. As a result, our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements as of and for the year ended December 31, 2009 with respect to this uncertainty. We have no current source of revenue to sustain our present activities, and we do not expect to generate revenue for the foreseeable future. Accordingly, our ability to continue as a going concern will require us to

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obtain additional financing to fund our operations and there can be no assurance that additional financing will be available to us or that such financing, if available, will be available on terms favorable to us.

While we believe that our current cash and cash equivalents and the net proceeds from this offering and the interest earned on the proceeds will be sufficient to fund our current operations at least through the end of 2012, we may raise additional funds within this period of time through collaborations, public or private debt or equity financings. However, we do not expect that our existing capital resources and the net proceeds received from this offering will be sufficient to enable us to fund the completion of the development of our current product candidates, and 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.

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 prospectus:

	Year Ended December 31,			Nine Months Ended September 30,	
	2007	2008	2009	2009	2010
				(Unaudited)	
			(in thousands)		
Net cash used in operating activities	\$(8,861)	\$(18,903)	\$(19,418)	\$(15,241)	\$(9,042)
Net cash (used in) provided by investing activities	(2,217)	(9,935)	8,616	12,524	4,865
Net cash (used in) provided by financing activities	525	31,899	11,880	(1,627)	4,585

Cash Flows from Operating Activities

Net cash used in operating activities amounted to \$8.9 million, \$18.9 million, \$19.4 million, \$15.2 million and \$9.0 million for the years ended December 31, 2007, 2008, 2009 and the nine months ended September 30, 2009 and 2010. The primary use of cash for our operating activities during these periods was to fund the development of our product candidates. Our cash used for operating activities also reflected changes in our working capital and adjustments for non-cash charges, such as depreciation and amortization of our fixed assets, stock-based compensation, interest expense related to our debt financings, and the revaluation of our convertible preferred stock warrant liability.

Cash used in operating activities of \$9.0 million for the nine months ended September 30, 2010 reflected a net loss of \$10.8 million, partially offset by aggregate non-cash charges of \$2.5 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, \$0.8 million for the revaluation of the convertible preferred stock warrant liability and \$1.1 million in stock-based compensation. The net change in our operating assets and liabilities was primarily a result of accounts payable of \$0.3 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

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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 used in operating activities of \$8.9 million during the year ended December 31, 2007 reflected a net loss of \$9.6 million, partially offset by aggregate non-cash charges of \$0.3 million and a net change of \$0.4 million in our net operating assets and liabilities. Non-cash charges included \$0.2 million of depreciation and amortization and \$0.1 million of stock-based compensation. The net change in our operating assets and liabilities was primarily a result of the \$0.6 million increase in the deferred rent liability during the year ended December 31, 2007 relating to the tenant improvement allowance we received from our landlord when we entered into our lease agreement for the office and laboratory facilities and also as a result of a \$0.4 million increase in our prepaids and other assets.

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 nine months ended September 30, 2010, cash provided by investing activities was \$4.9 million primarily as a result of \$9.7 million in proceeds from the sale of our investments, partially offset by \$4.8 million of purchases of 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.

During the year ended December 31, 2007, cash used in investing activities of \$2.2 million was primarily a result of our capital expenditures of \$1.6 million relating to the acquisition of pharmaceutical and development equipment and \$8.1 million in purchases of investments, partially offset by \$7.5 million in proceeds received from sales of our investments.

Cash Flows from Financing Activities

To date, we have financed our operations primarily with proceeds from the sale of convertible preferred stock and the proceeds received from our debt financings. As of September 30, 2010, we had outstanding debt of \$14.4 million.

During the nine months ended September 30, 2010, cash provided by financing activities was \$4.6 million, primarily as a result of the receipt of \$8.0 million in borrowings received from the convertible

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note agreement entered into in September 2010 with certain existing investors, partially offset by principal repayments on our long-term debt of \$3.5 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 proceeds from our loan and security agreement in November 2008.

During the year ended December 31, 2007, cash provided by financing activities of \$0.5 million was primarily a result of the receipt of \$0.6 million from the issuance of long-term debt, partially offset by principal repayments on our long-term debt of \$0.1 million.

Contractual Obligations

The following table summarizes our outstanding contractual obligations and commitments as of December 31, 2009:

Contractual Obligations:	Payment by Period			2012 and Beyond
	Total	2010	2011	
Long-term debt obligations, including current portion ⁽¹⁾⁽²⁾	\$ 10,772	\$ 5,307	\$ 5,465	\$ —
Operating lease agreements ⁽³⁾	783	338	348	97
Total	\$ 11,555	\$ 5,645	\$ 5,813	\$ 97

⁽¹⁾ Long-term debt includes principal and accrued interest (\$1.0 million) under the \$12.0 million loan and security agreement entered into in September 2008. As of September 30, 2010, our outstanding obligations under the loan and security agreement have decreased to \$6.4 million, of which \$5.0 million is the current portion, due to regular loan repayments of \$3.4 million during the nine months ended September 30, 2010.

⁽²⁾ Long-term debt obligations as of December 31, 2009 do not reflect our obligations under the convertible note agreement entered into in September 2010, of which \$8.0 million in proceeds were received. The principal and accrued interest under the convertible note agreement is repayable on September 14, 2011 unless certain conversion criteria have been achieved, including the completion of a qualified initial public offering, other qualified equity financing or liquidation event, which would result in the notes converting into certain equity securities depending on the event that triggers the conversion.

⁽³⁾ Operating lease agreements represent our obligation to make payments under our non-cancelable lease agreement for office and laboratory facilities in Redwood City, California. During the nine months ended September 30, 2010, we made regular lease payments of \$0.3 million under the operating lease agreements.

Off-Balance Sheet Arrangements

Through September 30, 2010, we had not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Segment Information

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

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include risk related to interest rate sensitivities.

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Interest Rate Risk

Our exposure to market risk for changes in interest rates relates primarily to our investment portfolio and our outstanding debt obligations. Our cash, cash equivalents and investment accounts as of September 30, 2010 total \$8.1 million and consist primarily of cash, money market funds and U.S. government obligations with maturities of less than one year from the date of purchase. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of the interest rates in the United States. However, because of the short-term nature of the instruments in our portfolio, a sudden change in market interest rates would not be expected to have a material impact on our financial condition or our results of operation.

We have long-term debt of \$14.4 million as of September 30, 2010 consisting of our outstanding obligations under a loan and security agreement and a convertible note agreement. Our obligations under these debt agreements carry interest rates that are fixed and are not subject to fluctuations. However, to the extent in the future we enter into other long-term debt arrangements, we would be subject to fluctuations in interest rates which could have a material impact on our future financial condition and results of operation.

Recent Accounting Pronouncements

In October 2009, the Financial Accounting Standards Board, or FASB, issued an accounting standards update that provides application guidance on whether multiple deliverables exist, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. This update establishes a selling price hierarchy for determining the selling price of a deliverable. The selling price used for each deliverable will be based on vendor-specific objective evidence, if available, third-party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. We will be required to apply this guidance prospectively for revenue arrangements entered into or materially modified after January 1, 2011. We have not recognized any revenue since inception. Therefore, adoption of this guidance is not expected to have a material impact on our financial statements.

In January 2010, the FASB issued an amendment to an accounting standard which requires new disclosures for fair value measurements and provides clarification for existing fair value disclosure requirements. The amendment will require an entity to disclose separately the amounts of significant transfers in and out of Levels I and II fair value measurements and to describe the reasons for the transfers; and to disclose information about purchases, sales, issuances and settlements separately in the reconciliation for fair value measurements using significant unobservable inputs, or Level III inputs. This amendment clarifies existing disclosure requirements for the level of disaggregation used for classes of assets and liabilities measured at fair value and require disclosures about the valuation techniques and inputs used to measure fair value for both recurring and nonrecurring fair value measurements using Level II and Level III inputs. This guidance is effective for interim and annual reporting periods beginning after December 15, 2009, except for certain Level 3 activity disclosure requirements that will be effective for reporting periods beginning after December 15, 2010. Accordingly, we adopted this amendment on January 1, 2010, except for the additional Level 3 requirements which will be adopted in 2011.

In April 2010, the FASB issued an accounting standards update which provides guidance on the criteria to be followed in recognizing revenue under the milestone method. The milestone method of recognition allows a vendor who is involved with the provision of deliverables to recognize the full amount of a milestone payment upon achievement, if, at the inception of the revenue arrangement, the milestone is determined to be substantive as defined in the standard. The guidance is effective on a prospective basis for milestones achieved in fiscal years and interim periods within those fiscal years, beginning on or after June 15, 2010. We have not recognized any revenue since inception. Therefore, adoption of this guidance is not expected to have a material impact on our financial statements.

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 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.

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.
- *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

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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.

<u>Opioid</u>	<u>Therapeutic Index</u>
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.

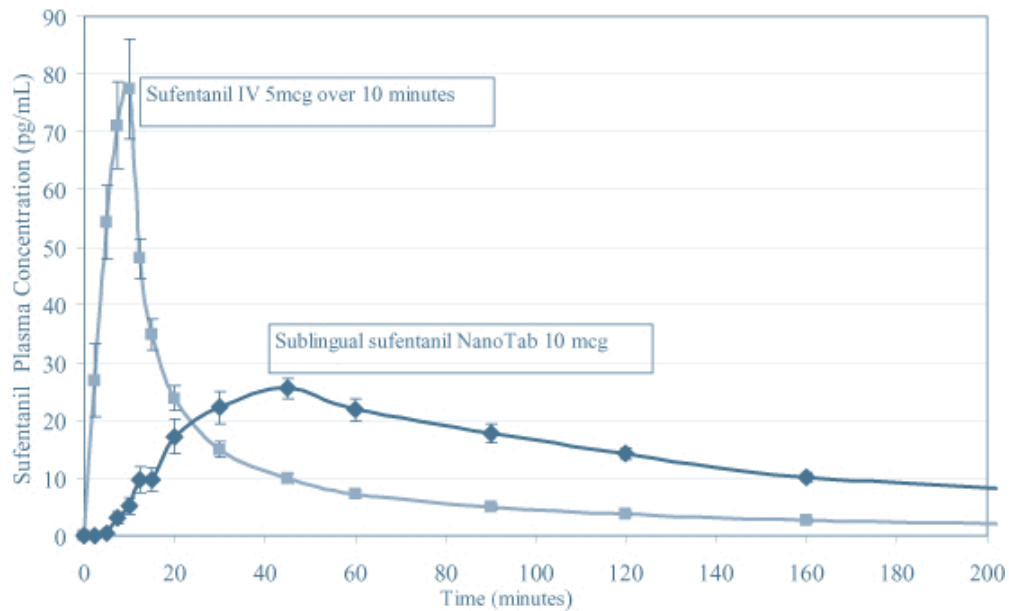
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Sublingual Delivery of Sufentanil: Summary of Phase 1 Clinical Studies Results

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.

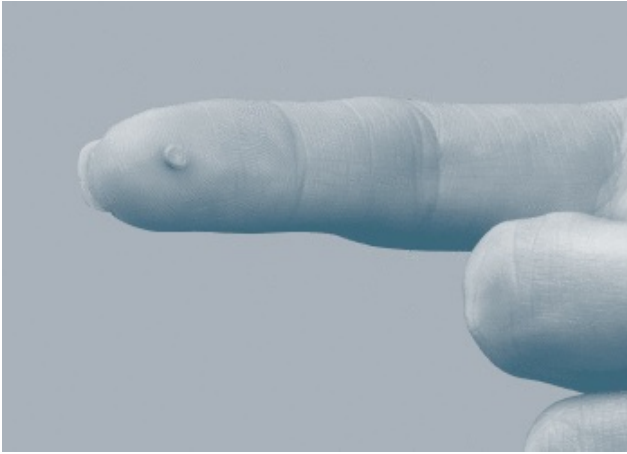
The chart below illustrates the PK profile of sublingual sufentanil NanoTab compared to IV delivery of sufentanil from one of our completed Phase 1 PK studies.



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.

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



None of our product candidates have been approved by the 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.

<u>Product Candidate</u>	<u>Description</u>	<u>Target Indication</u>	<u>Development Status</u>
ARX-01	Sufentanil NanoTab PCA System	Acute post-operative pain	<ul style="list-style-type: none">• 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 is anticipated to begin in the second half of 2011
ARX-02	Sufentanil NanoTab BTP Management System	Cancer breakthrough pain	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• Phase 2 clinical trial and End of Phase 2 meeting successfully completed• Two efficacy trials planned in Phase 3

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 index 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 10 mcg or 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

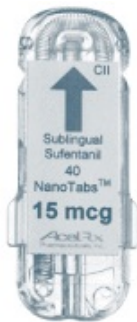


Figure 2, Dispenser Tip

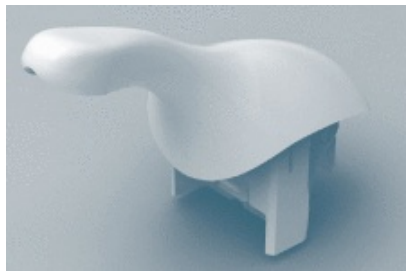


Figure 3, Controller



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;

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- a security tether that is designed to prevent theft and misuse; and
- fully automated inventory record of NanoTabs usage.

To set up the handheld PCA device, the nurse or healthcare professional turns on the controller and follows 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 trial in the second half of 2011. We expect to receive the top-line data from this trial in the first half of 2012 and expect to complete all studies by the end of 2012, with a potential NDA submission 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 220 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.

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Our second 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 330 patients will be randomly assigned to treatment with sufentanil or placebo. The primary endpoint also will be the SPID-48.

In addition, we plan to conduct an open label study to complete the safety database. We plan to conduct this study as an active comparator study of ARX-01 versus morphine IV PCA in patients undergoing orthopedic or abdominal surgery. Approximately 660 patients will be randomly assigned to treatment with Sufentanil NanoTab PCA System or morphine IV PCA. The primary endpoint will be the demonstration of 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.

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)

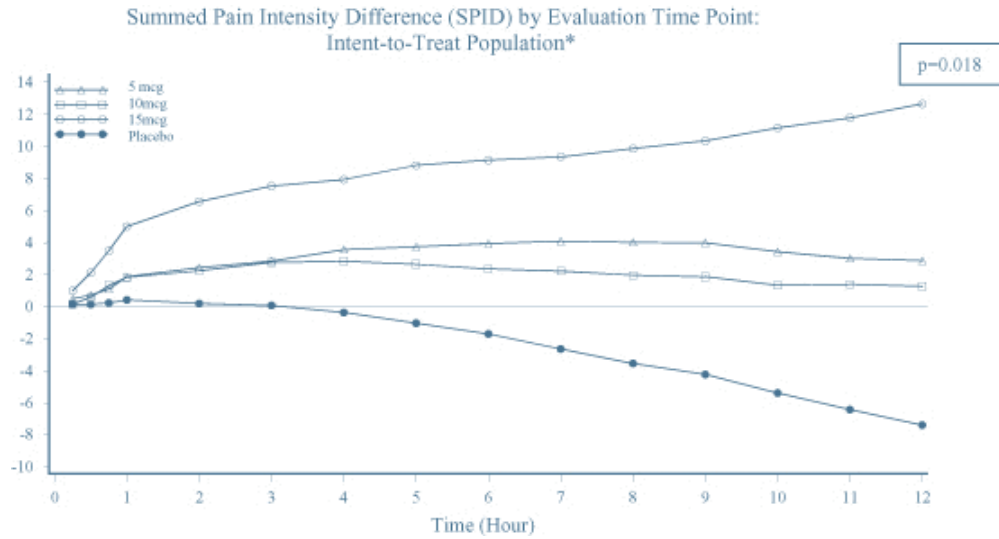
In the first Phase 2 study, we conducted a randomized, double-blind, placebo-controlled, multicenter Phase 2 clinical study to evaluate the efficacy, safety and tolerability of sublingual sufentanil NanoTabs in patients undergoing elective unilateral knee replacement. The study enrolled 101 male and 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

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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.

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.

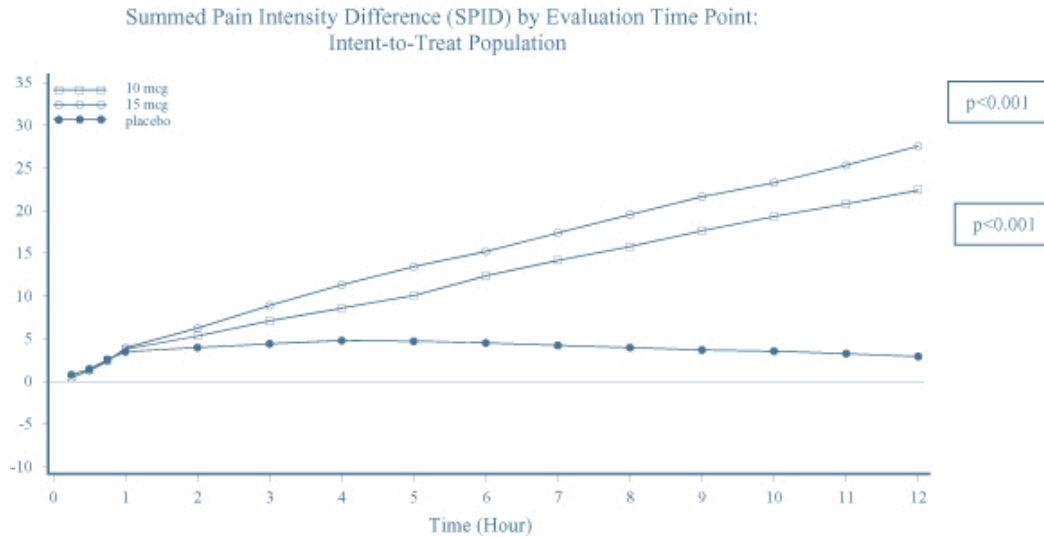


* Intent-to-Treat Population: The intent-to-treat, or ITT, population includes all randomized patients regardless of whether they received or adhered to the allocated treatment group. ITT analysis provides unbiased comparisons among the treatment groups and is the primary statistical analysis used by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

<u>Adverse Events</u>	<u>Placebo N=54</u>	<u>Sufentanil NanoTab (5 mcg) N=24</u>	<u>Sufentanil NanoTab (10 mcg) N=55</u>	<u>Sufentanil NanoTab (15 mcg) N=79</u>
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



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 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.

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.

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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.

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.

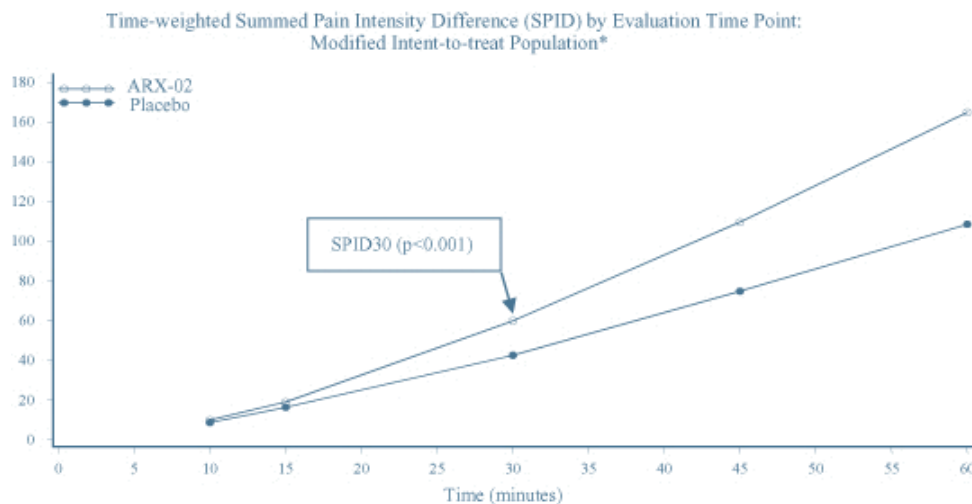
Patients were screened and, if qualified for the study, would titrate to an effective dose of sufentanil that provided adequate relief of cancer breakthrough pain without producing intolerable side effects. Patients

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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 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 ($p < 0.001$).

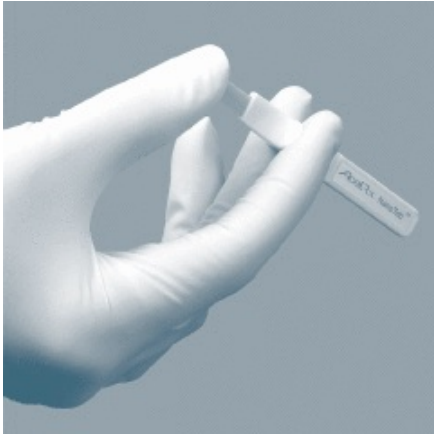
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Three patients reported an SAE; however, all SAEs were considered unrelated to study drug. The most common AEs were nervous system disorders, general disorders, and gastrointestinal disorders. The most common nervous system disorder was dysgeusia, 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.

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.

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ARX-03—Sufentanil/Triazolam NanoTabs



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.

anxiety reduction and analgesia for painful procedures conducted in a physician's office without the need for specialized personnel to monitor the patient.

The Market Opportunity for ARX-03

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

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 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

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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 this offering, we plan to commence clinical development of this product concept for the treatment of moderate-to-severe acute pain in a medically supervised setting.

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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 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 plan to advance ARX-01 into Phase 3 trials, 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 our Phase 3 development program 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.

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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;
- 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 “Risk Factors—Risks Related to Our Intellectual Property.”

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 41 foreign national or regional counterpart 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.

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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.

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.

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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-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.

<u>Product Name</u>	<u>Company</u>	<u>Formulation</u>	<u>Commercial Market</u>
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.

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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.

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;
- 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.

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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.
- *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.

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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.

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

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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 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,

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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 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.

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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 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;

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- 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, \$18.3 million and \$15.5 million in 2007, 2008 and 2009, and \$6.4 million for the nine months ended September 30, 2010. 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.

Facilities

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.

Legal Proceedings

We are not currently a party to any legal proceedings.

MANAGEMENT

Directors, Executive Officers and Key Employees

The following table sets forth information regarding our directors, executive officers and key employees as of December 31, 2010:

<u>Name</u>	<u>Age</u>	<u>Position</u>
Directors and Executive Officers		
Thomas A. Schreck ⁽¹⁾	53	Chairman and Co-Founder
Richard A. King	46	Director, President and Chief Executive Officer
Pamela P. Palmer, M.D., Ph.D.	47	Director, Chief Medical Officer and Co-Founder
Stephen J. Hoffman, Ph.D., M.D. ⁽¹⁾	56	Director
Guy P. Nohra ⁽²⁾⁽³⁾	50	Director
Howard B. Rosen ⁽²⁾⁽³⁾	52	Director
Mark Wan ⁽¹⁾⁽³⁾	45	Director
James H. Welch	53	Chief Financial Officer
Lawrence G. Hamel	59	Chief Development Officer
Badri Dasu	47	Chief Engineering Officer
Key Employees		
Carter J. King	39	Vice President, Finance
Nigel Ray	49	Vice President, Business Development

⁽¹⁾Member of nominating and corporate governance committee.

⁽²⁾Member of audit committee.

⁽³⁾Member of compensation committee.

The following includes a brief biography for each of our directors, executive officers and key employees, with each director biography including information regarding the experiences, qualifications, attributes or skills that caused our board of directors to determine that each member of our board of directors should serve as a director as of the date of this prospectus. There are no family relationships among any of our directors or executive officers.

Directors and Executive Officers

Thomas A. Schreck. Mr. Schreck has served as our Chairman since he co-founded AcelRx in July 2005, and as our President and Chief Executive Officer from July 2005 until April 2010. Since June 2010, Mr. Schreck has been co-founder and Chief Executive Officer of Sinusys Corporation, a medical device company. Prior to July 2005, he served as a founding President, and then Chief Financial Officer and a director of DURECT Corporation, an emerging specialty pharmaceutical company he co-founded in June 1998. Prior to 1998, Mr. Schreck held various investment banking positions in the San Francisco Bay Area and London, including Montgomery Securities and Manufacturers Hanover Limited. Mr. Schreck holds a B.A. in American Studies from Williams College. Mr. Schreck's historical knowledge of our company, his financial background and experience and his experience in the pharmaceutical industry provide him with the qualifications and skills to serve as a director.

Richard A. King. Mr. King has served as our director and President and Chief Executive Officer since May 2010. From April 2009 until May 2010, Mr. King acted as an independent consultant to a number of private and public biotechnology and venture capital companies. From October 2008 to April 2009, Mr. King served as President and General Manager of Tercica, Inc., a biotechnology company that was acquired by Ipsen, SA in 2008, and from February 2008 to October 2008, Mr. King served as President and Chief Operating Officer of Tercica, Inc., and from February 2007 until February 2008, served as Chief Operating Officer of Tercica, Inc. From January 2002 to October 2006, Mr. King served as

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Executive Vice President of Commercial Operations of Kos Pharmaceuticals, Inc., a pharmaceutical company that was acquired by Abbott Laboratories, a global, broad-based health care company, in 2006. From January 2000 to January 2002, Mr. King served as Senior Vice President of Commercial Operations at Solvay Pharmaceuticals, a pharmaceutical company that was acquired by Abbott Laboratories in 2009. From April 1992 to January 2000, Mr. King held various marketing positions at SmithKline Beecham Pharmaceuticals, now known as GlaxoSmithKline, a global pharmaceutical company. Mr. King holds a B.Sc. in Chemical Engineering from University of Surrey and an M.B.A. from Manchester Business School. Mr. King's extensive experience as an executive officer in public pharmaceutical companies and his knowledge of the day-to-day operations of our company provide him with the qualifications and skills to serve as a director.

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

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

Guy P. Nohra. Mr. Nohra has served as our director since August 2006. Mr. Nohra co-founded Alta Partners, a venture capital firm investing in life science companies in 1996, and has served as Managing Director of Alta Partners since 1996. Mr. Nohra was also a partner at Burr, Egan, Deleage & Co., a venture capital firm, which he joined in 1989. From January 1984 until June 1987, Mr. Nohra was Product Manager of Medical Products with Security Pacific Trading Corporation, a consumer and commercial bank. Currently, Mr. Nohra serves on the board of directors of numerous private companies, including Carbylan Biosurgery, Inc., Coapt Systems, PneumRx, Inc. and Vertiflex, Inc., and is the Chairman of the Board of USGI Medical, Inc. In addition, Mr. Nohra previously served on the board of directors of ATS Medical, Inc., a company focused on the manufacture of cardiac surgery products, that was acquired by Medtronic, Inc., a medical device company, in 2010 and Cutera, Inc., a global medical

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device company. Mr. Nohra also serves on the board of directors of the Medical Device Manufacturing Association, a national trade organization that advocates for entrepreneurial medical technology companies. Mr. Nohra holds a B.A. in History from Stanford University and an M.B.A. from the University of Chicago. Mr. Nohra's medical technology and venture capital industry experience provides him with the qualifications and skills to serve as a director.

Howard B. Rosen. Mr. Rosen has served as our director since 2008. Mr. Rosen has served as interim President and Chief Executive Officer of Pearl Therapeutics, Inc. since June 2010. From 2004 to 2008, Mr. Rosen was Vice President of Commercial Strategy at Gilead Sciences, Inc., a biopharmaceutical company. Mr. Rosen was President of ALZA Corporation, a pharmaceutical and medical systems company that merged with Johnson & Johnson in 2001, from 2003 until 2004 and Vice President, Product Development from 2002 until 2003. Prior to that, from 1994 until 2002, Mr. Rosen held various positions at ALZA Corporation. From 1993 to 1994, Mr. Rosen managed the west coast practice of Integral, Inc., a consulting firm. From 1989 until 1993, Mr. Rosen was Director of Corporate Development at GenPharm International, Inc., a company focusing on transgenic animal technology that was acquired by Medarex, Inc., in 1997 and later acquired by Bristol-Myers Squibb Company, a global biopharmaceutical company, in 2009. Mr. Rosen is also a member of the board of directors of PavVax, Inc., a biotechnology company, CNS Therapeutics, Inc., a pharmaceutical company and Pearl Therapeutics, Inc., a company focused on developing combination therapies for the treatment of highly prevalent chronic respiratory diseases. Previously, Mr. Rosen served on the board of directors of Pharsight Corporation, a company focused on providing software products and consulting services to pharmaceutical and biotechnology companies that was acquired by Tripos International, a company focused on drug discovery informatics products and services in 2008. Mr. Rosen also served on the board of directors of CoTherix, Inc., a biopharmaceutical company that was acquired by Actelion Pharmaceuticals Ltd, a biopharmaceutical company in 2007. Mr. Rosen holds a B.S. in Chemical Engineering from Stanford University, an M.S. in Chemical Engineering from the Massachusetts Institute of Technology and an M.B.A. from the Stanford Graduate School of Business. Mr. Rosen's experience in the biopharmaceutical industry, including his specific experience with commercialization of pharmaceutical products, provides him with the qualifications and skills to serve as a director.

Mark Wan. Mr. Wan has served as our director since August 2006. Mr. Wan is a founding general partner of Three Arch Partners, a venture capital firm. Prior to co-founding Three Arch Partners in 1993, Mr. Wan was a general partner at Brentwood Associates, a private equity firm from 1987 until 1993. Since 1999, Mr. Wan has served on the board of directors of Epocrates, Inc., a company focused on providing mobile drug reference tools. Mr. Wan also serves as a director of Biosensors International Group, Ltd. a company focused on the development, manufacture and marketing of medical devices for interventional cardiology and critical care procedures. Mr. Wan also serves on the board of directors of numerous private companies, including Ascend Health Corporation, Eleme Medical, Inc., Ingenuity Systems, Inc., TriReme Medical, Inc. and Quattro Vascular Pte Ltd. Mr. Wan holds a B.S. in Engineering and a B.A. in Economics from Yale University and an M.B.A. from the Stanford Graduate School of Business. Mr. Wan's financial experience and extensive knowledge of our company provides him with the qualifications and skills to serve as a director.

James H. Welch. Mr. Welch has served as our Chief Financial Officer since October 1, 2010. From June 2006 until September 2010 Mr. Welch served as Chief Financial Officer and Corporate Secretary for Cerimon Pharmaceuticals, a biopharmaceutical company. Mr. Welch served as Vice President, Chief Financial Officer and Corporate Secretary for Rigel Pharmaceuticals, Inc., a drug development company from October 2000 until May 2006, and as Vice President, Finance and Administration from May 1999 until October 2000. From June 1998 until May 1999, Mr. Welch served as an independent consultant at various companies. Mr. Welch served as Chief Financial Officer of Biocircuits Corporation, a company focused on developing immunodiagnostic testing systems from February 1997 until June 1998, and from

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June 1992 until February 1997, he served as Corporate Controller. Mr. Welch holds a B.A. in Business Administration from Whitworth College and an M.B.A. from Washington State University.

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

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

Key Employees

Carter J. King. Mr. King has served as our Vice President, Finance since July 2006. From September 2002 to June 2006, Mr. King served as Associate Director, Corporate Planning at ALZA Corporation. From September 1998 to June 2002, Mr. King held a number of positions at Coulter Pharmaceutical/Corixa Corporation, a developer of immunotherapeutics, including Director of Finance. Prior to 1998, Mr. King spent four years in various finance roles at OnCare Inc., an oncology focused healthcare services firm, and at GATX Capital, a provider of leasing and related services to customers operating rail, marine and other targeted assets. Mr. King holds a B.A. in Business Economics from the University of California Santa Barbara and an M.B.A. from the Haas School of Business at the University of California, Berkeley.

Nigel Ray. Mr. Ray has served as our Vice President of Business Development since October 2009. From January 2009 until September 2009, Mr. Ray served as Vice President of Business Development at Limerick BioPharma, a biopharmaceutical company. From 1999 until 2009, Mr. Ray served in a variety of business development roles at DURECT Corporation, most recently as Executive Director of Business Development. Previously, Mr. Ray served in a variety of marketing and business roles for ALZA Corporation. Mr. Ray holds a B.A. in Human Biology from Stanford University and an M.B.A. from the University of California Los Angeles Anderson School of Business.

Director Independence

Upon the completion of this offering, our common stock is expected to be listed on the NASDAQ Global Market. Under the rules of the NASDAQ Stock Market, LLC, or NASDAQ, “independent” directors must comprise a majority of a listed company’s board of directors within a specified period following that company’s listing date in conjunction with its initial public offering. In addition, applicable NASDAQ rules require that, subject to specified exceptions, each member of a listed company’s audit, compensation and nominating committees be independent within the meaning of applicable NASDAQ rules. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

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In November 2010, our board of directors undertook a review of the independence of each director and considered whether any director has a material relationship with us that could compromise his ability to exercise independent judgment in carrying out his responsibilities. As a result of this review, our board of directors determined that all of our directors, other than Messrs. King and Schreck and Dr. Palmer, qualify as “independent” directors within the meaning of the NASDAQ rules. Accordingly, a majority of our directors are independent, as required under applicable NASDAQ rules. In making this determination, our board considered Mr. Nohra’s affiliation with Alta Partners, one of our stockholders, Dr. Hoffman’s affiliation with Skyline Ventures, one of our stockholders and Mr. Wan’s affiliation with Three Arch Partners, one of our stockholders. As required under applicable NASDAQ rules, we anticipate that our independent directors will meet in regularly scheduled executive sessions at which only independent directors are present.

Voting Agreement

We are party to a voting agreement under which holders of our preferred stock, including our principal stockholders with which certain of our directors are affiliated, have agreed to vote in a certain way on certain matters, including with respect to the election of directors. Pursuant to the voting agreement, holders of our preferred stock have agreed to vote such that one director be a designee of Three Arch Partners IV, L.P. or its affiliates, who is currently Mark Wan; one director be a designee of ACP IV, L.P. or its affiliates, who is currently Guy Nohra; and one director be a designee of Skyline Venture Partners Qualified Purchaser Fund IV, L.P. or its affiliates, who is currently Stephen Hoffman. Upon the closing of this offering, the voting agreement will terminate in its entirety and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors.

Board Composition

Our board of directors may establish from time to time by resolution the authorized number of directors. Currently, seven directors are authorized. In accordance with our amended and restated certificate of incorporation to be in effect immediately prior to the closing of this offering, our board of directors will be divided into three classes with staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. After the completion of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Messrs. Schreck and Nohra, and their terms will expire at the annual meeting of stockholders to be held in 2011;
- the Class II directors will be Mr. King and Drs. Hoffman and Palmer, and their terms will expire at the annual meeting of stockholders to be held in 2012; and
- the Class III directors will be Messrs. Rosen and Wan, and their terms will expire at the annual meeting of stockholders to be held in 2013.

Our amended and restated certificate of incorporation will provide that the authorized number of directors may be changed only by resolution of the board of directors.

Board Committees

Our board of directors has an audit committee, a compensation committee and a nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our board.

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Audit Committee

Our audit committee consists of Messrs. Rosen and Nohra, each of whom is a non-employee member of our board of directors. We expect to add one additional member to the audit committee prior to the completion of this offering. Mr. Rosen serves as the chair of our audit committee. Our board of directors has determined that each of the directors serving on our audit committee meets the requirements for financial literacy under applicable rules and regulations of the SEC and NASDAQ. We are currently seeking an audit committee member who will be a financial expert as defined under the applicable rules and regulations of the SEC and who has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. The audit committee will be comprised of independent directors, subject to the phase-in periods available to companies listing on NASDAQ in connection with an initial public offering. Each member of the audit committee will be financially literate at the time such member is appointed. The composition of the audit committee will satisfy the independence and other requirements of NASDAQ and the SEC. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ and which will be available on our website prior to the completion of this offering at www.ancelrx.com.

The functions of our audit committee include, among other things:

- evaluating the performance, independence and qualifications of our independent registered public accounting firm and determining whether to retain our existing independent registered public accounting firm or engage new independent registered public accounting firm;
- reviewing and approving the engagement of our independent registered public accounting firm to perform audit services and any permissible non-audit services;
- monitoring the rotation of partners of our independent registered public accounting firm on our engagement team as required by law;
- reviewing our annual and quarterly financial statements and reports and discussing the statements and reports with our independent registered public accounting firm and management;
- reviewing with our independent registered public accounting firm and management significant issues that arise regarding accounting principles and financial statement presentation, and matters concerning the scope, adequacy and effectiveness of our internal control over financial reporting;
- reviewing with management and our registered public accounting firm any earnings announcements and other public announcements regarding material developments;
- establishing procedures for the receipt, retention and treatment of complaints received by us regarding financial controls, accounting or auditing matters and other matters;
- preparing the audit committee report that the SEC requires in our annual proxy statement;
- reviewing and providing oversight with respect to any related party transactions and monitoring compliance with our code of ethics; and
- reviewing and evaluating, at least annually, the performance of the audit committee, including compliance of the audit committee with its charter.

Compensation Committee

Our compensation committee consists of Messrs. Nohra, Rosen and Wan. Mr. Nohra serves as the chair of our compensation committee. All members of our compensation committee satisfy the independence requirements under applicable NASDAQ rules and regulations. The compensation committee operates

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under a written charter that satisfies the applicable standards of NASDAQ and which will be available on our website prior to the completion of this offering at www.aceirx.com.

The functions of our compensation committee include, among other things:

- approving or recommending for approval to our board of directors the compensation and other terms of employment of our executive officers;
- approving or recommending to our board of directors performance goals and objectives relevant to the compensation of our executive officers and assessing their performance against these goals and objectives;
- evaluating and approving the equity incentive plans, compensation plans and similar programs, as well as modification or termination of existing plans and programs;
- evaluating and recommending to our board of directors the type and amount of compensation to be paid or awarded to board members;
- administering our equity incentive plans;
- establishing policies with respect to equity compensation arrangements;
- reviewing the competitiveness of our executive compensation programs and evaluating the effectiveness of our compensation policy and strategy in achieving expected benefits to us;
- approving or recommending to our board of directors the terms of any employment agreements, severance arrangements, change in control protections and any other compensatory arrangements for our executive officers;
- reviewing with management our disclosures under the caption “Compensation Discussion and Analysis” and recommending to the full board its inclusion in our reports to be filed with the SEC;
- preparing the compensation committee report that the SEC requires in our annual proxy statement;
- reviewing the adequacy of our compensation committee charter on a periodic basis; and
- reviewing and evaluating, at least annually, the performance of the compensation committee.

Nominating and Corporate Governance Committee

Our nominating and corporate governance committee consists of Messrs. Wan, Hoffman and Schreck. Mr. Wan serves as the chair of our nominating and corporate governance committee. Currently, our board of directors has determined that Messrs. Wan and Hoffman satisfy the NASDAQ independence requirements for service on the Nominating and Corporate Governance Committee, and we expect that membership of this committee will be changed to comply with these requirements prior to the end of the phase-in period permitted by NASDAQ. The nominating and corporate governance committee operates under a written charter that satisfies the applicable standards of NASDAQ and which will be available on our website prior to the completion of this offering at www.aceirx.com.

The functions of our nominating and corporate governance committee include, among other things:

- identifying, reviewing and evaluating candidates to serve on our board of directors;
- determining the minimum qualifications for service on our board of directors;
- evaluating director performance on the board and applicable committees of the board;
- interviewing, evaluating, nominating and recommending individuals for membership on our board of directors;

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- considering nominations by stockholders of candidates for election to our board;
- considering and assessing the independence of members of our board of directors;
- developing, as appropriate, a set of corporate governance principles, and reviewing and recommending to our board of directors any changes to such principles;
- periodically reviewing our policy statements to determine their adherence to our code of business conduct and ethics and considering any request by our directors or executive officers for a waiver from such code;
- reviewing the adequacy of its charter on an annual basis; and
- evaluating, at least annually, the performance of the nominating and corporate governance committee.

Compensation Committee Interlocks and Insider Participation

The current members of our compensation committee are Messrs. Wan, Nohra and Rosen. None of the members of our compensation committee has at any time during the past three years been one of our officers or employees. None of our executive officers currently serves or in the prior three years has served as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board or compensation committee. For information regarding certain transactions with entities that members of our compensation committee are affiliated with, see the section entitled “Certain Relationships and Related Party Transactions” appearing elsewhere in this prospectus.

Board Leadership Structure and Role in Risk Oversight

Our board has a Chairman, Mr. Schreck, who has authority, among other things, to preside over board meetings, including meetings of the independent directors. Accordingly, the Chairman has substantial ability to shape the work of our board. We currently believe that separation of the roles of Chairman and Chief Executive Officer reinforces the independence of our board in its oversight of the business and affairs of our company. However, no single leadership model is right for all companies and at all times. The board recognizes that depending on the circumstances, other leadership models, such as combining the role of Chairman with the role of Chief Executive Officer, might be appropriate. Accordingly, the board may periodically review its leadership structure.

Our board is generally responsible for the oversight of corporate risk in its review and deliberations relating to our activities and has determined that our principal source of risk falls into two categories, financial and product development. The audit committee oversees management of financial risks; our board regularly reviews information regarding our cash position, liquidity and operations, as well as the risks associated with each. The board regularly reviews plans, results and potential risks related to our lead therapeutic development programs and other preclinical programs as well as financial and strategic risk related to our operations.

In addition, our nominating and corporate governance committee monitors the effectiveness of our corporate governance guidelines and policies and manages risks associated with the independence of the board and potential conflicts of interest. Our compensation committee oversees risk management as it relates to our compensation plans, policies and practices for all employees including executives particularly whether our compensation programs may create incentives for our employees to take excessive or inappropriate risks which could have a material adverse effect on the Company. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board is regularly informed through committee reports about such risks.

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Code of Business Conduct and Ethics

We adopted a code of business conduct and ethics that applies to all of our employees, officers and directors including those officers responsible for financial reporting. Upon the completion of this offering, the code of business conduct and ethics will be available on our website at www.acerlx.com. We intend to disclose future amendments to the code, or any waivers of its requirements on our website to the extent permitted by the applicable rules and exchange requirements. The inclusion of our website address in this prospectus does not include or incorporate by reference the information on our website into this prospectus.

EXECUTIVE COMPENSATION

Compensation Discussion and Analysis

Overview

This Compensation Discussion and Analysis explains our compensation philosophy, policies and practices for the following executives, our named executive officers:

Richard A. King	President and Chief Executive Officer
James H. Welch	Chief Financial Officer
Thomas A. Schreck	Former Chief Executive Officer and Former Principal Financial Officer
Pamela P. Palmer, M.D., Ph.D.	Chief Medical Officer
Lawrence G. Hamel	Chief Development Officer
Badri Dasu	Chief Engineering Officer

Compensation Philosophy and Objectives

We believe in providing a total compensation package to our executive management team through a combination of base salary, discretionary annual bonuses, grants under our long-term equity incentive compensation plan, and severance and change of control benefits, as well as broad-based health and welfare benefits programs that are available to all salaried employees. Our executive compensation programs are designed to achieve the following objectives:

- attract and retain talented and experienced executives, whose knowledge, skills and performance are critical to our success;
- motivate executives to achieve our business objectives;
- create a meaningful link between pay and performance;
- promote teamwork while also recognizing the role each executive plays in our success; and
- align the interests of our executive officers and stockholders.

We believe that our executive compensation programs should include short-term and long-term components, including cash and equity-based compensation, and should reward performance that consistently meets or exceeds expectations, including by increasing base salary levels, awarding cash bonuses and granting additional equity awards.

When setting executive compensation in any given year, we may consider a number of factors, including the following:

- corporate and/or individual performance, including specific business challenges for a given year, as we believe this encourages our executive officers to focus on achieving our business objectives;
- the experiences and individual knowledge of the members of our board of directors regarding compensation programs at other companies, as we believe this approach helps us to compete in hiring and retaining the best possible talent while at the same time maintaining a reasonable and responsible cost structure;
- compensation paid by other companies, as publicly reported by such companies or as reported in third party surveys, although in any given year, and with respect to any specific compensation element, we may or may not benchmark to any specified level of compensation;

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- internal pay equity of the compensation paid to one executive officer as compared to another—that is, that the compensation paid to each executive should reflect the importance of his or her role to the company as compared to the roles of the other executives;
- the potential dilutive effect on our stockholders of equity awards granted to executive officers, as well as the potentially dilutive effect on our employees of financings undertaken prior to this offering;
- broader economic conditions, in order to ensure that our pay strategies are effective yet responsible, particularly in the face of any unanticipated consequences of the broader economy on our business; and
- individual negotiations with executives, particularly in connection with their initial compensation package, as these executives may be leaving meaningful compensation opportunities at their prior employer in order to work for us, as well as negotiations upon their departures, as we recognize the benefit to our stockholders of smooth transitions.

Our historical practice and our intent going forward is to perform at least an annual review of our executive officers' overall compensation packages to determine whether they meet our compensation objectives.

Role of Our Board and Our Compensation Committee in Setting Executive Compensation

Prior to this offering, our compensation committee had the primary responsibility for approving the cash compensation packages for our executive officers and making recommendations to the board with regard to setting equity compensation. Certain elements of our compensation program, such as granting equity incentive awards and approving severance and change of control benefits, were determined by the board in consultation with the compensation committee. As part of its responsibility, the compensation committee has considered both the aggregate level of compensation offered (without necessarily benchmarking to a specific level of total target compensation, although with a view toward providing total cash compensation at or around the 50th to 75th percentile of survey data, as described in more detail below) and the mix of individual compensation elements (without necessarily trying to achieve a specific weighting as between the elements). As further described under the specific elements of compensation below, the compensation committee considered the recommendations of management with respect to the various elements of compensation and then either made a recommendation to the board or, with respect to cash compensation, made the final determination of base salary levels or bonus amounts. Following this offering, our compensation committee will generally be responsible for reviewing, modifying, approving and otherwise overseeing the compensation policies and practices applicable to our employees (including our executive officers), including the administration of our equity and cash incentive plans.

As part of its deliberations in any given year, the board and the compensation committee may review and consider factors such as the achievement of predefined milestones, the company's financial condition, operational data, tax and accounting consequences, the total compensation that may become payable to executives in various hypothetical scenarios, executive stock ownership information, company stock performance, analyses of historical executive compensation levels and current company-wide compensation levels, and the recommendations of our Chief Executive Officer.

Role of Our Management

Our Chief Executive Officer evaluates the performance of the other executive officers and employees on an annual basis and makes recommendations to the compensation committee with respect to salary adjustments, bonuses and stock option grants. Our Chief Executive Officer also makes recommendations on new hire compensation packages. Our board and our compensation committee review the

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performance of our Chief Executive Officer. Our Chief Executive Officer also makes recommendations regarding the design of compensation programs applicable to our executive officers and other senior executives, changes to existing compensation programs, and financial and other performance targets to be achieved under those programs. Our finance department works with our Chief Executive Officer to gather compensation data that he reviews in making his recommendations.

No executive officer participated directly in the final determinations or deliberations of our compensation committee (or our board of directors, as applicable) regarding the amount of any component of his or her own compensation package. From time to time members of our finance team attend meetings (or portions of meetings) of the board and the compensation committee in order to present survey and financial data and answer questions.

Limited Role of Compensation Consultants

Prior to this offering, neither our board nor our compensation committee had retained its own independent compensation consultant. In October 2010, in connection with preparations for this offering, the company retained Kara Halvorson Consulting LLC to assist management in reviewing human resources and compensation matters. The consultant has been working directly with the company's management team to review employment agreements and our compensation practices in connection with preparations for this offering. This consultant is paid by the company and has not been present at the deliberations of the board or the compensation committee. Following this offering, the compensation committee will consider retaining its own independent compensation consultant.

Benchmarking

We have not established a peer group of companies. As is the case with many private companies, our compensation committee and our board have discussed compensation levels in the context of the experiences and individual knowledge of each board member. This approach called for our board members to use their reasonable business judgment in determining compensation levels that would allow us to compete in hiring and retaining the best possible employees, without the cost of engaging a compensation consultant. In making its determinations with respect to 2009 and 2010 compensation, our board members reviewed compensation data as compiled by our finance department from the following surveys:

- 2008 Thelander Pre-IPO Survey: a survey of 193 pre-IPO companies, predominantly in life sciences, located primarily on the west coast, with an average stage of financing of less than \$50 million;
- 2008 E&Y Life Sciences Survey: a survey of 189 pre-IPO and post-IPO life science companies located across the country, with an average stage of financing of less than three venture rounds; and
- 2007 BEDC Compensation Survey: a survey of 87 public and private life science companies, many of whom had fewer than 50 employees, located in the greater San Diego area.

In setting compensation for 2009, the finance department provided our compensation committee with the data points from only the Thelander Survey for total cash compensation and percentage stock ownership for each executive officer position, at the 50th and 75th percentiles. In setting compensation for 2010, the finance department provided our compensation committee with an average of all three of the surveys above, as adjusted by 4.5% to reflect cost of living increases since the dates of the surveys, at each of the 50th and 75th percentiles, for total cash compensation and percentage stock ownership for each executive.

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Our compensation committee has used the survey data to check their own assumptions and expectations about compensation levels. The board and the compensation committee may, but do not always, aim to set a specific element of compensation at or around the 50th to 75th percentiles as reflected by this survey data. We believe this approach helps us hire and retain the best possible talent while at the same time maintaining a reasonable and responsible cost structure. The board has not selected a peer group or benchmarking level to be used following this offering. Information about whether a given element of compensation was benchmarked in a given year is provided below under the discussion of each element.

Elements of Executive Compensation

The compensation program for our executive officers consists principally of base salary and long-term compensation in the form of stock options, with discretionary cash bonuses paid from time to time. We also offer limited severance protection through the terms of our stock options and certain employment agreements with our executive officers, with the benefits generally in the form of accelerated vesting of stock options in the case of termination of employment following a change of control. We believe that this mix of compensation elements appropriately retains executives, provides longer term incentives and rewards, and allows us to conserve our cash for use in the development of the our products. We do not affirmatively set out in any given year to apportion compensation in any specific ratio between cash and equity. Rather, in any given year, total compensation may skew more heavily toward either element, as a result of cash constraints, company performance, the value of our common stock and other factors described in the following table and narrative.

<u>Compensation element</u>	<u>Material factors considered in 2009 and 2010</u>	<u>Objective</u>
Base salary	<ul style="list-style-type: none">• Board members' experience and knowledge• Historical salary levels• Achievement of corporate objectives• Lack of a formal cash bonus plan• Expected future cash flows• Internal pay equity• Survey data• Individual negotiations	<ul style="list-style-type: none">• Attract and retain experienced executives• Reward executives for achievement of company objectives
Cash bonuses	<ul style="list-style-type: none">• Board members' experience and knowledge• Achievement of corporate objectives• Subjective review of each executive's overall individual performance• Internal pay equity• Expected future cash flows• Survey data• Individual negotiations	<ul style="list-style-type: none">• Attract and retain experienced executives• Reward executives for achievement of company objectives• Link performance with compensation paid

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<u>Compensation element</u>	<u>Material factors considered in 2009 and 2010</u>	<u>Objective</u>
Long-term equity incentive awards	<ul style="list-style-type: none">• Board members' experience and knowledge• Achievement of corporate objectives• Subjective review of an executive's overall individual performance• Internal pay equity• Survey data• The potential dilutive effect on our stockholders• The potential dilutive effect of our financings on our employees' equity awards• Individual negotiations	<ul style="list-style-type: none">• Attract and retain experienced executives• Motivate and reward executives for achievement of company objectives• Link performance with compensation paid• Provide incentives to promote our growth and create stockholder value• Align the financial interests of our executive officers with those of our stockholders
Severance benefits	<ul style="list-style-type: none">• Board members' experience and knowledge• Internal pay equity• Individual negotiations	<ul style="list-style-type: none">• Attract and retain experienced executives• Motivate executives to achieve company objectives• Align the financial interests of the executive officers with those of our stockholders
Employee benefits	<ul style="list-style-type: none">• Board members' experience and knowledge• Internal pay equity	<ul style="list-style-type: none">• Attract and retain experienced executives

Base Salary

We provide base salary as a fixed source of compensation for our executives, allowing them a degree of certainty in the face of working for a privately held biotechnology company and having a meaningful portion of their compensation "at risk" in the form of options to purchase shares of such private company. The compensation committee recognizes the importance of base salaries as an element of compensation that helps to attract and retain our executives.

Base salaries for our executives are established based in part on individual negotiations with the executives when they join the company, and reflect the scope of their anticipated responsibilities, the individual experience they bring to the company, the committee members' experiences and knowledge in compensating similarly situated individuals at other companies, the company's annual budget for salary increases, internal pay equity among executives, reference to survey data, and performance (company and/or individual) in the prior year. Historically, base salaries have been reviewed, and, if necessary, adjusted annually, typically in connection with our annual performance review process. The compensation committee does not apply specific formulas to determine increases. While the compensation committee members consider existing salaries plus any discretionary bonuses awarded as compared to the 50th and 75th percentiles of total cash compensation paid to similarly situated executives using the survey data described above, such reference points are not solely determinative.

In the first quarter of 2009, our compensation committee reviewed the base salaries of our executive officers, as well as Dr. Palmer's then current rate of consulting fees, taking into account the factors described above. In particular, our compensation committee considered the achievement in 2008 of a number of significant company milestones, including successful preparation for Phase 2 studies, efficient completion of the first Phase 2 study and the first positive Phase 2 data for the ARX-01 program, the limited financial budget that the board had allocated for salary increases on a company-wide basis in

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2009, and attention to internal pay equity as among officers. Specifically, given our limited budget for salary increases due to our expected cash flow constraints, more of the salary increase budget was allocated to our Chief Executive Officer and Dr. Palmer (that is, an increase in her consulting fees), reflecting the compensation committee deference to internal pay equity (that is, their greater level of duties and responsibilities in running the company as compared to our other executives) and so that their total cash compensation would be closer to the 50th to 75th percentile of total cash compensation (given that we do not have a formal cash bonus program) as reflected in the survey data. The compensation committee determined that since the majority of the base salary compensation increases were awarded to Mr. Schreck and Dr. Palmer, only limited salary increases were made to Messrs. Hamel and Dasu. Therefore, the compensation committee awarded cash bonuses in respect of 2008 performance in the first quarter of 2009 to Messrs. Hamel and Dasu (and not Mr. Schreck or Dr. Palmer given their salary increases), in recognition of the significant roles Messrs. Hamel and Dasu played in 2008 in achieving the first positive Phase 2 data for the ARX-01 program and advancing the Company's engineering efforts and so that their total cash compensation would be closer to the 50th to 75th percentile of total cash compensation as reflected in the survey data. Based on these factors, our compensation committee decided to adjust base salaries, retroactive to January 1, 2009, as set forth in the table below.

In July 2009, Dr. Palmer transitioned from her role as a consultant to a full time executive officer and employee. In connection with this transition, the compensation committee set her base salary for 2009 at \$375,000 on an annual basis, representing, on an annual basis, an increase from her consulting fee rates of \$350,000 per year (that is, from the level determined in the first quarter of 2009). The compensation committee set her base salary at this level based on her prior consulting rates, her individual negotiations and through assessment of internal pay equity (that is, the committee believed that as a founder and an executive officer, and given the scope of her responsibility, Dr. Palmer's salary should be closer to that of Mr. Schreck than the other executives).

In the first quarter of 2010, our compensation committee reviewed base salaries for our executive officers. The compensation committee considered the expected transition of Mr. Schreck from CEO and Dr. Palmer's recent hiring (and therefore the adequacy of her salary given her recent transition to full time employment) and did not make any adjustments to their salaries. However, the compensation committee wished to increase the base salary levels for Messrs. Hamel and Dasu to a level more reflective of their responsibilities and the importance of their role to the company's successful development of its products. The adjustments set forth in the table below were made so that their base salaries would be closer to the 50th percentile of total cash compensation (given that we do not have a formal cash bonus program) as reflected in the survey data. Based on these factors, our compensation committee decided to adjust base salaries, retroactive to January 1, 2010, as set forth in the table below.

In the spring of 2010, the company hired Mr. King and in October 2010, hired Mr. Welch. In connection with these new hires, the compensation committee set their base salaries on an annual basis as set forth in the table below. These decisions were based on individual negotiations (which reflect, in part, base salaries that these executives were being paid by their prior employers), internal pay equity (that is, Mr. King's salary should be greater than the other executive officers) and the scope of their expected responsibilities, particularly in connection with the company's preparations for this offering.

<u>Executive Officer</u>	<u>First quarter 2009 increase in base salary for 2009</u>	<u>New 2009 base salary</u>	<u>Percentile against Survey Data⁽¹⁾</u>	<u>Increase in base salary for 2010</u>	<u>New 2010 base salary</u>	<u>Percentile against Survey Data⁽¹⁾</u>
Richard A. King	N/A	N/A	N/A	N/A	\$ 400,000	>75 th (2)
James H. Welch	N/A	N/A	N/A	N/A	\$ 290,000	>75 th (2)
Thomas A. Schreck	\$ 50,000	\$ 375,000	<50 th	—	\$ 375,000	<50 th
Pamela P. Palmer, M.D., Ph.D.	\$ 50,000 ⁽³⁾	\$ 375,000 ⁽⁴⁾	<50 th	—	\$ 375,000	50 th – 75 th
Lawrence G. Hamel	\$ 17,500	\$ 262,500	<50 th	\$ 12,500	\$ 275,000	<50 th
Badri Dasu	\$ 12,500	\$ 247,500	50 th – 75 th	\$ 15,000	\$ 262,500	50 th

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⁽¹⁾Percentile of the executive's base salary, plus any bonus awarded to him or her for the applicable year (as set forth in the table below), as compared to total cash compensation reported in the surveys.

⁽²⁾Assumes achievement of target bonus.

⁽³⁾Increase in annual consulting fee level from \$300,000 to \$350,000 that occurred in the first quarter of 2009 prior to Dr. Palmer joining as an employee.

⁽⁴⁾Upon joining as an employee in July 2009.

Cash Bonuses

In addition to base salaries, from time to time we have paid discretionary cash bonuses to reward our executives for achieving our strategic objectives or to provide a one time additional cash payment in lieu of providing a salary increase in order to manage budgetary constraints. As part of our annual performance reviews, the compensation committee reviews the company's performance, as well as each executive's contributions to the company in the prior year and makes decisions regarding cash bonuses to be paid in respect of such performance. Prior to this offering, the company has not set in advance specific performance goals related to bonus amounts that may be earned by our executive officers. Rather, as with many private companies, our compensation committee has decided to use a discretionary cash bonus system that looked at performance at the conclusion of the applicable year, and awarded cash bonuses based on its evaluation of performance, budgetary constraints, internal pay equity, the board members' experiences and knowledge in compensating similarly situated individuals at other companies, and, from time to time, compiled survey data.

At the conclusion of 2009, the compensation committee considered the company's financial position, including a reduction in force in December 2009, partnering status, and achievement against financing milestones. As a result, no cash bonuses were earned or paid in respect of 2009 performance.

Historically, the company has not set target bonus amounts, expressed as a percentage of base salary or otherwise, for its executive officers. However, in 2010, in connection with hiring Messrs. King and Welch, the compensation committee approved annual cash bonus targets of 35% of base salary for Mr. King and 30% of base salary for Mr. Welch. The compensation committee approved these levels based on individual negotiations which reflect, in part, target bonus opportunities that these executives were foregoing from their prior employers, the board members' experiences, and internal pay equity. On December 17, 2010, upon recommendation of the compensation committee, the board, in its discretion, based on the company's progress toward an IPO and Mr. King's general performance, and without weighting any specific factors, approved Mr. King's bonus of \$94,500. The compensation committee has not set any performance goals for Mr. Welch's annual cash bonus for 2010, and any such prorated bonus will be made in the board's discretion when the board makes that determination later in 2011. No other named executive officers are eligible for bonus payments in 2010 pursuant to their offer letters.

Long-Term Equity Incentive Awards

We utilize long-term equity incentive awards in the form of options to purchase our common stock that, prior to this offering, have been granted under our 2006 Stock Plan. We believe that by providing our executives the opportunity to increase their ownership of our stock, the best interests of stockholders and executives will be more aligned and our executives will be encouraged to focus on long-term performance. These stock options enable our executive officers to benefit like stockholders from any increases in the value of our shares, while also exposing them to the risk of loss from any decrease in the value of our shares. We also believe that equity compensation is an integral component of our efforts to attract exceptional executives, senior management and employees.

As noted above, we believe that properly structured equity compensation works to align the long-term interests of stockholders and employees by creating a strong, direct link between employee compensation and stock price appreciation. Specifically, because we grant stock options with an exercise price not less than the fair market value of our common stock on the date of grant (which in the past has been determined by our board of directors, as described below under "Equity granting policies"), these

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options will have value to our executive officers only if the fair market value of our common stock increases after the date of grant and the date of vesting. Typically, stock options granted to our executive officers vest over 48 months, with 25% of the options vesting after 12 months, and the remainder vesting monthly over the next 36 months. This vesting schedule provides a retention incentive to our executive officers. Typically, the grants are made with a vesting commencement date of January 1 of the year of the grant to reflect that the grants are made with respect to prior year performance. In addition, we have agreed to the accelerated vesting of stock options held by our executive officers upon an involuntary termination of employment following certain material corporate transactions, subject to executing an effective release of claims. We believe these accelerated vesting provisions reflect current market practices, based on the collective knowledge and experiences of our board members (and without reference to any specific peer group data), and allow us to attract and retain highly qualified executives. In addition, these accelerated vesting provisions allow our executive officers to focus on closing a transaction that may be in the best interest of our stockholders even though the transaction may otherwise result in a termination of their employment and, absent such accelerated vesting, a forfeiture of their unvested equity awards. In addition, we believe the automatic accelerated vesting upon a change of control (regardless of a termination event) that was approved by the board in 2010 for Mr. Schreck is appropriate given his transition in 2010 from a member of the company's management team to Chairman of the board as the other board members have this vesting provision. Additional information regarding accelerated vesting prior to, upon or following a change in control is discussed below under "Executive Employment Agreements and Termination Benefits."

In early 2008, the board established a fiscal budget and set of corporate objectives against which company performance would generally be evaluated. However, the board did not prospectively establish a specific pool of shares or weighting of individual milestones that would result in equity awards to our executive officers. Major objectives for 2008 included the successful preparation for, initiation and completion of the ARX-01 Phase 2 knee replacement study, advancing ARX-02 towards initiation of a Phase 2 study, and the completion of the ARX-03 Phase 1 study. In mid-2008, the board approved the addition of a second ARX-01 Phase 2 study start in abdominal surgery as a company goal. In early 2009, the compensation committee reviewed achievement against these goals and the recommendations our Chief Executive Officer on grant size. The compensation committee considered the role each executive played in achieving these goals, internal pay equity (that is, more of the grants should be allocated to the Chief Executive Officer and Chief Medical Officer given their responsibilities for running the company), and the compensation committee's judgment based on its experience and knowledge. The board met in March 2009 and tentatively approved the compensation committee's recommendations, including an option grant to Mr. Schreck for 25,000 shares, with all of the option grants to be made at a future board meeting upon receipt of a third party valuation. In July 2009, the board met after considering a third party valuation and other factors, and formally approved the grants that were tentatively approved in March 2009. In addition, the board reflected on the fact that certain anticipated hires had not occurred in the interim, freeing up additional shares to be used for additional grants from the company's available share pool, and their evaluation of the need for an additional grant to Mr. Schreck to reward and motivate him, and granted an additional option award to him covering an additional 25,000 shares on the same date (for a total award on July 1, 2009 of 50,000 shares).

In early 2009, the board established a budget of 150,000 to 180,000 shares for equity grants to be made to all of our employees, including executive officers, in respect of performance in 2009 – that is, it was intended that annual equity grants for 2009 would be made from this pool of shares at the end of the year based on achievement of certain performance goals. The pool was set at a level that the board determined would provide adequate compensation for employees while limiting the dilutive impact on stockholders and prior to our preparations for the Series C preferred stock financing. The performance goals focused on milestones in the development of ARX-01, ARX-02 and ARX-03, including the completion of the ARX-01 Phase 2 abdominal surgery study, the completion of the ARX-01 device functionality study, completion of the ARX-01 End of Phase 2 meeting, initiation of the ARX-02 Phase 2

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cancer breakthrough pain study, and completion of the ARX-03 Phase 2 study. These goals were proposed by management and approved by the compensation committee. Any award of options at the end of 2009 after achievement of these goals was to be made entirely in the discretion of the board without any reference to a formula or specific weighting.

In early 2010, the board determined achievement against these goals. However, notwithstanding our actual achievement against these goals, the board used its discretion and eliminated the original pool as a result of the dilution to employees caused by the closing of our Series C preferred stock financing that closed in November 2009. Instead, the board determined the number of shares each executive officer was eligible to receive (based on factors described below) once the fair market value of our common stock could be reasonably determined, but did not make the actual grants of the options, as it was awaiting a third party valuation of our common stock. After considering that valuation and other factors, the board met in June 2010 and made grants to our executive officers as set forth in the table below. The size of these grants reflected the board's subjective consideration of internal pay equity (including the belief that more of the grants should be allocated to the Chief Executive Officer and Chief Medical Officer given their founder status and responsibilities for running the company), the board's judgment based on its experiences and knowledge, and, most importantly the fact that the equity holdings of our employees, including our executive officers, were substantially diluted due to the closing of the Series C preferred stock financing. Prior to the closing of the Series C preferred stock financing, we had approximately 4.75 million shares outstanding; after the closing of the Series C preferred stock financing, we had approximately 11.5 million shares outstanding. Therefore, the grants made in 2010 as set forth in the table below reflect the decision to offset approximately 50% of the dilution the officers suffered as a result of the Series C financing. The grants that were specifically intended to address the impact of the Series C financing contained vesting provisions such that 25% of the stock option shares were vested on January 1, 2010 with the remaining 75% of the stock option shares vesting over three years. Management requested, and the board approved, this special vesting schedule to help ameliorate the impact of the dilution from the financing. The board also, at that time, made an additional merit grant to Mr. Dasu in light of the importance of his role as the engineering leader of the ARX-01 device functionality study that achieved positive Phase 2 results. This grant was made with our standard four year vesting schedule. These grants were priced at 100% of the fair market value of our common stock, as determined by our board based in part on an independent third party valuation as of December 31, 2009.

In early 2010, our board established a budget of 175,000 to 237,500 shares for equity grants to all of our then-current employees (that is, exclusive of Messrs. King and Welch) to be granted in 2011 based on the achievement of certain performance goals in 2010. The pool was set at a level that the board determined would provide adequate compensation for employees while limiting the dilutive impact on stockholders. These performance goals focused on milestones in the development of ARX-01, ARX-02 and ARX-03 as well as broader strategic objectives. These goals were proposed by management and approved by the compensation committee. Any award of options at the end of 2010 after achievement of these goals will be made entirely at the discretion of the board without any reference to a formula or specific weighting.

In the spring of 2010, the company hired Mr. King and in the fall of 2010, the company hired Mr. Welch. In connection with these new hires, the board granted stock options to these executives, in the amounts set forth below, based primarily on individual negotiations (which reflect, in part, equity awards that these executives were eligible for with their prior employers), and survey data providing for grants at the 50th percentile to chief executive officers in an amount equal to 4.8% of the outstanding stock of such companies and chief financial officers in an amount equal to 1% of the outstanding stock of such companies. Mr. King negotiated a limited severance vesting provision for his initial option grant that expired in May 2010, and the board agreed to it as an inducement to have Mr. King join. The grants shown in the table below are equal to approximately 4% of the company for Mr. King and 1% of the company for Mr. Welch, on a fully diluted basis. In addition, Mr. King is eligible to be granted an option

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to purchase 115,208 shares of common stock of the company upon achievement of one of the following corporate milestones prior to June 30, 2011:

(i) completion by the company of a qualifying partnering transaction, (ii) completion of this offering, or (iii) completion of a private financing raising at least \$15 million from new investors. Mr. Welch is eligible to be granted an option covering 25,000 shares if we complete this offering or a private financing raising at least \$15 million from new investors prior to June 30, 2011. All of these new hire grants are separate and apart from the 2010 pool described above, which pool was not increased as a result of the hiring of these executives.

<u>Executive officer</u>	<u>Number of options related to 2008 performance (granted 2009)</u>	<u>Number of options related to Series C dilution (granted in 2010)</u>	<u>Merit and special grants in 2010 (including new hire grants)</u>
Richard A. King	N/A	N/A	456,610
James H. Welch	N/A	N/A	125,000
Thomas A. Schreck	50,000	218,750	N/A
Pamela P. Palmer, M.D., Ph.D.	37,500	250,000	N/A
Lawrence G. Hamel	12,500	62,500	N/A
Badri Dasu	6,250	30,000	25,000

In December 2010, our board of directors, out of an abundance of caution, allowed eligible optionees, including our named executive officers, to increase the exercise price of stock options granted to them on June 15, 2010 in light of the potential risk of adverse tax consequences under 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. When setting the exercise price for the June 15, 2010 stock option grants, the board 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 as described in more detail under “Management’s Discussion and Analysis of our Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation”. 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. We believe that the board’s determination of the fair market value of our common stock on June 15, 2010 in reliance upon all material facts available to the board 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 decided, out of an abundance of caution, to make the offer to amend. All of our eligible named executive officers accepted the offer, and their eligible options were amended on December 27, 2010 (as further set forth in the 2010 Grants of Plan-Based Awards Table below).

Equity Granting Policies

- We encourage our named executive officers to hold a significant equity interest in our company, but have not set specific ownership guidelines.
- While our board of directors has delegated authority to our compensation committee to make stock option grants to executive officers, all stock option grants previously awarded to our executive officers have been granted by our full board of directors.
- Prior to this offering, we did not have any program, plan or obligation that required us to grant equity compensation on specified dates and, because we have not been a public company, we have not made equity grants in connection with the release or withholding of material non-public information.
- In the absence of a public trading market for our common stock, our board of directors has historically determined the fair market value of our common stock in good faith based upon

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consideration of a number of relevant factors including our financial condition, the likelihood of a liquidity event, the liquidation preference of our participating preferred stock, the price at which our preferred stock was sold, the enterprise values of comparable companies, our cash needs, operating losses, progress in the research and development of our product candidates, market conditions, material risks to our business and valuation reports obtained from independent valuation firms.

Severance and Change in Control Benefits

The employment of all of our executive officers is “at will.” However, Messrs. King, Welch and Schreck and Dr. Palmer have been eligible to receive cash severance benefits upon certain involuntary terminations of employment under the terms of their respective offer letter agreements. In addition, our executive officers are eligible for accelerated vesting upon an involuntary termination following a change in control and Mr. Schreck, in his capacity as a board member, is now eligible for accelerated single trigger vesting upon a change of control, as described in more detail under “Long-term Equity Incentive Awards.” The terms of these severance and change in control benefits are further described below under “—Employment Agreements and Arrangements—Executive Employment Agreements and Termination Benefits.” These benefits reflect the negotiations of each of the applicable executive officers with the company, as well as a desire to reflect internal pay equity among our executive officers with respect to their potential severance benefits (for instance, only our Chief Executive Officer, Chief Financial Officer and Chief Medical Officer are currently offered cash severance benefits, and the severance benefits offered to our current Chief Executive Officer provide for a greater number of months of salary continuation than to our Chief Financial Officer or Chief Medical Officer, due to the breadth of his responsibilities within the company). We consider these severance benefits critical to attracting and retaining high caliber executives and our board believes the benefits are comparable to benefits provided to similarly situated executives at other private companies. In addition, we believe that change in control severance benefits, including accelerated vesting provisions, if structured appropriately, serve to minimize the distractions to an executive and reduce the risk that an executive officer terminates his employment with us before an acquisition is consummated. We believe that our existing arrangements allow our executive officers to focus on continuing normal business operations and, in the case of change in control benefits, on the success of a potential business combination, rather than being distracted by how business decisions that may be in the best interest of our stockholders will impact each executive officer’s own financial security. Specifically, our board believes these existing arrangements help ensure stability among our executive officers, and will help enable our executive officers to maintain a balanced perspective in making overall business decisions during periods of uncertainty.

Other Employee Benefits

We provide the following benefits to the executive officers, on the same terms and conditions as provided to all other eligible employees:

- health, dental and vision insurance benefits;
- a limited life insurance benefit of \$15,000 as part of our health insurance plan; and
- participation in a 401(k) plan, with non-discretionary 3% safe harbor profit sharing contribution.

We believe these benefits are important to attracting and retaining experienced executives. Like many private companies, the company does not currently provide perquisites to the executive officers, given our attention to the cost-benefit tradeoff of such benefits, and the boards’ knowledge of the benefit offerings at other private companies.

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Tax Deductibility of Compensation

Following the offering, Section 162(m) of the Code will limit our deduction for federal income tax purposes to not more than \$1.0 million of compensation paid to certain executive officers in a calendar year. Compensation above \$1.0 million may be deducted if it is “performance-based compensation.” The compensation committee has not yet established a policy for determining which forms of incentive compensation awarded to our executive officers will be designed to qualify as “performance-based compensation.” To maintain flexibility in compensating our executive officers in a manner designed to promote our objectives, the compensation committee has not adopted a policy that requires all compensation to be deductible. However, the compensation committee intends to evaluate the effects of the compensation deduction limits of Section 162(m) on any compensation it proposes to grant, and the compensation committee intends to provide future compensation in a manner consistent with the best interests of our stockholders.

Compensation Recovery Policies

The compensation committee has not determined whether it would attempt to recover bonuses from our executive officers if the performance objectives that led to the bonus determination were to be restated, or found not to have been met to the extent originally believed by the compensation committee. However, as a public company subject to the provisions of Section 304 of the Sarbanes-Oxley Act of 2002, if we are required as a result of misconduct to restate our financial results due to our material noncompliance with any financial reporting requirements under the federal securities laws, our chief executive officer and chief financial officer may be legally required to reimburse us for any bonus or other incentive-based or equity-based compensation they receive. In addition, the company will comply with the requirements of the Dodd-Frank Wall Street Reform and Consumer Protection Act and will adopt a compensation recovery policy once final regulations on the subject have been adopted.

Accounting Considerations

We account for equity compensation paid to our employees under ASC 718, which requires us to estimate and record an expense over the service period of the award. Our cash compensation is recorded as an expense at the time the obligation is accrued. The accounting impact of our compensation programs is one of many factors that are considered in determining the size and structure of our programs.

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Summary Compensation Table

The following table sets forth certain summary information for the year indicated with respect to the compensation earned by our Chief Executive Officer, our Chief Financial Officer, our former President and Chief Executive Officer (and acting principal financial officer) who resigned effective April 30, 2010, and each of our three other most highly compensated executive officers as of December 31, 2010. We refer to these individuals as our “named executive officers” elsewhere in this prospectus.

2010 and 2009 Summary Compensation Table

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (S)</u>	<u>Bonus (S)</u>	<u>Option Awards (S)⁽¹⁾</u>	<u>All Other Compensation (S)⁽²⁾</u>	<u>Total (S)⁽³⁾</u>
Richard A. King ⁽⁴⁾ <i>President and Chief Executive Officer</i>	2010	306,667	94,500	925,032	6,000	1,332,199
	2009	—	—	—	—	—
James H. Welch ⁽⁵⁾ <i>Chief Financial Officer</i>	2010	72,500	⁽⁶⁾	450,426	—	522,926
	2009	—	—	—	—	—
Thomas A. Schreck ⁽⁷⁾ <i>Former President, Chief Executive Officer and Principal Financial Officer</i>	2010	125,000	—	432,142	214,082 ⁽⁸⁾	771,224
	2009	375,000	—	98,071	7,350	480,421
Lawrence G. Hamel <i>Chief Development Officer</i>	2010	275,000	—	123,469	7,350	405,819
	2009	262,500	—	24,518	7,350	294,368
Badri Dasu <i>Chief Engineering Officer</i>	2010	262,500	—	109,912	7,350	379,762
	2009	247,500	—	12,259	7,350	267,109
Pamela P. Palmer, M.D., Ph.D. <i>Chief Medical Officer</i>	2010	375,000	—	493,876	7,350	876,226
	2009	187,500	—	73,554	177,813 ⁽⁹⁾	438,867

⁽¹⁾The dollar amounts in this column represent the aggregate grant date fair value of all option awards granted during the indicated year. These amounts have been calculated in accordance with FASB ASC Topic 718, or ASC 718, using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 10 to our financial statements and the discussion under “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” included elsewhere in this prospectus. These amounts do not necessarily correspond to the actual value that may be recognized from the option awards by the named executive officers. The modification of stock option awards originally granted in June 2010 as described under “— Employment Agreements and Arrangements—Employee Benefit and Stock Plans—Option Exercise Price Increase” did not result in an increase in the fair value of such stock option awards under ASC 718.

⁽²⁾Except as otherwise noted, the dollar amounts in this column represent company profit sharing contributions under our 401(k) plan.

⁽³⁾For 2009, represents total compensation earned in 2009. For 2010, represents total compensation earned in 2010 other than with respect to Mr. Welch. For 2010 for Mr. Welch, represents total compensation earned in 2010, not including expected bonus compensation.

⁽⁴⁾Mr. King has served as our President and Chief Executive Officer since May 1, 2010 and did not receive any compensation from us in any capacity during the year ended December 31, 2009. Mr. King also served as our principal financial officer from May 1, 2010 until September 30, 2010.

⁽⁵⁾Mr. Welch has served as our Chief Financial Officer since October 1, 2010 and did not receive any compensation from us in any capacity during the year ended December 31, 2009.

⁽⁶⁾Mr. Welch is eligible to receive a prorated cash bonus for 2010 of up to \$21,750, expected to be determined in the first quarter of 2011; however, no bonus determination has been made by the board as of the date of this prospectus.

⁽⁷⁾Mr. Schreck resigned as our President and Chief Executive Officer effective April 30, 2010 but continues to serve on our board of directors. Mr. Schreck also served as our principal financial officer until his resignation.

⁽⁸⁾Represents \$7,350 in company profit sharing contributions under our 401(k) plan, \$187,500 in base salary continuation and \$19,232 in company-paid health coverage and benefits. For more information regarding Mr. Schreck’s post-employment

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compensatory arrangements, please see “— Employment Agreements and Arrangements—Executive Employment Agreements and Termination Benefits—Thomas Schreck Employment and Resignation Agreements”.

⁽⁹⁾Represents \$2,813 in company profit sharing contributions under our 401(k) plan and \$175,000 in consulting fees.

Grants of Plan-Based Awards Table

The following table provides information regarding grants of plan-based awards to each of our named executive officers during the year ended December 31, 2010. During the year ended December 31, 2010, none of our named executive officers were awarded any equity incentive plan awards, non-equity incentive plan awards or stock awards.

2010 Grants of Plan-Based Awards Table

<u>Name</u>	<u>Grant Date⁽¹⁾</u>	<u>All Other Option Awards: Number of Securities Underlying Options (#)⁽²⁾</u>	<u>Exercise or Base Price of Option Awards (\$/Sh)⁽³⁾</u>	<u>Grant Date Fair Value of Stock and Option Awards (\$)⁽⁴⁾</u>
Richard A. King	06/15/10	456,610 ⁽⁵⁾	1.20	925,032
	12/27/10	⁽⁶⁾	2.56	—
James H. Welch	11/04/10	125,000 ⁽⁷⁾	5.32	450,426
Thomas A. Schreck	06/15/10	218,750 ⁽⁸⁾	1.20	432,142
	12/27/10	⁽⁶⁾	2.56	—
Lawrence G. Hamel	06/15/10	62,500 ⁽⁸⁾	1.20	123,469
	12/27/10	⁽⁶⁾	2.56	—
Badri Dasu	06/15/10	30,000 ⁽⁸⁾	1.20	59,265
	12/27/10	⁽⁶⁾	2.56	—
	06/15/10	25,000 ⁽⁹⁾	1.20	50,647
	12/27/10	⁽⁶⁾	2.56	—
Pamela P. Palmer, M.D., Ph.D.	06/15/10	250,000 ⁽⁸⁾	1.20	493,876
	12/27/10	⁽⁶⁾	2.56	—

⁽¹⁾Grant date of the option awards or, in the case of repriced option awards, the date of repricing.

⁽²⁾The stock options reflected in this column were granted under our 2006 Plan. For a description of the terms of stock options granted under our 2006 Plan, please see “— Employment Agreements and Arrangements—Employee Benefit and Stock Plans—2006 Stock Plan.”

⁽³⁾Our common stock was not publicly traded during 2010, and the exercise price of the options was determined by our board of directors on the grant date based on its determination of the fair market value of our common stock on such grant date. For more information on our methodology for determining the exercise price of the options, see “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” appearing elsewhere in this prospectus.

⁽⁴⁾The dollar amounts in this column represent the grant date fair value of each option award calculated in accordance with ASC 718 using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 10 to our financial statements and the discussion under “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” included elsewhere in this prospectus. These amounts do not necessarily correspond to the actual value that may be recognized by the named executive officers.

⁽⁵⁾28,538 of the shares subject to the option award were vested as of the grant date, 85,614 of the shares subject to the option award will vest on March 3, 2011, and the remaining shares subject to the option award will vest on an equal monthly basis over the following 36 months.

⁽⁶⁾Shows the increase in the exercise price of the option award referenced in the line immediately above. As described under “—Employment Agreements and Arrangements—Employee Benefit and Stock Plans—Option Exercise Price Increase,” certain of the option awards granted to our named executive officers in 2010 were amended to increase the exercise price of the option awards from \$1.20 per share to \$2.56 per share. The repricing did not result in an increase in the fair value of these option awards under ASC 718.

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⁽⁷⁾The shares subject to this option award will vest as to 1/4th of the shares subject to the option award on September 30, 2011 with the remaining shares subject to the option award vesting on an equal monthly basis over the following 36 months.

⁽⁸⁾The shares subject to this option award vested as to 1/2 of the shares subject to the option award on December 31, 2010 with the remaining shares subject to the option award vesting on an equal monthly basis over the following 24 months.

⁽⁹⁾The shares subject to this option award vested as to 1/4th of the shares subject to the option award on December 31, 2010 with the remaining shares subject to the option award vesting on an equal monthly basis over the following 36 months.

Employment Agreements and Arrangements

Executive Employment Agreements and Termination Benefits

Thomas Schreck Employment and Resignation Agreements

In August 2006, we entered into an employment agreement with Mr. Schreck that provides for an initial base salary and discretionary bonus eligibility, as well as certain severance benefits. Under the employment agreement, in the event that Mr. Schreck's employment had terminated without cause or had terminated as a result of a voluntary termination by Mr. Schreck for certain stated reasons within 18 months after a change of control, as these terms are used in the employment agreement, Mr. Schreck would have been entitled to the following severance benefits, subject to Mr. Schreck executing a general release of claims in favor of us:

- a single lump-sum payment equal to six months of his base salary in effect as of the date of his termination;
- full vesting acceleration of all stock options and stock awards granted to Mr. Schreck under the 2006 Plan; and
- the same level of company-paid health coverage and benefits in effect for Mr. Schreck as of immediately prior to his termination date for a period of up to six months provided, among other things, that Mr. Schreck would have timely elected continuation under the Consolidated Omnibus Budget Reconciliation Act of 1985, or COBRA.

In addition, under the employment agreement, in the event that Mr. Schreck's employment had terminated without cause or had terminated as a result of a voluntary termination by Mr. Schreck for certain stated reasons before a change of control, as these terms are used in the employment agreement, Mr. Schreck would have been entitled to the same benefits described above except for the stock option and stock award vesting acceleration.

Effective April 30, 2010, Mr. Schreck resigned as our President and Chief Executive Officer, but continues to serve on our board of directors. In connection with his resignation, we entered into a resignation letter agreement with Mr. Schreck that provides for continuation of his base salary in effect as of the effective date of resignation (\$375,000) for six months, commencing within 30 days after the effective date of his resignation, and the same level of company-paid health coverage and benefits in effect for Mr. Schreck as of the effective date of his termination for a period of six months (subject to his timely COBRA election). The resignation letter agreement also provides for continued vesting of his stock option awards and restricted stock for so long as he continues to serve on our board of directors or as a consultant to us, and provides for a general release of claims in favor of us. Please refer to "Stock Option Vesting Acceleration" below for description of Mr. Schreck's current stock option vesting acceleration.

Offer Letter Agreements

We have entered into offer letter agreements with each of our executive officers, other than Mr. Schreck, in connection with each named executive officer's commencement of employment with us. These offer letter agreements provide for the named executive officer's initial base salary, eligibility to participate in our standard benefit plans and in certain cases, the named executive officer's initial stock option grant along with vesting provisions with respect to that initial stock option grant. We amended and restated

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these offer letter agreements in December 2010 to clarify certain terms for compliance with tax laws, to specify the terms of the option to be granted to Mr. King upon achievement of certain milestones and to provide additional change of control severance benefits to Mr. Welch and Dr. Palmer.

Under Mr. King's, Mr. Welch's and Dr. Palmer's respective offer letter agreements, in the event that such executive's employment is terminated by us without cause, or such executive resigns for good reason, or in a manner that constitutes an involuntary termination, in each case within one year following a change in control, as these terms are defined in the offer letters, each will be entitled to base salary and health benefits continuation for a period of twelve months in the case of Mr. King, and six months in the case of each of Mr. Welch and Dr. Palmer. Mr. King is also entitled to base salary and health benefits continuation for a period of twelve months in connection with a termination by us without cause that is not in connection with a change of control. Dr. Palmer's offer letter agreement also provides for a lump sum cash severance payment if she is terminated by us without cause (other than in connection with a change of control) during the first two years of her employment, which commenced on July 1, 2009, equal to four months of Dr. Palmer's base salary at the time of her termination plus two weeks of salary for every full year of regular, full time employment she has completed with us as of her termination. Please refer to "Stock Option Vesting Acceleration" below for description of the current stock option vesting acceleration for each of our executive officers. In order to receive severance benefits, each such executive must sign a waiver and release of claims.

Mr. King's and Mr. Welch's offer letters also provide for an opportunity to earn a target annual bonus of 35% and 30% of base salary, respectively, and Mr. King is entitled to an additional option grant covering 115,208 shares of our common stock upon achievement of one of the following corporate milestones prior to June 30, 2011: (i) completion by the company of a qualifying partnering transaction, (ii) completion of this offering, or (iii) completion of a private financing raising at least \$15 million from new investors. Mr. Welch is entitled to an additional option grant covering 25,000 shares if we complete this offering or a private financing raising at least \$15 million from new investors prior to June 30, 2011.

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

Stock Option Vesting Acceleration

Each of our executive officers, other than Mr. Schreck, are entitled to full "double-trigger" stock option vesting acceleration benefits (for all currently outstanding stock options and any stock options that may be granted in the future) in the event their service with us is terminated by us without cause, or such executive resigns for good reason, or in a manner that constitutes an involuntary termination, in each case within 18 months following a change in control, subject to signing an effective release of claims. Mr. Schreck was entitled to double-trigger vesting acceleration benefits while he served as our President and Chief Executive Officer. In September 2010, we amended the terms of each of Mr. Schreck's stock options to provide for full stock option vesting acceleration on a "single-trigger" basis, meaning that he is entitled to full stock option vesting acceleration immediately upon such a change in control transaction.

Founder's Vesting Agreements

Each of Mr. Schreck and Dr. Palmer, our co-founders, entered into founder's vesting agreements with us in August 2006. Under these agreements, 125,000 of the 250,000 shares of our common stock held by each of Mr. Schreck and Dr. Palmer became restricted and made subject to vesting in equal monthly installments over a four year period commencing on September 15, 2006. As of August 15, 2010, all of these restricted shares had vested in full. Under the founder's vesting agreement with Dr. Palmer, in the event that Dr. Palmer's service with us as an employee or consultant had terminated without cause or

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had terminated as a result of a voluntary termination by Dr. Palmer for certain stated reasons within 18 months after a change of control, as these terms are used in her founder's vesting agreement, and Dr. Palmer had signed a general release of claims in favor of us, any of her unvested restricted shares then held would have become fully vested as of the date of her termination.

Employee Benefit and Stock Plans

2006 Stock Plan

Our board of directors adopted, and our stockholders approved, the 2006 Stock Plan, or 2006 Plan, in August 2006. The 2006 Plan was subsequently amended by our board of directors and approved by our stockholders in each of February 2008 and November 2009. The 2006 Plan provides for the grant of incentive stock options, nonstatutory stock options and rights to acquire restricted stock. Upon the execution and delivery of the underwriting agreement for this offering, no additional stock options or other stock awards will be granted under the 2006 Plan. All outstanding stock options and other stock awards previously granted under the 2006 Plan will remain subject to the terms of the 2006 Plan.

Share reserve. There are 2,093,059 shares of common stock reserved for issuance under the 2006 Plan. As of September 30, 2010, 32,569 shares of common stock had been issued upon the exercise of stock options or pursuant to stock awards granted under the 2006 Plan, options to purchase 1,892,860 shares of common stock were outstanding at a weighted average exercise price at September 30, 2010 of \$1.88 per share (or \$2.76 per share assuming that the December 2010 stock option modification described under "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation" had occurred as of September 30, 2010) and 167,630 shares remained available for future grant under the 2006 Plan.

Administration. Our board of directors administers our 2006 Plan. Our board of directors, referred to as the plan administrator, has the authority to interpret, amend, suspend and terminate the 2006 Plan, as well as to determine the terms of a stock award or amend the terms of a stock award. No amendment to the 2006 Plan or any award agreement thereunder may adversely affect the rights under any outstanding stock award unless the holder consents to that amendment. However, the plan administrator may unilaterally amend the 2006 Plan or the terms of an outstanding award agreement to conform the 2006 Plan or such stock award to any law, regulation or rule applicable to the 2006 Plan, including, but not limited to, Section 409A of the Code, as the plan administrator deems necessary or advisable.

Eligibility. The 2006 Plan provides for the grant of options and stock awards to our employees, directors and consultants. Incentive stock options may be granted only to employees. Nonstatutory stock options and stock awards may be granted to employees, directors and consultants.

Stock option provisions generally. In general, the exercise price of a stock option cannot be less than 100% of the fair market value of our common stock on the date of grant. However, an incentive stock option granted to a person who on the date of grant owns more than 10% of the combined voting power of all classes of our stock or any of our affiliates' stock must have an exercise price that is at least 110% of the fair market value on the date of grant.

Generally, an optionee may not transfer his or her stock option other than by will or by the laws of descent and distribution. Shares subject to options under the 2006 Plan generally vest and become exercisable in periodic installments. With the exception of stock options issued to an officer, a director or a consultant, shares subject to stock options under the 2006 Plan must vest and become exercisable at a rate not less than 20% per year over a period of five years from the date of grant of the option, subject to the optionee's continued service.

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The aggregate fair market value, determined at the time of grant, of shares of our common stock with respect to which incentive stock options are exercisable for the first time by an optionee during any calendar year under all of our stock plans may not exceed \$100,000. Options or portions thereof that exceed such limit will be treated as nonstatutory stock options.

The plan administrator determines the term of stock options granted under the 2006 Plan, up to a maximum of 10 years, provided that incentive stock options granted to persons who own more than 10% of the combined voting power of all classes of our stock or any of our affiliates' stock may not have a term of more than five years. Unless the terms of an optionee's stock option agreement provide otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee generally may exercise the vested portion of any stock options for a period of three months following the cessation of service. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within three months following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months. The option term may be further extended in the event that exercise of the stock option following termination of the optionee's service is prohibited by applicable securities laws. In no event may an option be exercised beyond the expiration of its term. In the event of a termination for cause, options generally terminate immediately upon the termination of the optionee's service. Unless otherwise defined in an optionee's award agreement or in a written employment agreement or contract of service between an optionee and us, cause refers to an optionee's termination due to (1) the optionee's theft, dishonesty, willful misconduct, breach of fiduciary duty for personal profit, or falsification of any of our documents or records; (2) the optionee's material failure to abide by a code of conduct or other policies of ours (including, without limitation, policies relating to confidentiality and reasonable workplace conduct); (3) the optionee's unauthorized use, misappropriation, destruction or diversion of any tangible or intangible asset or corporate opportunity of ours (including, without limitation, the optionee's improper use or disclosure of our confidential or proprietary information); (4) any intentional act by the optionee which has a material detrimental effect on our reputation or business; (5) the optionee's repeated failure or inability to perform any reasonable assigned duties after written notice from us of, and a reasonable opportunity to cure, such failure or inability; (6) any material breach by the optionee of any employment or service agreement between the optionee and us, which breach is not cured pursuant to the terms of such agreement; or (7) the optionee's conviction (including any plea of guilty or nolo contendere) of any criminal act involving fraud, dishonesty, misappropriation or moral turpitude, or which impairs the optionee's ability to perform his or her duties with us.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option will be determined by the plan administrator and may include (a) cash, check or cash equivalent, (b) the tender to us, or attestation to the ownership, of shares of our common stock previously owned by the optionee, (c) a broker-assisted cashless exercise, (d) other legal consideration approved by the plan administrator or (e) any combination of the foregoing.

Stock purchase rights generally. Rights to acquire restricted stock may be granted pursuant to restricted stock purchase agreements adopted under the 2006 Plan. The purchase price for restricted stock purchase rights cannot be less than 85% of the fair market value of our common stock on the date of grant or the date the purchase is consummated, provided that the purchase price for restricted stock purchase rights granted to a person who on the date of grant owns or is deemed to own more than 10% of the total combined voting power of all classes of our stock or any of our affiliates' stock must be at least 100% of the fair market value on the date of grant or the date the purchase is consummated. Payment of the purchase price for restricted stock purchase rights may be made using (1) cash, check or a cash equivalent, (2) past services provided to us or our affiliates, (3) other legal consideration permitted by the plan administrator or (4) any combination of the foregoing. Shares of common stock acquired under a restricted stock purchase right may, but need not, be subject to a share repurchase option in our

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favor in accordance with a vesting schedule to be determined by the plan administrator, in which case, if a participant's service relationship with us terminates, we may repurchase any or all of the shares of common stock subject to the restricted stock purchase award that have not vested as of the date of termination. With the exception of shares acquired under a restricted stock purchase right award by an officer, a director or a consultant, our repurchase right with respect to shares subject to vesting in connection with a restricted stock purchase award must lapse at the rate of at least 20% of the shares per year over the period of five years from the date of grant of the restricted stock purchase right. A holder of a stock purchase right may not transfer his or her stock purchase right other than by will or by the laws of descent and distribution.

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

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

- accelerate the vesting of a stock award;
- arrange for the assumption, continuation or substitution of a stock award by the surviving or acquiring entity or its parent company; or
- cancel or arrange for the cancellation of the stock award in exchange for a payment in (1) cash, (2) stock, or (3) other property, and in any such case in an amount equal to the fair market value of the consideration to be paid per share of stock in the change of control over the exercise price per share.

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

Option Exercise Price Increase

In December 2010, our board of directors, out of an abundance of caution, allowed eligible optionees, including our named executive officers, to increase the exercise price of stock options granted to them on June 15, 2010 in light of the potential risk of adverse tax consequences under 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. When setting the exercise price for the June 15, 2010 stock option grants, the board 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 as described in more detail under "Management's Discussion and Analysis of our Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation". 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. We believe that the board's determination of the fair market value of our common stock on June 15, 2010 in reliance upon all material facts available to the board 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 decided, out of an abundance of caution, to make the offer to amend. All of our eligible named executive officers accepted the offer, and their eligible options were amended on December 27, 2010 (as further set forth in the 2010 Grants of Plan-Based Awards Table above).

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2011 Equity Incentive Plan

Our board of directors adopted, and our stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan, in January 2011 as a successor to the 2006 Plan. We expect the 2011 Incentive Plan will become effective immediately upon the execution and delivery of the underwriting agreement for this offering. The 2011 Incentive Plan will terminate on January 4, 2021, unless sooner terminated by our board of directors. Our board of directors may amend or suspend the 2011 Incentive Plan at any time, although no such action may impair the rights under any then-outstanding award without the holder's consent.

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

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

No person may be granted stock awards covering more than 1,000,000 shares of our common stock under our 2011 Incentive Plan during any calendar year pursuant to stock options, stock appreciation rights and other stock awards whose value is determined by reference to an increase over an exercise or strike price of at least 100% of the fair market value on the date the stock award is granted. Additionally, no person may be granted in a calendar year a performance stock award covering more than 750,000 shares or a performance cash award having a maximum value in excess of \$1,000,000. Such limitations are designed to help assure that any deductions to which we would otherwise be entitled with respect to such awards will not be subject to the \$1,000,000 limitation on the income tax deductibility of compensation paid to any covered executive officer imposed by Section 162(m) of the Code.

If a stock award granted under the 2011 Incentive Plan expires or otherwise terminates without being exercised in full, or is settled in cash, the expiration, termination or settlement shall not reduce (or otherwise offset) the number of shares of common stock that may be available for issuance under the 2011 Incentive Plan. In addition, the following types of shares under the 2011 Incentive Plan may become available for the grant of new stock awards under the 2011 Incentive Plan: (1) shares that are forfeited to or repurchased by us prior to becoming fully vested; (2) shares withheld to satisfy income or employment withholding taxes; or (3) shares used to pay the exercise price of an option. Shares issued under the 2011 Incentive Plan may be previously unissued shares or reacquired shares bought by us on the open market. As of the date hereof, no awards have been granted and no shares of our common stock have been issued under the 2011 Incentive Plan.

Administration. Our board of directors, or a duly authorized committee thereof, has the authority to administer the 2011 Incentive Plan. Our board of directors has delegated its authority to administer the 2011 Incentive Plan to our compensation committee under the terms of the compensation committee's

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charter. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than other officers) to be recipients of stock options or stock appreciation rights, and (2) determine the number of shares of common stock to be subject to such stock awards, provided that our board of directors must specify the total number of shares of common stock that may be subject to stock awards granted by such officer and that such officer may not grant a stock award to himself or herself. Subject to the terms of the 2011 Incentive Plan, our board of directors or the authorized committee or officer, referred to as the plan administrator, determines recipients, dates of grant, the numbers and types of stock awards to be granted and the terms and conditions of the stock awards, including the period of their exercisability and vesting schedule applicable to a stock award. Subject to the limitations set forth below, the plan administrator will also determine the exercise price, strike price or purchase price of awards granted and the types of consideration to be paid for the award.

The plan administrator has the authority to reduce the exercise price (or strike price) of any outstanding option or stock appreciation right, cancel and re-grant any outstanding option or stock appreciation right or take any other action that is treated as a repricing under U.S. generally accepted accounting principles, with the consent of any adversely affected participant.

Stock options. Incentive and nonstatutory stock options are granted pursuant to stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for a stock option, within the terms and conditions of the 2011 Incentive Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2011 Incentive Plan vest at the rate specified by the plan administrator.

The plan administrator determines the term of stock options granted under the 2011 Incentive Plan, up to a maximum of 10 years. Unless the terms of an optionee's stock option agreement provides otherwise, if an optionee's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the optionee may generally exercise any vested options for a period of three months following the cessation of service. The option term may be extended in the event that exercise of the option or sale of shares received upon exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If an optionee's service relationship with us, or any of our affiliates, ceases due to disability or death, or an optionee dies within a certain period following cessation of service, the optionee or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the occurrence of the event giving rise to the right to terminate the individual for cause. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option will be determined by the plan administrator and may include (1) cash, check, bank draft or money order, (2) a broker-assisted cashless exercise, (3) the tender of shares of our common stock previously owned by the optionee, (4) a net exercise of the option if it is a nonstatutory option, and (5) other legal consideration approved by the plan administrator.

Unless the plan administrator provides otherwise, options generally are not transferable except by will, the laws of descent and distribution, or pursuant to a domestic relations order. An optionee may designate a beneficiary, however, who may exercise the option following the optionee's death.

Tax limitations on incentive stock options. The aggregate fair market value, determined at the time of grant, of our common stock with respect to incentive stock options that are exercisable for the first time by an optionee during any calendar year under all of our stock plans may not exceed \$100,000. Options or portions thereof that exceed such limit will generally be treated as nonstatutory stock options. No

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incentive stock option may be granted to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant, and (2) the term of the incentive stock option does not exceed five years from the date of grant.

Restricted stock awards. Restricted stock awards are granted pursuant to restricted stock award agreements adopted by the plan administrator. Restricted stock awards may be granted in consideration for (1) cash, check, bank draft or money order, (2) past services rendered to us or our affiliates, or (3) any other form of legal consideration. Common stock acquired under a restricted stock award may, but need not, be subject to a share repurchase option in our favor in accordance with a vesting schedule to be determined by the plan administrator. Rights to acquire shares under a restricted stock award may be transferred only upon such terms and conditions as set by the plan administrator.

Restricted stock unit awards. Restricted stock unit awards are granted pursuant to restricted stock unit award agreements adopted by the plan administrator. The plan administrator will determine the vesting terms of restricted stock unit awards. The plan administrator will determine the consideration to be paid, if any, by the participant upon delivery for each share subject to a restricted stock unit award, which may be paid in any form of legal consideration acceptable to the plan administrator. A restricted stock unit award may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted stock unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit award. Except as otherwise provided in the applicable award agreement, restricted stock units that have not vested will be forfeited upon the participant's cessation of continuous service for any reason.

Stock appreciation rights. Stock appreciation rights are granted pursuant to stock appreciation right grant agreements adopted by the plan administrator. The plan administrator determines the strike price for a stock appreciation right, which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Upon the exercise of a stock appreciation right, we will pay the participant an amount equal to the product of (1) the excess of the per share fair market value of our common stock on the date of exercise over the strike price, multiplied by (2) the number of shares of common stock with respect to which the stock appreciation right is exercised. A stock appreciation right granted under the 2011 Incentive Plan vests at the rate specified in the stock appreciation right grant agreement as determined by the plan administrator.

The plan administrator determines the term of stock appreciation rights granted under the 2011 Incentive Plan, up to a maximum of ten years. Unless the terms of a participant's stock appreciation right grant agreement provides otherwise, if a participant's service relationship with us, or any of our affiliates, ceases for any reason other than cause, disability or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. The stock appreciation right term may be further extended in the event that exercise of the stock appreciation right or the sale of shares received upon exercise of the stock appreciation right following such a termination of service is prohibited by applicable securities laws. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested stock appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, stock appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the right to terminate the individual for cause. In no event may a stock appreciation right be exercised beyond the expiration of its term.

Performance awards. The 2011 Incentive Plan permits the grant of performance-based stock and cash awards that may qualify as performance-based compensation not subject to the \$1,000,000 limitation on

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the income tax deductibility of compensation paid to a covered executive officer imposed by Section 162(m) of the Code. To help assure that the compensation attributable to performance-based awards will so qualify, our compensation committee can structure such awards so that stock or cash will be issued or paid pursuant to such award only after the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: (1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) total stockholder return; (5) return on equity or average stockholders' equity; (6) return on assets, investment, or capital employed; (7) stock price; (8) margin (including gross margin); (9) income (before or after taxes); (10) operating income; (11) operating income after taxes; (12) pre-tax profit; (13) operating cash flow; (14) sales or revenue targets; (15) increases in revenue or product revenue; (16) expenses and cost reduction goals; (17) improvement in or attainment of working capital levels; (18) economic value added (or an equivalent metric); (19) market share; (20) cash flow; (21) cash flow per share; (22) share price performance; (23) debt reduction; (24) implementation or completion of projects or processes; (25) customer satisfaction; (26) stockholders' equity; (27) capital expenditures; (28) debt levels; (29) operating profit or net operating profit; (30) workforce diversity; (31) growth of net income or operating income; (32) billings; and (33) to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by our board of directors.

The performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise (1) in the award agreement at the time the award is granted or (2) in such other document setting forth the performance goals at the time the goals are established, the plan administrator will appropriately make adjustments in the method of calculating the attainment of performance goals as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated goals; (3) to exclude the effects of changes to U.S. generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of any "extraordinary items" as determined under U.S. generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; (8) to exclude the effect of any change in the outstanding shares of our common stock by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock based compensation and/or the award of bonuses under our bonus plans; and (10) to exclude the effect of any other unusual, non-recurring gain or loss or other extraordinary item. In addition, the plan administrator retains the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of the goals and to define the manner of calculating the performance criteria it selects to use for a performance period. The performance goals may differ from participant to participant and from award to award.

Other stock awards. The plan administrator may grant other awards based in whole or in part by reference to our common stock. The plan administrator will set the number of shares under the stock award and all other terms and conditions of such awards.

Changes to capital structure. In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, the plan administrator shall appropriately and proportionately adjust: (a) the class(es) and maximum number of shares reserved for issuance under the 2011 Incentive Plan and the class(es) and maximum number of shares by which the share reserve may

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increase automatically each year, (b) the class(es) and maximum number of shares that may be issued upon the exercise of incentive stock options, (c) the class(es) and maximum number of shares subject to stock awards that can be granted in a calendar year (as established under the 2011 Incentive Plan pursuant to Section 162(m) of the Code) and (d) the class(es) and number of shares and price per share of stock subject to outstanding stock awards.

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

- arrange for the assumption, continuation or substitution of a stock award by a surviving or acquiring entity or parent company;
- arrange for the assignment of any reacquisition or repurchase rights held by us to the surviving or acquiring entity or parent company;
- accelerate the vesting of the stock award and provide for its termination prior to the effective time of the corporate transaction;
- arrange for the lapse of any reacquisition or repurchase right held by us;
- cancel or arrange for the cancellation of the stock award in exchange for such cash consideration, if any, as our board of directors may deem appropriate; or
- make a payment equal to the excess of (a) the value of the property the participant would have received upon exercise of the stock award over (b) the exercise price otherwise payable in connection with the stock award.

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

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

2011 Employee Stock Purchase Plan

Our board of directors adopted, and our stockholders approved, the 2011 Employee Stock Purchase Plan, or ESPP, in January 2011. We expect the ESPP will become effective immediately upon the execution and delivery of the underwriting agreement for this offering.

Share reserve. The ESPP initially authorizes the issuance of 250,000 shares of our common stock pursuant to purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by our board of directors. If a purchase right granted under the ESPP terminates without having been exercised, the shares of our common stock not purchased under such purchase right will be available for issuance under the ESPP.

Administration. Our board of directors, or a duly authorized committee thereof, has the authority to administer the ESPP. Our board of directors has delegated its authority to administer the ESPP to our

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compensation committee. Our board of directors or the authorized committee is referred to as the plan administrator.

Purchase rights. The ESPP is implemented through a series of offerings of purchase rights to eligible employees. Purchase rights are generally not transferable. Under the ESPP, we may specify offerings with a duration of not more than 27 months, and may specify one or more shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for the employees who are participating in the offering. An offering may be terminated early under certain circumstances such as a material change in control of AcclRx. The plan administrator has the discretion to structure an offering so that if the fair market value of the shares of our common stock on the first day of a new purchase period within such offering is less than or equal to the fair market value of the shares of our common stock on the first day of the offering, then (a) that offering shall terminate immediately, and (b) the participants in such terminated offering shall be automatically enrolled in a new offering beginning on the first day of such new purchase period.

Payroll deductions. Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings toward the purchase of our common stock under the ESPP. Unless otherwise determined by the plan administrator, common stock will be purchased for participating employees at a price per share equal to the lower of (a) 85% of the fair market value of a share of our common stock on the first date of an offering, or (b) 85% of the fair market value of a share of our common stock on the date of purchase.

Limitations. Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by the plan administrator: (a) customary employment with us or one of our affiliates for more than 20 hours per week and more than five months per calendar year or (b) continuous employment with us or one of our affiliates for a minimum period of time prior to the first date of an offering, provided that such minimum period may not to exceed two years. No employee may purchase shares under the ESPP at a rate in excess of \$25,000 worth of our common stock, based on the fair market value per share of our common stock at the beginning of an offering, for each calendar year in which such purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if, immediately after such rights are granted, such employee owns our stock possessing five percent or more of the total combined voting power or value of all classes of our outstanding capital stock.

Changes to capital structure. In the event that there is a specified type of change in our capital structure such as a stock split or recapitalization, appropriate adjustments will be made to (a) the class(es) and maximum number of shares reserved under the ESPP, (b) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (c) the class(es) and number of shares subject to, and purchase price applicable to, all outstanding purchase rights, and (d) any limits on the class(es) and number of shares that may be purchased in an ongoing offering.

Corporate transactions. In the event of certain significant corporate transactions, such as an acquisition of the AcclRx that results in a material change in the ownership of AcclRx, any then-outstanding purchase rights under the ESPP may be assumed, continued or substituted for by any surviving or acquiring entity or its parent company, provided that the rights of any participant under any such assumption, continuation or substitution will not be impaired. If the surviving or acquiring entity or its parent company elects not to assume, continue or substitute for such purchase rights, then the participants' accumulated contributions will be used to purchase shares of our common stock within 10 business days prior to such corporate transaction, and such purchase rights will terminate immediately thereafter.

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Plan amendments. The plan administrator has the authority to amend, suspend or terminate the ESPP, provided any such action will not be taken without the consent of an adversely affected participant except as necessary to comply with any laws, listing requirements or governmental regulations or to maintain favorable tax, listing or regulatory treatment. We will obtain stockholder approval of any amendment to our ESPP as required by applicable law.

401(k) Plan

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

Pension Benefits

We do not maintain any pension or retirement plans.

Nonqualified Deferred Compensation

We do not maintain any nonqualified deferred compensation plans.

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Outstanding Equity Awards at December 31, 2010

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2010.

2010 Outstanding Equity Awards at Fiscal Year-End Table

Name	Option Awards			
	Number of Securities Underlying Unexercised Options (#)	Number of Securities Underlying Unexercised Options (#)	Option Exercise Price (\$ ⁽¹⁾)	Option Expiration Date
	Exercisable	Unexercisable		
Richard A. King	28,538	428,072 ⁽²⁾	2.56	06/15/2020
James H. Welch	—	125,000 ⁽³⁾	5.32	11/04/2020
Thomas A. Schreck	109,375	109,375 ⁽⁴⁾	2.56	06/15/2020
	12,500	12,500 ⁽⁴⁾	5.52	07/01/2019
	12,500	12,500 ⁽⁴⁾	5.52	07/01/2019
	28,125	9,375 ⁽⁶⁾	4.00	08/14/2018
	18,750	— ⁽⁷⁾	1.32	04/03/2017
Lawrence G. Hamel	31,250	31,250 ⁽⁴⁾	2.56	06/15/2020
	6,250	6,250 ⁽⁴⁾	5.52	07/01/2019
	14,062	4,688 ⁽⁸⁾	1.20	12/05/2017
	25,000	— ⁽⁹⁾	1.20	04/03/2017
	12,500	— ⁽⁷⁾	1.20	04/03/2017
Badri Dasu	15,000	15,000 ⁽⁴⁾	2.56	06/15/2020
	6,250	18,750 ⁽⁵⁾	2.56	06/15/2020
	3,125	3,125 ⁽⁴⁾	5.52	07/01/2019
	30,468	7,032 ⁽¹⁰⁾	1.20	10/25/2017
Pamela P. Palmer, M.D., Ph.D.	125,000	125,000 ⁽⁴⁾	2.56	06/15/2020
	18,750	18,750 ⁽⁴⁾	5.52	07/01/2019
	28,125	9,375 ⁽⁶⁾	4.00	08/14/2018
	25,000	— ⁽⁷⁾	1.32	04/03/2017

⁽¹⁾The dollar amounts in this column reflect the increase in the exercise price of the options we granted to our named executive officers on June 15, 2010 as described under “— Employment Agreements and Arrangements—Employee Benefit and Stock Plans—Option Exercise Price Increase.”

⁽²⁾The shares subject to this stock option vested as to 28,538 of the shares subject to the option on June 15, 2010, with 85,614 of the shares subject to the stock option vesting on March 3, 2011 and the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽³⁾The shares subject to this stock option will vest as to 1/4th of the shares subject to the option on September 30, 2011, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽⁴⁾The shares subject to this stock option vested as to 1/2 of the shares subject to the option on December 31, 2010 with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 24 months.

⁽⁵⁾The shares subject to this stock option vested as to 1/4th of the shares subject to the option on December 31, 2010 with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽⁶⁾The shares subject to this stock option vested as to 1/4th of the shares subject to the option on December 31, 2008, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽⁷⁾The shares subject to this stock option vested as to 1/4th of the shares subject to the option on December 31, 2007, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽⁸⁾ The shares subject to this stock option vested as to 1/4th of the shares subject to the option on December 4, 2008, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

⁽⁹⁾ The shares subject to this stock option vested as to 1/4th of the shares subject to the option on September 20, 2007, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

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⁽¹⁰⁾ The shares subject to this stock option vested as to 1/4th of the shares subject to the option on September 25, 2008, with the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months.

Option Exercises and Stock Vested

The following table shows information regarding the vesting of restricted stock held by our named executive officers during the year ended December 31, 2010. No stock options were exercised by our named executive officers during the year ended December 31, 2010.

2010 Option Exercises and Stock Vested Table

Name	Stock Awards	
	Number of Shares Acquired on Vesting (#)	Value Realized on Vesting (\$) ⁽¹⁾
Richard A. King	—	—
James H. Welch	—	—
Thomas A. Schreck	20,833	270,829
Lawrence G. Hamel	—	—
Badri Dasu	—	—
Pamela P. Palmer, M.D., Ph.D.	20,833	270,829

⁽¹⁾The value realized on vesting has been calculated assuming a price per share of \$13.00, which is the mid-point of the price range set forth on the cover page of this prospectus, multiplied by the number of shares vested. More information about the restricted stock held by Mr. Schreck and Dr. Palmer can be found under “Employment Agreements and Arrangements—Executive Employment Agreements and Termination Benefits—Founder’s Vesting Agreements.”

Potential Payments Upon Termination or Change in Control

Please refer to the section entitled “— Employment Agreements and Arrangements—Executive Employment Agreements and Termination Benefits” above for a description of the compensation and benefits payable to each of our named executive officers in certain termination situations. The amount of compensation and benefits payable to each named executive officer, other than Mr. Schreck, in various termination situations has been estimated in the tables below, assuming the applicable termination event occurred on December 31, 2010. All of the potential compensation and benefits listed in the tables below are compensation or benefits that would have been made, pursuant to the terms of the offer letter agreements with our named executive officers and the terms of the 2006 Plan and the stock option agreements thereunder. For purposes of the tables below, we have assumed that none of the potential compensation and benefits would be subject to the excise tax imposed pursuant Section 4999 of the Code and therefore reduced in accordance with the terms of the applicable agreements.

We entered into a resignation letter agreement with Mr. Schreck in connection with his resignation as our President and Chief Executive Officer as described under “— Employment Agreements and Arrangements—Executive Employment Agreements and Termination Benefits.” Pursuant to the resignation letter agreement with Mr. Schreck, we continued to pay his base salary that was in effect as of the effective date of his resignation for a six month period following his resignation, or a total of \$187,500 in base salary continuation payments, and provided Mr. Schreck with six months of continued company-paid health coverage and benefits at a cost to us of \$19,232 in the aggregate. The resignation letter agreement also provides for continued vesting of his stock option awards and restricted stock for so long as he continues to serve on our board of directors or as a consultant to us, and provides for a general release of claims in favor of us.

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Richard A. King

<u>Compensation and Benefits</u>	<u>Termination Without Cause Not in Connection With a Change in Control (\$)</u>	<u>Change in Control and Termination Without Cause or For Good Reason (\$)</u>
Base continuation ⁽¹⁾	400,000	400,000
Continued health coverage ⁽²⁾	19,320	19,320
Stock option vesting acceleration ⁽³⁾	—	4,469,069

⁽¹⁾Represents twelve months of base salary continuation payments.

⁽²⁾Represents twelve months of continued company-paid health coverage.

⁽³⁾The value of vesting acceleration is calculated assuming a price per share of \$13.00, which is the mid-point of the price range set forth on the cover page of this prospectus, with respect to unvested option shares subject to acceleration minus the exercise price of these unvested option shares.

James H. Welch

<u>Compensation and Benefits</u>	<u>Change in Control and Termination Without Cause or Eligible Voluntary Termination (\$)</u>
Base continuation ⁽¹⁾	145,000
Continued health coverage ⁽²⁾	11,197
Stock option vesting acceleration ⁽³⁾	960,000

⁽¹⁾Represents six months of base salary continuation payments.

⁽²⁾Represents six months of continued company-paid health coverage.

⁽³⁾The value of vesting acceleration is calculated assuming a price per share of \$13.00, which is the mid-point of the price range set forth on the cover page of this prospectus, with respect to unvested option shares subject to acceleration minus the exercise price of these unvested option shares.

Pamela P. Palmer, M.D., Ph.D.

<u>Compensation and Benefits</u>	<u>Upon Termination Prior to Employment Anniversary Not in Connection With a Change in Control (\$)⁽¹⁾</u>	<u>Change in Control and Termination Without Cause or Eligible Voluntary Termination (\$)</u>
Severance payment	140,625	—
Base continuation ⁽²⁾	—	187,500
Continued health coverage ⁽³⁾	—	5,742
Stock option vesting acceleration ⁽⁴⁾	—	1,529,625

⁽¹⁾Dr. Palmer is entitled to severance in the event her employment is terminated during the first two years of her employment, which commenced on July 1, 2009. The amount listed in this column represents a severance payment equal to four months of Dr. Palmer's base salary plus two weeks of salary for the full year of regular, full time employment Dr. Palmer had completed with us as of December 31, 2010.

⁽²⁾Represents six months of base salary continuation payments.

⁽³⁾Represents six months of continued company-paid health coverage.

⁽⁴⁾The value of stock option vesting acceleration is calculated assuming a price per share of \$13.00, which is the mid-point of the price range set forth on the cover page of this prospectus, with respect to unvested option shares subject to acceleration minus the exercise price of these unvested option shares.

Other Named Executive Officers

<u>Name</u>	<u>Change in Control and Termination Without Cause or Eligible Voluntary Termination Stock Option Vesting Acceleration (\$)⁽¹⁾</u>
Lawrence G. Hamel	386,238
Badri Dasu	458,694

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⁽¹⁾The value of vesting acceleration is calculated assuming a price per share of \$13.00, which is the mid-point of the price range set forth on the cover page of this prospectus, with respect to unvested option shares subject to acceleration minus the exercise price of these unvested option shares.

Non-Employee Director Compensation

Cash Compensation Arrangements

Other than respect to Mr. Rosen, our non-employee directors do not currently receive any cash compensation for their services as members of our board of directors or any committee of our board of directors. Mr. Rosen currently receives an annual retainer of \$30,000 per year. Our non-employee directors are reimbursed for travel, lodging and other reasonable expenses incurred in connection with their attendance at board of director or committee meetings.

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

- the board chair will receive an additional annual retainer of \$25,000;
- the audit committee chair will receive an additional annual retainer of \$10,000;
- the compensation committee chair will receive an additional annual retainer of \$5,000;
- the nominating and corporate governance committee chair will receive an additional annual retainer of \$5,000; and
- each committee member will receive \$1,000 as a meeting fee for each committee meeting attended by the non-employee director in person.

All board and committee retainers accrue and are payable on a quarterly basis at the end of each calendar quarter of service. After this offering, we will continue to reimburse our non-employee directors for their travel and other reasonable expenses incurred in attending board of director or committee meetings.

Equity Compensation Arrangements

Our non-employee directors are currently eligible to receive stock awards under our 2006 Stock Plan, as amended, or the 2006 Plan. To date, Mr. Rosen is our only non-employee director who has received any stock awards under the 2006 Plan while serving in such capacity. In August 2008, we granted a stock option to purchase 22,500 shares of common stock at an exercise price of \$4.00 per share to Mr. Rosen under the 2006 Plan. This option has a four year vesting schedule, with 1/4th of the shares vesting one day prior to the one year anniversary of the vesting commencement date and the remaining shares vesting on an equal monthly basis over the following 36 months. We also granted a stock option to Mr. Rosen to purchase 16,250 shares of common stock at an exercise price of \$1.20 per share under the 2006 Plan in June 2010. This option was subsequently amended in December 2010 to increase the exercise price to \$2.56 per share as described in more detail under “— Employment Agreements and Arrangements—Employee Benefit and Stock Plans—Option Exercise Price Increase.” This option has a three year vesting schedule, with 1/4th of the shares vested on the vesting commencement date and the remaining shares subject to the stock option vesting on an equal monthly basis over the following 36 months. In the event of a change in control transactions involving us, such as our liquidation or dissolution of or an event that results in a material change in the ownership of our company, the vesting of all shares subject to each option granted to Mr. Rosen will accelerate in full and be fully exercisable. Upon the execution and

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delivery of the underwriting agreement for this offering, no additional stock options or other stock awards will be granted under the 2006 Plan. For a description of the terms of the 2006 Plan, see “Executive Compensation—Employment Agreements and Arrangements—Employee Benefit and Stock Plans—2006 Stock Plan.”

Our non-employee director compensation policy, which will be effective for all of our non-employee directors effective upon the execution and delivery of the underwriting agreement for this offering, provides for automatic grants of stock options to our non-employee directors under our 2011 Incentive Plan following this offering. Upon election or appointment to our board, each non-employee director will receive an initial grant of a stock option to purchase 15,000 shares of our common stock, which will vest as to 1/36th of the shares subject to the option on an equal monthly basis over a three-year period. Additionally, on the date of each annual meeting of stockholders, each non-employee director who is then serving as a director or who is elected to the board on the date of such annual meeting will receive a grant of a stock option to purchase 12,500 shares of our common stock, which will vest as to 1/24th of the shares subject to the option on an equal monthly basis over a two-year period. All these options will be granted with an exercise price equal to the fair market value of our common stock on the date of the grant, and shall be entitled to full vesting acceleration as of immediately prior to the effective date of certain change in control transactions involving us, such as our liquidation or a dissolution of or an event that results in a material change in the ownership of our company. For a description of the terms of the 2011 Incentive Plan, see “Executive Compensation—Employment Agreements and Arrangements—Employee Benefit and Stock Plans—2011 Equity Incentive Plan.”

Director Compensation Table

The following table sets forth certain summary information for the year ended December 31, 2010 with respect to the compensation of our non-employee directors. Neither Mr. King (who has served as our President and Chief Executive Officer since May 1, 2010) nor Dr. Palmer, each of whom are executive officers, received or receives any additional compensation for serving on our board of directors or its committees. In addition, Mr. Schreck, who served as our President and Chief Executive Officer until April 30, 2010, did not receive any additional compensation for serving on our board of directors or its committees during the year ended December 31, 2010, and all of his compensation for 2010 is summarized under “— Summary Compensation Table” above.

2010 Director Compensation Table

<u>Name</u>	<u>Fees Earned or Paid in Cash (\$)</u>	<u>Option Awards (\$(1))</u>	<u>Total (\$)</u>
Howard B. Rosen	30,000	32,102	62,102
Stephen J. Hoffman Ph.D., M.D.	—	—	—
Guy P. Nohra	—	—	—
Mark Wan	—	—	—

⁽¹⁾The dollar amount in this column for Mr. Rosen represents the grant date fair value of the stock option award granted to Mr. Rosen on June 15, 2010. This amount has been calculated in accordance with ASC 718 using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 10 to our financial statements and the discussion under “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates—Stock-Based Compensation” included elsewhere in this prospectus. These amounts do not necessarily correspond to the actual value that may be recognized from the option award by Mr. Rosen. The modification of Mr. Rosen’s stock option award originally granted on June 15, 2010 as described under “— Employment Agreements and Arrangements—Employee Benefit and Stock Plans—Option Exercise Price Increase” did not result in an increase in the fair value of the stock option award under ASC 718. As of December 31, 2010, Mr. Rosen held stock options exercisable for 22,656 shares of our common stock. A description of the terms of these options can be found under the heading “Equity Compensation Arrangements” above. None of the other non-employee directors listed in the table above were granted any option awards during 2010 nor did they hold any outstanding stock options at December 31, 2010.

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Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation and amended and restated bylaws, each to be effective upon the completion of this offering, will provide that we will indemnify our directors and officers, and may indemnify our employees and other agents, to the fullest extent permitted by the Delaware General Corporation Law. However, Delaware law prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or to our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; and
- any transaction from which the director derived an improper personal benefit.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated certificate of incorporation does not eliminate a director's duty of care and, in appropriate circumstances, equitable remedies, such as injunctive or other forms of non-monetary relief, remain available under Delaware law. This provision also does not affect a director's responsibilities under any other laws, such as the federal securities laws or other state or federal laws. Under our amended and restated bylaws, we will also be empowered to enter into indemnification agreements with our directors, officers, employees and other agents and to purchase insurance on behalf of any person whom we are required or permitted to indemnify.

In addition to the indemnification required in our amended and restated certificate of incorporation and amended and restated bylaws, we have entered into indemnification agreements with each of our current directors, officers and some employees before the completion of this offering. These agreements provide for the indemnification of such persons for all reasonable expenses and liabilities incurred in connection with any action or proceeding brought against them by reason of the fact that they are or were serving in such capacity. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors, officers and employees. Furthermore, we have obtained director and officer liability insurance to cover liabilities our directors and officers may incur in connection with their services to us and expect to increase the level upon completion of this offering.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a summary of transactions since January 1, 2007 to which we have been a party in which the amount involved exceeded \$120,000 and in which any of our executive officers, directors or holders of more than 5% of our capital stock, or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than compensation arrangements which are described under the section of this prospectus entitled “Executive Compensation.”

Private Placement Financings

Preferred Stock Financings

The following table summarizes purchases of our Series B preferred stock and Series C preferred stock since January 1, 2007 by holders of more than 5% of our capital stock and their affiliated entities.

Name	Series B Preferred Stock	Aggregate Purchase Price of Series B Preferred Stock	Series C Preferred Stock	Aggregate Purchase Price of Series C Preferred Stock
Funds affiliated with Three Arch Partners ⁽¹⁾	656,249	\$ 10,500,000	1,752,337	\$ 6,909,117
Funds affiliated with Skyline Venture Partners ⁽²⁾	312,500	5,000,000	915,798	3,610,810
Funds affiliated with Alta Partners ⁽³⁾	218,750	3,500,000	810,129	3,194,178
Funds affiliated with Kaiser Foundation Hospitals ⁽⁴⁾	62,500	1,000,000	278,989	1,100,001
Approximate price per share	\$16.00		\$3.94	
Dates of purchase	2/4/08-2/15/08		11/23/09	

⁽¹⁾Includes 16,741 shares of Series B preferred stock held by Three Arch Associates III, L.P., 7,088 shares of Series B preferred stock held by Three Arch Associates IV, L.P., 311,384 shares of Series B preferred stock held by Three Arch Partners III, L.P. and 321,036 shares of Series B preferred stock held by Three Arch Partners IV, L.P. Includes 44,702 shares of Series C preferred stock held by Three Arch Associates III, L.P., 18,928 shares of Series C preferred stock held by Three Arch Associates IV, L.P., 831,466 shares of Series C preferred stock held by Three Arch Partners III, L.P. and 857,241 shares of Series C preferred stock held by Three Arch Partners IV, L.P. Mark Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares.

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

⁽³⁾These shares are held by ACP IV, L.P. Guy Nohra is one of our directors and is a director of ACMP IV, LLC, the general partner of ACP IV, L.P., and shares voting and investment power with respect to such shares. Mr. Nohra disclaims beneficial ownership of these shares.

⁽⁴⁾Includes 31,250 shares of Series B preferred stock held by Kaiser Foundation Hospitals and 31,250 shares of Series B preferred stock held by The Permanente Federation LLC – Series G. Includes 139,494 shares of Series C preferred stock held by Kaiser Foundation Hospitals and 139,495 shares of Series C preferred stock held by The Permanente Federation LLC – Series I.

2010 Bridge Loan Financing

On September 14, 2010, we sold convertible promissory notes, or the 2010 notes, and warrants, or the 2010 warrants, to purchase shares of our equity securities to certain of our existing investors for an aggregate purchase price of \$8.0 million. Upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 notes outstanding, we will sell an additional \$4.0 million of 2010 notes and corresponding 2010 warrants. However, this \$4.0 million call option will expire upon the closing of this offering.

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The 2010 notes accrue interest at a rate of 4.0% per annum. No payment of principal or interest has been paid on the 2010 notes since their issuance and the aggregate amount of principal outstanding is \$8.0 million as of September 30, 2010. In connection with this offering, the outstanding principal and interest of the 2010 notes will automatically convert into common stock at a conversion price equal to eighty percent of the initial public offering price.

The 2010 warrants are not currently exercisable but will become exercisable by their terms for an aggregate of 507,249 shares of Series C preferred stock at an exercise price of approximately \$3.94 immediately prior to this offering. The 2010 warrants terminate if they are not exercised prior to the closing of this offering. Each 2010 warrant contains a customary net issuance feature, which allows the warrant holder to pay the exercise price of the warrant by forfeiting a portion of the exercised warrant shares with a value equal to the aggregate exercise price. All of the holders of the 2010 warrants have elected to exercise the 2010 warrants on a net issuance basis contingent upon and effective immediately prior to the completion of this offering.

The following table summarizes the participation in the 2010 bridge financing by holders of more than 5% of our capital stock and their affiliated entities:

<u>Name</u>	<u>Aggregate Loan Amount</u>	<u>Aggregate Shares of Series C Preferred Stock Issuable Upon Exercise of 2010 Warrants Prior to this Offering⁽¹⁾</u>
Funds affiliated with Three Arch Partners ⁽²⁾	\$ 3,793,273	240,516
Funds affiliated with Skyline Venture Partners ⁽³⁾	1,977,503	125,386
Funds affiliated with Alta Partners ⁽⁴⁾	1,742,044	110,457
Funds affiliated with Kaiser Foundation Hospitals ⁽⁵⁾	487,180	30,890

⁽¹⁾The above table and footnotes do not give effect to the exercise, on a net issuance basis, of the 2010 warrants, which exercise is contingent upon and effective immediately prior to the completion of this offering.

⁽²⁾Includes a note held by Three Arch Associates III, L.P. with a principal amount of \$96,767, a note held by Three Arch Associates IV, L.P. with a principal amount of \$40,973, a note held by Three Arch Partners III, L.P. with a principal amount of \$1,799,869 and a note held by Three Arch Partners IV, L.P. with a principal amount of \$1,855,663. Includes a warrant held by Three Arch Associates III, L.P., exercisable into 6,135 shares of Series C preferred stock, a warrant held by Three Arch Associates IV, L.P., exercisable into 2,597 shares of Series C preferred stock, a warrant held by Three Arch Partners III, L.P., exercisable into 114,123 shares of Series C preferred stock and a warrant held by Three Arch Partners IV, L.P., exercisable into 117,661 shares of Series C preferred stock. Mark Wan, one of our directors, is managing partner of Three Arch Management II, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the securities owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these securities.

⁽³⁾This note and warrant are held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Stephen Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all securities held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of these securities.

⁽⁴⁾This note and warrant are held by ACP IV, L.P. Guy Nohra is one of our directors and is a director of ACMP IV, LLC, the general partner of ACP IV, L.P., and shares voting and investment power with respect to such securities. Mr. Nohra disclaims beneficial ownership of these securities.

⁽⁵⁾Includes a note held by Kaiser Foundation Hospitals with a principal amount of \$243,590 and a note held by The Permanente Federation LLC – Series I with a principal amount of \$243,590. Includes a warrant held by Kaiser Foundation Hospitals, exercisable into 15,445 shares of Series C preferred stock and a warrant held by The Permanente Federation LLC – Series I, exercisable into 15,445 shares of Series C preferred stock.

Investors' Rights Agreement

We entered into an investors' rights agreement with certain purchasers of our preferred stock and warrants to purchase our preferred stock, including our principal stockholders with which certain of our directors are affiliated. Pursuant to the investor's rights agreement, these holders are entitled to rights with respect to the registration of their shares under the Securities Act. For a description of these registration rights, please see the section entitled "Description of Capital Stock—Registration Rights."

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Voting Agreement

We are party to a voting agreement under which holders of our preferred stock, including our principal stockholders with which certain of our directors are affiliated, have agreed to vote in a certain way on certain matters, including with respect to the election of directors. Pursuant to the voting agreement, holders of our preferred stock have agreed to vote such that one director be a designee of Three Arch Partners IV, L.P. or its affiliates, who is currently Mark Wan; one director be a designee of ACP IV, L.P. or its affiliates, who is currently Guy Nohra; and one director be a designee of Skyline Venture Partners Qualified Purchaser Fund IV, L.P. or its affiliates, who is currently Stephen Hoffman. Upon the closing of this offering, the voting agreement will terminate in its entirety and none of our stockholders will have any special rights regarding the election or designation of members of our board of directors.

Other Transactions

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

We have entered into indemnification agreements with each of our current directors and officers. See “Executive Compensation—Limitation on Liability and Indemnification Matters.”

Policies and Procedures for Related Party Transactions

In January 2011, our board of directors adopted an audit committee charter that will be in effect prior to the closing of this offering that provides that the audit committee will review and approve all related party transactions. Accordingly, following this offering, all future related party transactions will be reviewed and approved by our audit committee. This review will cover any material transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, and a related party had or will have a direct or indirect material interest, including, purchases of goods or services by or from the related party or entities in which the related party has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related party. All of the transactions described above were entered into prior to the adoption of this audit committee charter and were approved by our board of directors.

PRINCIPAL STOCKHOLDERS

The following table sets forth information known to us about the beneficial ownership of our common stock at December 31, 2010, as adjusted to reflect the sale of the shares of common stock in this offering, by:

- each named executive officer;
- each of our directors;
- each person known to us to be the beneficial owner of more than 5% of our common stock; and
- all of our executive officers and directors as a group.

Unless otherwise noted below, the address of each beneficial owner listed on the table is c/o AcelRx Pharmaceuticals, Inc., 575 Chesapeake Drive, Redwood City, CA 94063. We have determined beneficial ownership in accordance with the rules of the SEC. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons and entities named in the tables below have sole voting and investment power with respect to all shares of common stock that they beneficially own, subject to applicable community property laws.

In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed outstanding shares of common stock subject to options held by that person that are currently exercisable or exercisable within 60 days of December 31, 2010. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person.

We have based our calculation of beneficial ownership prior to the offering on 9,230,066 shares of common stock outstanding on December 31, 2010, which assumes the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock. We have based our calculation of beneficial ownership after the offering on 16,134,660 shares of our common stock outstanding immediately after the completion of this offering, which gives effect to the issuance of 5,770,000 shares of common stock in this offering and the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock and assumes:

- the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010 that we issued in connection with a bridge loan financing in September 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus; and
- the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes, or the 2010 notes, into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011.

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The actual numbers of shares issued upon exercise of the 2010 warrants and conversion of the 2010 notes is based on the assumptions set forth above and will likely differ from the numbers appearing in this discussion and the following table and footnotes. See “Prospectus Summary—The Offering.” Ownership information assumes no exercise of the underwriters’ over-allotment option.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned		Percentage of Common Stock Beneficially Owned	
	Prior to Offering	After Offering	Prior to Offering	After Offering
Funds affiliated with Three Arch Entities ⁽¹⁾	3,965,752	4,503,730	42.97%	27.91%
Funds affiliated with Skyline Venture Partners ⁽²⁾	2,067,366	2,347,825	22.40%	14.55%
Funds affiliated with Alta Partners ⁽³⁾	1,821,097	2,068,162	19.73%	12.82%
Funds affiliated with Kaiser Foundation Hospitals ⁽⁴⁾	509,301	578,393	5.52%	3.58%
Named Executive Officers and Directors:				
Richard King ⁽⁵⁾	28,538	28,538	0.31%	0.18%
Jim Welch	—	—	—	—
Pamela Palmer ⁽⁶⁾	460,415	460,415	4.88%	2.82%
Anil Dasu ⁽⁷⁾	58,957	58,957	0.63%	0.36%
Thomas Schreck ⁽⁸⁾	509,941	509,941	5.41%	3.12%
Lawrence G. Hamel ⁽⁹⁾	92,967	92,967	1.00%	0.57%
Mark Wan ⁽¹⁰⁾	3,965,752	4,503,730	42.97%	27.91%
Stephen J. Hoffman ⁽¹¹⁾	2,067,366	2,347,825	22.40%	14.55%
Guy Nohra ⁽¹²⁾	1,821,097	2,068,162	19.73%	12.82%
Howard Rosen ⁽¹³⁾	24,270	24,270	0.26%	0.15%
All executive officers and directors as a group (10 persons) ⁽¹⁴⁾	9,029,303	10,094,805	97.58%	62.49%

⁽¹⁾ Includes 101,165 shares held by Three Arch Associates III, L.P., 42,835 shares held by Three Arch Associates IV, L.P., 1,881,711 shares held by Three Arch Partners III, L.P. and 1,940,041 shares held by Three Arch Partners IV, L.P. In addition, the number of shares beneficially owned after the offering includes (a) 9,449 shares of common stock issuable upon conversion of a 2010 note held by Three Arch Associates III, L.P., 4,001 shares of common stock issuable upon conversion of a 2010 note held by Three Arch Associates IV, L.P., 175,756 shares of common stock issuable upon conversion of a 2010 note held by Three Arch Partners III, L.P. and 181,204 shares of common stock issuable upon conversion of a 2010 note held by Three Arch Partners IV, L.P. and (b) 4,274 shares of common stock issuable upon the net exercise of a 2010 warrant held by Three Arch Associates III, L.P. and the concomitant conversion of the underlying Series C convertible preferred stock into common stock, 1,809 shares of common stock issuable upon the net exercise of a 2010 warrant held by Three Arch Associates IV, L.P. and the concomitant conversion of the underlying Series C convertible preferred stock into common stock, 79,510 shares of common stock issuable upon the net exercise of a 2010 warrant held by Three Arch Partners III, L.P. and the concomitant conversion of the underlying Series C convertible preferred stock into common stock, and 81,975 shares of common stock issuable upon the net exercise of a 2010 warrant held by Three Arch Partners IV, L.P. and the concomitant conversion of the underlying Series C convertible preferred stock into common stock. The voting and dispositive decisions with respect to the shares held by Three Arch Associates III, L.P. and Three Arch Partners III, L.P., are made by the following Managing Members of its general partner Three Arch Management III, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The voting and dispositive decisions with respect to the shares held by Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P. are made by the following Managing Members of its general partner, Three Arch Management IV, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The address for the funds affiliated with Three Arch Partners is 3200 Alpine Road, Portola Valley, CA 94028.

⁽²⁾ The 2,067,366 shares are held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. In addition, the number of shares beneficially owned after the offering includes (a) 193,102 shares of common stock issuable upon conversion of a 2010 note held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. and (b) 87,357 shares of common stock issuable upon the net exercise of a 2010 warrant held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. and the concomitant conversion of the underlying Series C convertible preferred stock into common stock. John G. Freund and Yasunori Kaneko are the Managing Members of Skyline Venture Management IV, LLC, which is the general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P., and as such Drs. Freund and Kaneko may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. In addition, Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Each of

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- Drs. Freund, Kaneko and Hoffman disclaims beneficial ownership of such shares. The address for Skyline Ventures is 525 University Avenue, Ste. 520, Palo Alto, CA 94301.
- (3) The 1,821,097 shares are beneficially owned by ACP IV, L.P., or ACPIV. In addition, the number of shares beneficially owned after the offering includes (a) 170,109 shares of common stock issuable upon conversion of a 2010 note held by ACPIV and (b) 76,956 shares of common stock issuable upon the net exercise of a 2010 warrant held by ACPIV and the concomitant conversion of the underlying Series C convertible preferred stock into common stock. ACMP IV, LLC, or ACMPIV, is the general partner of ACPIV. Jean Deleage, Dan Janney, David Mack, and Guy Nohra are directors of ACMPIV and they exercise shared voting and investment power with respect to the securities held by ACPIV. Mr. Deleage, Mr. Janney, Mr. Mack, and Mr. Nohra disclaim beneficial ownership of such securities. The address for ACPIV is One Embarcadero Center 37th Floor, San Francisco, CA 94111.
- (4) Includes 254,650 shares held by Kaiser Foundation Hospitals, or KFH, 115,156 shares held by The Permanente Federation LLC-Series G, or PFG, and 139,495 shares held by The Permanente Federation LLC-Series I, or PFI. In addition, the number of shares beneficially owned after the offering includes (a) 23,786 shares of common stock issuable upon conversion of a 2010 note held by KFH and 23,786 shares of common stock issuable upon conversion of a 2010 note held by PFI and (b) 10,760 shares of common stock issuable upon the net exercise of a 2010 warrant held by KFH and the concomitant conversion of the underlying Series C convertible preferred stock into common stock, and 10,760 shares of common stock issuable upon the net exercise of a 2010 warrant held by PFI and the concomitant conversion of the underlying Series C convertible preferred stock into common stock. The voting and dispositive decisions with respect to the shares held by KFH, PFI and PFG are made by Jordan M. Kramer, Robert Ward, Dave Schulte, Chris M. Grant and other employees of KFH, PFI and PFG, each of whom disclaims beneficial ownership of such shares. The address for the funds affiliated with Kaiser Foundation Hospitals is One Kaiser Plaza, 22nd Floor, Oakland, CA 94612.
- (5) Represents 28,538 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.
- (6) Includes 210,415 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.
- (7) Represents 58,957 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.
- (8) Includes 194,008 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010, and 16,482 shares held in trust for Mr. Schreck's children. Mr. Schreck disclaims beneficial ownership of the shares held in trust for Mr. Schreck's children.
- (9) Represents 92,967 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.
- (10) Mr. Wan is a managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares. The address of Mr. Wan is c/o Three Arch Partners, 3200 Alpine Road, Portola Valley, CA 94028.
- (11) Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of such shares. The address for Dr. Hoffman is c/o Skyline Ventures, 525 University Avenue, Suite 520, Palo Alto, CA 94301.
- (12) Mr. Nohra is a director of ACMPIV, and in such capacity he may be deemed to beneficially own the shares owned by ACPIV. Mr. Nohra disclaims beneficial ownership of these shares. The address for Mr. Nohra is c/o Alta Partners, One Embarcadero Center 37th Floor, San Francisco, CA 94111.
- (13) Represents 24,270 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.
- (14) Includes 609,155 shares issuable pursuant to stock options exercisable within 60 days of December 31, 2010.

DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering, our amended and restated certificate of incorporation will authorize us to issue up to 100,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share. As of September 30, 2010, after giving effect to the adjustments described below, there were outstanding:

- 10,364,660 shares of our common stock held by approximately 35 stockholders;
- 231,678 shares of common stock issuable upon the exercise of outstanding warrants that are expected to remain outstanding upon completion of this offering; and
- 1,892,860 shares of our common stock issuable upon exercise of outstanding stock options.

The number of shares of our common stock outstanding as of September 30, 2010 as shown above assumes:

- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
- the exercise, on a net issuance basis, of warrants outstanding as of September 30, 2010, or the 2010 warrants, which will be exercisable for shares of our Series C convertible preferred stock immediately prior to this offering, and the concomitant conversion of the shares of Series C convertible preferred stock into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus; and
- the automatic conversion of the principal and accrued interest outstanding under our \$8.0 million in aggregate principal amount of convertible promissory notes into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011.

The following description of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws that will be in effect upon completion of this offering. Copies of these documents will be filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur immediately upon completion of this offering.

Common Stock

Voting Rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all

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of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All of our outstanding shares of common stock are, and the shares of common stock to be issued pursuant to this offering will be, fully paid and nonassessable.

Preferred Stock

Upon the completion of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. Upon completion of this offering, no shares of preferred stock will be outstanding and we have no present plan to issue any shares of preferred stock.

2010 Notes

We issued convertible promissory notes in connection with our bridge loan financing in September 2010, or the 2010 notes. The 2010 notes accrue interest at a rate of 4.0% per annum. No payment of principal or interest has been paid on the 2010 notes since their issuance, and the aggregate amount of principal outstanding was \$8.0 million as of September 30, 2010. In connection with this offering, the outstanding principal and interest of 2010 notes will automatically convert into common stock at a conversion price equal to 80% of the initial public offering price.

Warrants

As of September 30, 2010, 2,500 shares of our Series A preferred stock were issuable upon exercise of an outstanding warrant to purchase Series A preferred stock with an exercise price of \$10.00 per share. This warrant was issued in connection with the execution of an equipment financing agreement we entered into with a lender. This warrant is immediately exercisable and will expire on March 15, 2017. This warrant has a net exercise provision under which the holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our common stock at the time of exercise of the warrant after deduction of the aggregate exercise price. The warrant contains provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of dilutive issuances affecting the Series A preferred stock and stock dividends, stock splits, reorganizations and reclassifications and consolidations.

As of September 30, 2010, 228,264 shares of our Series C preferred stock were issuable upon exercise of an outstanding warrant to purchase Series C preferred stock with an exercise price of approximately \$3.94 per share. This warrant was issued in connection with the execution of a loan and security agreement we entered into with a lender. This warrant is immediately exercisable and will expire on

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September 16, 2018. This warrant has a net exercise provision under which the holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our common stock at the time of exercise of the warrant after deduction of the aggregate exercise price. The warrant contains provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of diluting issuances affecting the Series C preferred stock and stock dividends, stock splits, reorganizations and reclassifications and consolidations.

In connection with the automatic conversion of all of our outstanding shares of preferred stock into common stock upon the closing of this offering:

- the warrant to purchase 2,500 shares of Series A preferred stock will automatically become exercisable for 3,414 shares of common stock; and
- the warrant to purchase 228,264 shares of Series C preferred stock will become exercisable for 228,264 shares of common stock.

We issued the 2010 warrants in connection with our bridge loan financing in September 2010. The 2010 warrants are not currently exercisable but will become exercisable by their terms for an aggregate of 507,249 shares of our Series C preferred stock at an exercise price of approximately \$3.94 per share immediately prior to the closing of this offering. The 2010 warrants terminate if they are not exercised prior to the closing of this offering. Each 2010 warrant contains a customary net issuance feature, which allows the warrant holder to pay the exercise price of the warrant by forfeiting a portion of the exercised warrant shares with a value equal to the aggregate exercise price. All of the holders of the 2010 warrants have elected to exercise the 2010 warrants on a net issuance basis contingent upon and effective immediately prior to the completion of this offering, which, if effected, would result in the issuance of 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus.

Registration Rights

Immediately following the closing of this offering, the holders of an aggregate of 9,140,792 shares of our common stock issued or issuable upon conversion of our preferred stock and the warrants described above (including 353,401 shares of our common stock issued upon the expected net exercise of the 2010 warrants and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise of the 2010 warrants into common stock upon completion of this offering, assuming an initial public price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus), which shares we refer to as registrable securities, will have the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing pursuant to an investors' rights agreement we entered into with certain of our stockholders. In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, these holders are entitled to notice of our registration and are entitled to certain piggyback registration rights allowing the holders to include their registrable securities in such registration, subject to certain marketing and other limitations. Pursuant to the investors' rights agreement, the holders of registrable securities have the right to require us to file a registration statement under the Securities Act in order to register the resale of their shares of registrable securities, provided that the registration meets certain thresholds. We may, in certain circumstances, defer such registrations. In an underwritten offering, the managing underwriter has the right, subject to specified conditions, to limit the number of registrable securities such holders may include. The holders of registrable securities have waived their rights to include any of their shares in this offering prior to the completion of this offering.

Anti-Takeover Provisions

Certificate of Incorporation and Bylaws to be in Effect Upon the Completion of this Offering

Our amended and restated certificate of incorporation and amended and restated bylaws, each to become effective immediately prior to the completion of this offering, will include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- *Issuance of undesignated preferred stock.* After the filing of our amended and restated certificate of incorporation, our board of directors will have the authority, without further action by the stockholders, to issue up to shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by the board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.
- *Classified board.* Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of the board.
- *Board of directors vacancies.* Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.
- *Stockholder action; special meetings of stockholders.* Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our amended and restated bylaws further provide that special meetings of our stockholders may be called only by a majority of our board of directors, the chairman of our board of directors, or our chief executive officer.
- *Advance notice requirements for stockholder proposals and director nominations.* Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at our annual meeting of stockholders.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage certain types of transactions that may involve an actual or threatened acquisition of us. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

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Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an “interested stockholder” as an entity or person who, together with the entity’s or person’s affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

The NASDAQ Global Market Listing

We have applied to have our common stock approved for listing on the NASDAQ Global Market under the symbol “ACRX.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent’s address is 250 Royall Street, Canton, Massachusetts 02021.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after these restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of September 30, 2010, upon the closing of this offering, 16,134,660 shares of common stock will be outstanding. The number of shares outstanding upon completion of this offering assumes:

- the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 8,555,713 shares of common stock upon completion of this offering;
- the exercise, on a net issuance basis, of the 2010 warrants and the concomitant conversion of the shares of Series C convertible preferred stock acquired upon exercise of the 2010 warrants into 353,401 shares of common stock upon completion of this offering, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus;
- the automatic conversion of the principal and accrued interest outstanding under the 2010 notes into 781,193 shares of common stock immediately prior to the closing of this offering at a conversion price equal to 80% of the initial public offering price, assuming an initial public offering price of \$13.00 per share, the mid-point of the price range set forth on the cover page of this prospectus, and assuming the conversion occurs on January 31, 2011;
- no exercise of the underwriters' over-allotment option; and
- no exercise of outstanding options or warrants, other than the 2010 warrants.

However, because the number of shares of common stock that will be issued upon exercise of the 2010 warrants and conversion of the 2010 notes depends upon the actual initial public offering price per share in this offering and, in the case of the 2010 notes, the closing date of this offering, the actual numbers of shares issuable upon such exercise and conversion will likely be different from the amounts we have assumed for purposes of this discussion. See "Prospectus Summary – The Offering."

All of the shares sold in this offering will be freely tradable unless purchased by our affiliates. The remaining 10,364,660 of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below or are otherwise subject to substantially similar lock-up agreements. Following the expiration of the lock-up period, all shares will be eligible for resale in compliance with Rule 144 or Rule 701.

Rule 144

In general, under Rule 144 under the Securities Act, once we have become subject to public company reporting requirements for at least 90 days, a person who is one of our affiliates and who has beneficially owned shares of our common stock for at least six months would be entitled to sell, within any three-month period, a number of shares that does not exceed the greater of:

- 1% of the number of shares of common stock then outstanding, which will equal approximately 161,346 shares immediately after the completion of this offering, based on shares of common stock outstanding on September 30, 2010 and the other assumptions set forth above; or

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- the average weekly trading volume of our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Sales under Rule 144 by affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

For a person who has not been our affiliate during the 90 days preceding a sale, sales of our securities held longer than six months, but less than one year, will be subject only to the current public information requirement.

A person who is not deemed to have been one of our affiliates at any time during the 90 days preceding a sale, and who has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than an affiliate, is entitled to sell the shares without complying with any of the requirements of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under “Underwriting” included elsewhere in this prospectus and will become eligible for sale only upon the expiration of the restrictions set forth in those agreements.

Lock-Up Agreements

We, along with our directors and executive officers and substantially all of our other security holders have agreed with the underwriters that, subject to certain exceptions, for a period of 180 days following the date of this prospectus, we or they will not offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, exercisable or exchangeable for or that represent the right to receive our common stock (including without limitation, common stock which may be deemed to be beneficially owned by such director, executive officer or security holder in accordance with rules and regulations of the SEC and securities that may be issued upon exercise of a stock option or warrant) whether owned or later acquired, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, or make any demand for, or exercise any right with respect to, the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, subject to specified exceptions, which exceptions include, in our case, our ability to issue up to 20% of our outstanding common stock to one or more counterparties in connection with certain strategic transactions, including partnering or collaboration arrangements, that we may enter into in the future. The underwriters may, in their sole discretion, at any time without prior notice, release all or any portion of the shares from the restrictions in any such agreement.

The 180-day lock-up period described in the preceding paragraph will be extended if:

- during the last 17 days of the 180-day lock-up period we issue an earnings release or material news or a material event relating to us occurs;
or
- prior to the expiration of the 180-day lock-up period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period,

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in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the release or the occurrence of the material news or material event, unless such extension is waived, in writing, by Piper Jaffray & Co. on behalf of the underwriters.

Registration Rights

We are party to an investors' rights agreement which provides that certain holders of our common stock have the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See "Description of Capital Stock—Registration Rights." Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon effectiveness of the registration statement, subject to the expiration of the lock-up period and to the extent these shares have been released from any repurchase option that we may hold.

Equity Compensation Plans

As soon as practicable after the completion of this offering, we intend to file a Form S-8 registration statement under the Securities Act to register shares of our common stock subject to options outstanding or reserved for issuance, as applicable, under our 2006 Plan, our 2011 Equity Incentive Plan and our 2011 Employee Stock Purchase Plan. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates and any lock-up agreements described above. For a more complete discussion of our equity compensation plans, see "Executive Compensation— Employment Agreements and Arrangements—Employee Benefit and Stock Plans."

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income and estate taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, “controlled foreign corporations,” “passive foreign investment companies,” corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment or other risk reduction strategy, partnerships and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a “capital asset” within the meaning of Section 1221 of the Code (generally, property held for investment).

The following discussion is for general information only and is not tax advice. Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a “Non-U.S. Holder” is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation), nor an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation). A “U.S. Holder” means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S.

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Holder generally will be required to provide us with a properly executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury Regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a non-taxable return of capital and will first reduce your adjusted basis in our common stock, but not below zero, and then will be treated as gain and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

A Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder's holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder's holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, unless a specific treaty

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exemption applies, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or otherwise establishes an exemption. The current backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. Rather, the amounts of tax withheld will be credits against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

Recently Enacted Legislation Affecting Taxation of Our Common Stock Held by or Through Foreign Entities

Recently enacted legislation generally will impose a U.S. federal withholding tax of 30% on dividends and the gross proceeds of a disposition of our common stock paid after December 31, 2012 to a foreign financial institution (as specifically defined for this purpose) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). The legislation also will generally impose a U.S. federal withholding tax of 30% on dividends and the gross proceeds of a disposition of our common stock paid after December 31, 2012 to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding direct and indirect U.S. owners of the entity. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. Holders are encouraged to consult with their own tax advisors regarding the possible implications of the legislation on their investment in our common stock.

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Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

UNDERWRITING

Piper Jaffray & Co. is acting as the book-running manager for this offering and as representative of the underwriters. We have entered into a firm commitment underwriting agreement with the representative. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has agreed to purchase, the number of shares listed next to its name in the following table:

<u>Underwriters</u>	<u>Number of Shares</u>
Piper Jaffray & Co.	
Canaccord Genuity Inc.	
Cowen and Company, LLC	
JMP Securities LLC	
Total	5,770,000

The underwriters have advised us that they propose to offer shares of our common stock to the public at \$ _____ per share. The underwriters propose to offer the common stock to certain dealers at the same price less a concession of not more than \$ _____ per share. The underwriters may allow, and the dealers may re-allow, a concession of not more than \$ _____ per share on sales to certain other brokers and dealers. After this offering, these figures may be changed by the underwriters.

We have granted to the underwriters an option to purchase up to an additional 865,500 shares of common stock from us at the same price to the public, and with the same underwriting discount, as set forth above. The underwriters may exercise this option any time during the 30-day period after the date of this prospectus, but only to cover over-allotments, if any. To the extent the underwriters exercise the option, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares as it was obligated to purchase under the purchase agreement.

We estimate that the total fees and expenses payable by us, excluding estimated underwriting discounts and commissions, will be approximately \$2,040,275. The estimated underwriting discounts and commissions are \$ _____ per share. The following table shows the underwriting fees to be paid to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the over-allotment option.

<u>Per Share</u>	<u>No Exercise</u>	<u>Full Exercise</u>
Total	\$ _____	\$ _____

We have agreed to indemnify the underwriters against certain liabilities, including civil liabilities under the Securities Act, or to contribute to payments that the underwriters may be required to make in respect of those liabilities.

Piper Jaffray has informed us that neither it, nor any other underwriter participating in the distribution of this offering, will make sales of the shares of common stock offered by this prospectus to accounts over which they exercise discretionary authority without the prior specific written approval of the customer.

We, along with our directors and executive officers and substantially all of our other security holders have agreed with the underwriters that, subject to certain exceptions, for a period of 180 days following the date of this prospectus, we or they will not offer, pledge, announce the intention to sell, sell, contract

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to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, make any short sale or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into, exercisable or exchangeable for or that represent the right to receive our common stock (including without limitation, common stock which may be deemed to be beneficially owned by such director, executive officer or security holder in accordance with rules and regulations of the SEC and securities that may be issued upon exercise of a stock option or warrant) whether owned or later acquired, or enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, or make any demand for, or exercise any right with respect to, the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, subject to specified exceptions, which exceptions include, in our case, our ability to issue up to 20% of our outstanding common stock to one or more counterparties in connection with certain strategic transactions, including partnering or collaboration arrangements, that we may enter into in the future. The underwriters may, in their sole discretion, at any time without prior notice, release all or any portion of the shares from the restrictions in any such agreement.

The 180-day lock-up period described in the preceding paragraph will be extended if:

- during the last 17 days of the 180-day lock-up period we issue an earnings release or material news or a material event relating to us occurs; or
- prior to the expiration of the 180-day lock-up period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period,

in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the release or the occurrence of the material news or material event, unless such extension is waived, in writing, by Piper Jaffray on behalf of the underwriters.

Prior to this offering, there has been no established trading market for the shares. The NASDAQ Global Market has approved the listing of shares of our common stock under the symbol "ACRX."

The initial public offering price for the common stock offered by this prospectus was negotiated by us and the underwriters. The factors considered in determining the initial public offering price include:

- the history of and the prospects for the industry in which we compete;
- our past and present operations;
- our historical results of operations;
- our prospects for future earnings;
- the recent market prices of securities of generally comparable companies; and
- the general condition of the securities markets at the time of this offering and other relevant factors.

There can be no assurance that the initial public offering price of the common stock will correspond to the price at which our common stock will trade in the public market subsequent to this offering or that an active public market for the common stock will develop and continue after this offering.

To facilitate this offering, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock during and after this offering. Specifically, the underwriters may over-allot or otherwise create a short position in the common stock for their own account by selling more common stock than we have sold to them. Short sales involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this

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offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of common stock or purchasing shares of common stock in the open market. In determining the source of common stock to close out the covered short position, the underwriters will consider, among other things, the price of common stock available for purchase in the open market as compared to the price at which they may purchase common stock through the over-allotment option. “Naked” short sales are sales in excess of this option. The underwriters must close out any naked short position by purchasing common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

In addition, the underwriters may stabilize or maintain the price of the common stock by bidding for or purchasing shares of common stock in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in this offering will be reclaimed if common stock previously distributed in this offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the common stock at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also affect the price of the common stock to the extent that it discourages resales of the common stock. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on the NASDAQ Global Market or otherwise and, if commenced, may be discontinued at any time. Some underwriters may also engage in passive market making transactions in our common stock. Passive market making consists of displaying bids on the NASDAQ Global Market limited by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the Securities and Exchange Commission limits the amount of net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of the common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

This prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses and prospectus supplements electronically.

From time to time in the ordinary course of their respective businesses, certain of the underwriters and their affiliates may in the future engage in commercial banking or investment banking transactions with us and our affiliates.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a “Relevant Member State”), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares of our common stock has been made or will be made to the public in that Member State, except that, with effect from and including such date, an offer of shares of our common stock may be made to the public in the Relevant Member State at any time:

- (a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and

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- (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or
- (d) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer of shares of our common stock to the public” in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression “Prospectus Directive” means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

United Kingdom

In the United Kingdom this document is being distributed only to, and is directed only at Qualified Investors who are permitted to carry on regulated activity in the United Kingdom by the UK Financial Services Authority under the Financial Services and Markets Act 2000, as amended, persons whose ordinary activities for the purpose of their businesses involve them in buying, selling, subscribing for or underwriting such securities or making arrangements for another person to do so (whether as principal or agent) or advising on investments or other persons who are Investment Professionals within the meaning given in paragraph 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005. Persons who are not permitted to carry on such regulated activity may not rely on this document.

Hong Kong

Our common stock may not be offered or sold by means of any document other than: (1) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (2) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules thereunder, or (3) in other circumstances which do not result in the document being a “prospectus” within the meaning of the Companies Ordinance. No advertisement, invitation or other document relating our common stock may be issued, whether in Hong Kong or elsewhere, where such document is directed at, or the contents are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the laws of Hong Kong), other than with respect to such common stock that is intended to be disposed of only to persons outside of Hong Kong or only to “professional investors” as defined in the Securities and Futures Ordinance and any rules thereunder.

LEGAL MATTERS

The validity of our common stock offered by this prospectus will be passed upon for us by Cooley LLP, Palo Alto, California. Cooley LLP and certain attorneys and investment funds affiliated with the firm collectively own an aggregate of 19,022 shares of our common stock. Certain legal matters in connection with this offering will be passed upon for the underwriters by Morgan, Lewis & Bockius LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2008 and 2009, and for each of the three years in the period ended December 31, 2009, and for the period from July 13, 2005 (inception) through December 31, 2009, as set forth in their report (which contains an explanatory paragraph describing conditions that raise substantial doubt about our ability to continue as a going concern as described in Note 1 to the financial statements). We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered in this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the accompanying exhibits and schedules. Some items included in the registration statement are omitted from this prospectus in accordance with the rules and regulations of the SEC. For further information with respect to us and the common stock offered in this prospectus, we refer you to the registration statement and the accompanying exhibits and schedules. Statements contained in this prospectus as to the contents of any contract, agreement or any other document are summaries of the material terms of these contract, agreement or other document. With respect to each of these contracts, agreements or other documents filed as an exhibit to the registration statement, reference is made to such exhibit for a more complete description of the matter involved. A copy of the registration statement, and the accompanying exhibits and schedules, may be inspected without charge and copied at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC's website is <http://www.sec.gov>.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and we will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at <http://www.acerx.com>. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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INDEX TO FINANCIAL STATEMENTS

**AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)**

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
AcelRx Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of AcelRx Pharmaceuticals, Inc. (a development stage company) (the Company) as of December 31, 2008 and 2009, and the related statements of operations, convertible preferred stock and of stockholders' equity (deficit), and cash flows for the years ended December 31, 2007, 2008 and 2009, and for the period from July 13, 2005 (inception) through December 31, 2009. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of AcelRx Pharmaceuticals, Inc. (a development stage company) at December 31, 2008 and 2009, and the results of its operations and its cash flows for the years ended December 31, 2007, 2008 and 2009, and for the period from July 13, 2005 (inception) through December 31, 2009, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 1 to the financial statements, the Company's recurring losses from operations raise substantial doubt about its ability to continue as a going concern. Management's plans as to these matters also are described in Note 1. The December 31, 2009, financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

San Francisco, California

June 30, 2010, except for the last paragraph of Note 1, as to which the date is January 28, 2011

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AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)
Balance Sheets
(in thousands, except share and per share data)

	<u>December 31,</u> <u>2008</u>	<u>December 31,</u> <u>2009</u>	<u>September 30,</u> <u>2010</u> <u>(Unaudited)</u>	<u>Pro Forma</u> <u>Stockholders'</u> <u>Equity as of</u> <u>September 30,</u> <u>2010</u> <u>(Unaudited)</u> <u>(Note 1)</u>
ASSETS				
CURRENT ASSETS:				
Cash and cash equivalents	\$ 6,072	\$ 7,150	\$ 7,558	
Short-term investments	14,135	5,396	524	
Prepaid expenses and other current assets	773	397	523	
Total current assets	20,980	12,943	8,605	
Property and equipment, net	1,412	1,280	926	
Restricted cash	205	205	205	
Other assets	82	63	50	
TOTAL ASSETS	\$ 22,679	\$ 14,491	\$ 9,786	
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)				
CURRENT LIABILITIES:				
Accounts payable	\$ 1,188	\$ 917	\$ 602	
Accrued liabilities	500	369	259	
Convertible notes	—	—	4,603	—
Long-term debt, current portion	2,842	4,726	5,035	
Total current liabilities	4,530	6,012	10,499	
Deferred rent	596	425	290	
Long-term debt, net of current portion	9,492	5,008	1,347	
Call option liability	—	—	476	—
Convertible preferred stock warrant liability	240	169	2,219	—
Total liabilities	14,858	11,614	14,831	
Commitments and Contingencies (Note 8)				
Convertible preferred stock, \$0.001 par value—13,736,125, 46,736,125 and 46,736,125 shares authorized as of December 31, 2008, 2009 and September 30, 2010 (unaudited); 3,375,274, 7,132,527 and 7,151,802 shares issued and outstanding as of December 31, 2008, 2009 and September 30, 2010 (unaudited); liquidation preference of \$56,148 and \$56,224 as of December 31, 2009 and September 30, 2010 (unaudited), actual; no shares issued and outstanding, pro forma (unaudited)				
	41,156	55,871	55,941	—
STOCKHOLDERS' EQUITY (DEFICIT):				
Preferred stock, \$0.001 par value—no shares authorized, issued and outstanding as of December 31, 2008, 2009 and September 30, 2010 (unaudited), no shares authorized, issued and outstanding, pro forma (unaudited)				
	—	—	—	—
Common stock, \$0.001 par value—25,000,000, 71,000,000 and 71,000,000 shares authorized as of December 31, 2008, 2009 and September 30, 2010 (unaudited); 524,127, 620,116 and 674,353 shares issued and outstanding as of December 31, 2008, 2009 and September 30, 2010 (unaudited), actual; 9,230,066 shares issued and outstanding, pro forma (unaudited)				
	1	1	1	9
Additional paid-in capital	725	1,226	4,053	67,284
Accumulated other comprehensive income (loss)	39	(2)	—	—
Deficit accumulated during the development stage	(34,100)	(54,219)	(65,040)	(65,040)
Total stockholders' equity (deficit)	(33,335)	(52,994)	(60,986)	\$ 2,253
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)	\$ 22,679	\$ 14,491	\$ 9,786	

See notes to financial statements.

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AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)
Statements of Operations
(in thousands, except share and per share data)

	<u>Year Ended December 31,</u>			<u>Period from</u> <u>July 13, 2005</u> <u>(Inception)</u> <u>Through</u> <u>December 31,</u> <u>2009</u>	<u>Nine Months Ended</u> <u>September 30,</u>		<u>Period from</u> <u>July 13, 2005</u> <u>(Inception)</u> <u>Through</u> <u>September 30,</u> <u>2010</u>
	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>2009</u>	<u>2009</u>	<u>2010</u>	<u>2010</u>
					(Unaudited)		(Unaudited)
Operating Expenses:							
Research and development	\$ 8,209	\$ 18,325	\$ 15,502	\$ 45,604	\$ 13,180	\$ 6,309	\$ 51,913
General and administrative	2,082	2,365	3,529	8,501	2,510	3,033	11,534
Total operating expenses	10,291	20,690	19,031	54,105	15,690	9,342	63,447
Loss from operations	(10,291)	(20,690)	(19,031)	(54,105)	(15,690)	(9,342)	(63,447)
Interest income	687	484	33	1,551	37	2	1,553
Interest expense	(25)	(404)	(1,242)	(1,733)	(965)	(656)	(2,389)
Other income (expense), net	(1)	(52)	121	68	196	(825)	(757)
Loss before provision for income taxes	(9,630)	(20,662)	(20,119)	(54,219)	(16,422)	(10,821)	(65,040)
Provision for income taxes	—	—	—	—	—	—	—
Net loss	\$ (9,630)	\$ (20,662)	\$ (20,119)	\$ (54,219)	\$ (16,422)	\$ (10,821)	\$ (65,040)
Net loss per share of common stock, basic and diluted	\$ (26.45)	\$ (43.69)	\$ (34.93)	\$ (29.09)	\$ (16.63)	\$ (16.63)	\$ (16.63)
Shares used in computing net loss per share of common stock, basic and diluted	364,039	472,914	576,021	564,571	650,774	650,774	650,774
Pro forma net loss per share of common stock, basic and diluted (unaudited) (Note 11)			\$ (3.51)			\$ (1.09)	
Shares used in computing pro forma net loss per share of common stock, basic and diluted (unaudited) (Note 11)			5,746,372			9,204,999	

See notes to financial statements.

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

	Convertible Preferred Stock		Common Stock			Deficit Accumulated During the Development Stage	Other Comprehensive Income (loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Additional Paid-in Capital			
Balance as of July 13, 2005 (Inception)	—	\$ —	—	\$ —	\$ —	\$ —	\$ —	\$ —
Net and comprehensive loss	—	—	—	—	—	(40)	—	(40)
Balance as of December 31, 2005	—	—	—	—	—	(40)	—	(40)
Issuance of restricted common stock to founders	—	—	250,000	1	—	—	—	1
Issuance of Series A convertible preferred stock (net of issuance costs of \$100)	2,111,639	21,016	—	—	—	—	—	—
Issuance of common stock upon the exercise of common stock warrants	—	—	25,534	1	50	—	—	51
Stock-based compensation related to restricted stock	—	—	20,833	—	42	—	—	42
Comprehensive loss:								
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	(1)	(1)
Net loss	—	—	—	—	—	(3,768)	—	(3,768)
Total comprehensive loss	—	—	—	—	—	(3,768)	—	(3,769)
Balance as of December 31, 2006	2,111,639	21,016	296,367	2	92	(3,808)	(1)	(3,715)
Stock-based compensation related to restricted stock	—	—	127,448	1	116	—	—	117
Stock-based compensation related to stock options	—	—	—	—	33	—	—	33
Comprehensive loss:								
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	6	6
Net loss	—	—	—	—	—	(9,630)	—	(9,630)
Total comprehensive loss	—	—	—	—	—	(9,630)	—	(9,624)
Balance as of December 31, 2007	2,111,639	21,016	423,815	3	241	(13,438)	5	(13,189)
Issuance of Series B convertible preferred stock (net of issuance costs of \$78)	1,263,635	20,140	—	—	—	—	—	—
Stock-based compensation related to restricted stock	—	—	97,812	—	271	—	—	271
Stock-based compensation related to stock options	—	—	—	—	197	—	—	197
Contribution of common stock to a charitable organization	—	—	2,500	—	14	—	—	14
Comprehensive loss:								
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	34	34
Net loss	—	—	—	—	—	(20,662)	—	(20,662)
Total comprehensive loss	—	—	—	—	—	(20,662)	—	(20,628)
Balance as of December 31, 2008	3,375,274	\$ 41,156	524,127	\$ 3	\$ 723	\$ (34,100)	\$ 39	\$ (33,335)

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

	<u>Convertible Preferred Stock</u>		<u>Common Stock</u>			<u>Deficit Accumulated During the Development Stage</u>	<u>Other Comprehensive Income (loss)</u>	<u>Total Stockholders' Equity (Deficit)</u>
	<u>Shares</u>	<u>Amount</u>	<u>Shares</u>	<u>Amount</u>	<u>Additional Paid-in Capital</u>			
Balance as of December 31, 2008	3,375,274	\$ 41,156	524,127	\$ 3	\$ 723	\$ (34,100)	\$ 39	\$ (33,335)
Issuance of Series C convertible preferred stock (net of issuance costs of \$99)	3,757,253	14,715	—	—	—	—	—	—
Stock-based compensation related to restricted stock	—	—	74,375	—	163	—	—	163
Stock-based compensation related to stock options	—	—	—	—	312	—	—	312
Issuance of common stock upon exercise of stock options	—	—	21,614	—	26	—	—	26
Comprehensive loss:								
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	(41)	(41)
Net loss	—	—	—	—	—	(20,119)	—	(20,119)
Total comprehensive loss								(20,160)
Balance as of December 31, 2009	7,132,527	55,871	620,116	3	1,224	(54,219)	(2)	(52,994)
Issuance of Series C convertible preferred stock (net of issuance costs of \$6) (unaudited)	19,275	70	—	—	—	—	—	—
Stock-based compensation related to restricted stock (unaudited)	—	—	43,282	—	93	—	—	93
Stock-based compensation related to stock options (unaudited)	—	—	—	—	1,014	—	—	1,014
Issuance of common stock upon exercise of stock options (unaudited)	—	—	10,955	—	21	—	—	21
Beneficial conversion feature related to convertible notes (unaudited)	—	—	—	—	1,699	—	—	1,699
Comprehensive loss:								
Change in unrealized gains and losses on investments, net of taxes (unaudited)	—	—	—	—	—	—	2	2
Net loss (unaudited)	—	—	—	—	—	(10,821)	—	(10,821)
Total comprehensive loss (unaudited)								(10,819)
Balance as of September 30, 2010 (unaudited)	7,151,802	\$55,941	674,353	\$ 3	\$ 4,051	\$ (65,040)	\$ —	\$ (60,986)

See notes to financial statements.

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

	Year Ended December 31,			Period from July 13, 2005 (Inception) Through December 31, 2009	Nine Months Ended September 30, (Unaudited)		Period from July 13, 2005 (Inception) Through September 30, 2010 (Unaudited)
	2007	2008	2009	2009	2009	2010	2010
CASH FLOWS FROM OPERATING ACTIVITIES:							
Net loss	\$ (9,630)	\$ (20,662)	\$ (20,119)	\$ (54,219)	\$ (16,422)	\$ (10,821)	\$ (65,040)
Adjustments to reconcile net loss to net cash used in operating activities:							
Depreciation and amortization	216	383	481	1,086	363	359	1,445
Interest expense related to debt financings	—	161	280	491	215	168	659
Stock-based compensation	128	456	463	1,089	317	1,107	2,196
Contribution of shares to charitable organizations	—	14	—	14	—	—	14
Revaluation of convertible preferred stock warrant liability	—	77	(71)	170	(168)	827	997
Realized gain on sale of investments	—	—	(29)	(29)	(32)	—	(29)
Changes in operating assets and liabilities:							
Prepays and other assets	(364)	109	138	(429)	28	(126)	(555)
Restricted cash	(28)	(27)	—	(205)	—	—	(205)
Accounts payable	422	319	(271)	917	745	(315)	602
Accrued liabilities	(251)	317	(119)	179	(159)	(106)	73
Deferred rent	646	(50)	(171)	425	(128)	(135)	290
Net cash used in operating activities	<u>(8,861)</u>	<u>(18,903)</u>	<u>(19,418)</u>	<u>(50,511)</u>	<u>(15,241)</u>	<u>(9,042)</u>	<u>(59,553)</u>
CASH FLOWS FROM INVESTING ACTIVITIES:							
Purchase of property and equipment	(1,558)	(547)	(111)	(2,365)	(110)	(4)	(2,369)
Purchase of investments	(8,109)	(14,088)	(13,906)	(40,378)	(8,537)	(4,823)	(45,201)
Proceeds from sale of investments	7,450	4,700	22,633	35,033	21,171	9,692	44,725
Net cash provided by (used in) investing activities	<u>(2,217)</u>	<u>(9,935)</u>	<u>8,616</u>	<u>(7,710)</u>	<u>12,524</u>	<u>4,865</u>	<u>(2,845)</u>
CASH FLOWS FROM FINANCING ACTIVITIES:							
Proceeds from the issuance long-term debt	621	12,000	—	12,621	—	—	12,621
Payment of long-term debt	(96)	(241)	(2,861)	(3,198)	(1,653)	(3,506)	(6,704)
Proceeds from issuance of convertible notes	—	—	—	1,000	—	8,000	9,000
Proceeds from issuance of common stock	—	—	26	77	26	21	98
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	20,140	14,715	54,871	—	70	54,941
Net cash provided by (used in) financing activities	<u>525</u>	<u>31,899</u>	<u>11,880</u>	<u>65,371</u>	<u>(1,627)</u>	<u>4,585</u>	<u>69,956</u>
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	(10,553)	3,061	1,078	7,150	(4,344)	408	7,558
CASH AND CASH EQUIVALENTS—Beginning of period	<u>13,564</u>	<u>3,011</u>	<u>6,072</u>	<u>—</u>	<u>6,072</u>	<u>7,150</u>	<u>—</u>
CASH AND CASH EQUIVALENTS—End of period	<u>\$ 3,011</u>	<u>\$ 6,072</u>	<u>\$ 7,150</u>	<u>\$ 7,150</u>	<u>\$ 1,728</u>	<u>\$ 7,558</u>	<u>\$ 7,558</u>
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:							
Cash paid for interest	<u>\$ 21</u>	<u>\$ 204</u>	<u>\$ 979</u>	<u>\$ 1,204</u>	<u>\$ 762</u>	<u>\$ 521</u>	<u>\$ 1,725</u>
NONCASH INVESTING AND FINANCING ACTIVITIES:							
Issuance of convertible preferred stock warrants	<u>\$ 1</u>	<u>\$ 162</u>	<u>\$ —</u>	<u>\$ 163</u>	<u>\$ —</u>	<u>\$ 1,223</u>	<u>\$ 1,386</u>
Beneficial conversion features related to convertible notes	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,699</u>	<u>\$ 1,699</u>
Issuance of call option related to convertible notes	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 476</u>	<u>\$ 476</u>

See notes to financial statements.

**AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)**

Notes to Financial Statements

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

1. Organization and Summary of Significant Accounting Policies

The Company

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

The Company is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. Since incorporation, primary activities have consisted of establishing facilities, recruiting personnel, conducting research and development of its products, developing intellectual property, and raising capital. To date, the Company has not yet commenced primary operations or generated any revenues and, accordingly, the Company is considered to be in the development stage.

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

The accompanying financial statements have been prepared assuming the Company will continue as a going concern. The Company has incurred recurring operating losses and negative cash flows from operating activities since inception through September 30, 2010. In addition, the Company had an accumulated deficit of \$54.2 million and \$65.0 million as of December 31, 2009 and September 30, 2010. Through September 30, 2010, the Company has relied primarily on the proceeds from equity offerings and loan proceeds to finance its operations. Management believes that currently available cash, cash equivalents and investments will provide sufficient funds to enable the Company to meet its obligations through at least March 2011. Management plans to continue to finance the Company's operations with a combination of equity issuances, debt arrangements and, in the longer term, revenues from collaborations with pharmaceutical companies, technology licenses and, ultimately, product sales and royalties. However, there is no assurance that additional funding will be available to the Company on acceptable terms on a timely basis, if at all, or that the Company will achieve profitable operations. If the Company is unable to raise additional capital to fund its operations, it will need to curtail planned activities to reduce costs. Doing so may affect the Company's ability to operate effectively. The accompanying financial statements do not include any adjustments that might result from the outcome of these uncertainties.

Subsequent Events

The Company applies Accounting Standards Codification, or ASC, Topic No. 855 for the accounting for and disclosure of events that occur after the balance sheet date but before financial statements are issued. For the financial statements as of December 31, 2008 and 2009, and the related statements of operations, convertible preferred stock and of stockholders' equity (deficit), and cash flows for the years ended December 31, 2007, 2008 and 2009, and for the period from July 13, 2005 (inception) through December 31, 2009, the Company has evaluated subsequent events through June 30, 2010, the date these financial statements were issued.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in

AcelRx Pharmaceuticals, Inc.
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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

the financial statements and accompanying notes. Such management estimates include the fair value of common stock, stock-based compensation expense, valuation of deferred tax assets and the fair value of the convertible preferred stock warrants. The Company bases its estimates on historical experience and also on assumptions that it believes are reasonable, however, actual results could differ from those estimates.

Unaudited Interim Financial Information

The accompanying interim balance sheet as of September 30, 2010, the interim statements of operations and cash flows for the nine months ended September 30, 2009 and 2010 and the period from July 13, 2005 (Inception) through September 30, 2010 and the interim statement of convertible preferred stock and of stockholders' equity (deficit) for the nine months ended September 30, 2010 are unaudited. The unaudited interim financial statements have been prepared on a basis consistent with the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company's financial position as of September 30, 2010 and its results of operations and cash flows for the nine months ended September 30, 2009 and 2010 and the period from July 13, 2005 (inception) through September 30, 2010. The financial data and the other financial information disclosed in these notes to the financial statements related to the nine month periods are also unaudited. The results of operations for the nine months ended September 30, 2010 are not necessarily indicative of the results to be expected for the year ending December 31, 2010 or for any other future annual or interim period.

Unaudited Pro Forma Stockholders' Equity

The unaudited pro forma stockholders' equity as of September 30, 2010 has been prepared assuming that immediately prior to the consummation of an initial public offering: (1) the automatic conversion of all outstanding shares of the Company's convertible preferred stock into shares of common stock; (2) the automatic conversion of the convertible notes into shares of common stock and the related reclassification of the convertible note liability to common stock and additional paid-in capital; and (3) the reclassification of the convertible preferred stock warrant liability to additional paid-in capital. The pro forma shares of common stock outstanding as of September 30, 2010 reflect the conversion of 7,151,802 shares of convertible preferred stock into 8,555,713 shares of common stock but does not reflect the shares of common stock that will be issued as a result of the assumed conversion of the convertible notes or any warrant exercises.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, short-term investments and restricted cash. Cash, cash equivalents, short-term investments and restricted cash are invested with banks and other financial institutions in the United States and are only invested in high-credit quality instruments. Such deposits may be in excess of insured limits provided on such deposits.

Cash and Cash Equivalents

Cash and cash equivalents are stated at cost, which approximates fair value. The Company considers highly liquid investments with original maturities from the date of purchase of 90 days or less to be cash equivalents. Cash and cash equivalents consist primarily of demand deposits and money market mutual funds and are held primarily by two domestic financial institutions with high credit standings.

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

Short-Term Investments

The Company's investments are all short-term and consist of high-credit quality U.S. government agency obligations that have maturities greater than 90 days, but less than 365 days from the date of purchase. Short-term investments are classified as available-for-sale and are, therefore, recorded at fair value, and unrealized gains and losses, net of any related tax effects, are not reflected in the statement of operations but are reported in the statement of stockholders' equity as a separate component of other comprehensive income (loss) until realized. The Company uses the specific-identification method to compute gains and losses on the investments. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in interest income or expense. Realized gains and losses and declines in fair value that are deemed to be other-than-temporary are reported in the statement of operations.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally three years for computer equipment and software, five years for research equipment, and seven years for furniture and fixtures. Leasehold improvements are amortized over the shorter of the estimated useful life of the improvements, generally five years, or the remaining lease term. Maintenance and repairs that do not extend the life or improve an asset are expensed in the period incurred.

Impairment of Long-Lived Assets

The Company periodically assesses the impairment of long-lived assets and, if indicators of asset impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through an analysis of the undiscounted future expected operating cash flows. If impairment is indicated, the Company records the amount of such impairment for the excess of the carrying value of the asset over its estimated fair value. As of September 30, 2010, the Company has not written down any of its long-lived assets as a result of impairment.

Restricted Cash

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

Research and Development Expenses

Research and development costs are charged to expense when incurred. Research and development expenses include salaries, employee benefits, laboratory supplies, costs associated with clinical trials and manufacturing, other professional services and facility costs. Expenses related to clinical trials generally are accrued based on the level of patient enrollment and activity according to the protocol. The Company monitors patient enrollment levels and related activity to the extent possible and adjusts accrual estimates accordingly.

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Notes to Financial Statements—(Continued)

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Comprehensive Loss

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

Fair Value of Financial Instruments

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

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

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

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

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

The Company's financial instruments consist of Level I and Level II assets and Level III liabilities. Level I securities include highly liquid money market funds. If quoted market prices are not available for the specific security, then the Company estimates fair value by using benchmark yields, reported trades, broker dealer quotes and issuer spreads. Such Level II instruments include U.S. government agency and corporate obligations. Level III liabilities that are measured at fair value on a recurring basis consist of convertible preferred stock warrant liabilities. The fair values of the outstanding convertible preferred stock warrants are measured using the Black-Scholes option-pricing model. Inputs used to determine estimated fair market value include the estimated fair value of the underlying stock at the valuation measurement date, the remaining contractual term of the warrants, risk-free interest rates, expected dividends and the expected volatility of the underlying stock.

Income Taxes

The Company estimates actual current tax exposure together with assessing temporary differences resulting from differences in accounting for reporting purposes and tax purposes for certain items, such as accruals and allowances not currently deductible for tax purposes. These temporary differences result in deferred tax assets and liabilities, which are included in the Company's balance sheets. In general, deferred tax assets represent future tax benefits to be received when certain expenses previously

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

recognized in the Company's statements of operations become deductible expenses under applicable income tax laws or when net operating loss or credit carryforwards are utilized. Accordingly, realization of the Company's deferred tax assets is dependent on future taxable income against which these deductions, losses and credits can be utilized.

The Company must assess the likelihood that the Company's deferred tax assets will be recovered from future taxable income, and to the extent the Company believes that recovery is not likely, the Company establishes a valuation allowance. The Company recorded a full valuation allowance as of December 31, 2008, 2009 and September 30, 2010. Based on the available evidence, the Company believed it was more likely than not that it would not be able to utilize its deferred tax assets in the future. The Company intends to maintain valuation allowance until sufficient evidence exists to support its reversal.

The Company regularly reviews its tax positions and for benefits to be realized, a tax position must be more likely than not to be sustained upon examination. The amount recognized is measured as the largest amount of benefit that is more likely than not to be realized upon settlement. The Company's policy is to recognize interest and penalties related to income tax matters as an income tax expense. Through September 30, 2010, the Company did not have any interest or penalties associated with unrecognized tax benefits.

Liability Associated with Warrants to Purchase Convertible Preferred Stock

The Company accounts for freestanding warrants to purchase shares of convertible preferred stock that are contingently redeemable as liabilities on the balance sheet at their estimated fair value because these warrants may obligate the Company to redeem these warrants at some point in the future. At the end of each reporting period, changes in the estimated fair value of the warrants to purchase shares of the convertible preferred stock during the period are recorded through other income in the statements of operations. The Company will continue to adjust the liability associated with the warrants to purchase convertible preferred stock for changes in the estimated fair value of the warrants until the earlier of the exercise of the warrants or the completion of a liquidation event, including the completion of an initial public offering, at which time the convertible preferred stock issuable upon exercise of the warrants will become common stock and the related liability will be reclassified to stockholders' equity.

Stock-Based Compensation

Compensation costs related to stock options and shares of restricted stock granted to employees of the Company are based on the fair value of the awards on the date of grant, net of estimated forfeitures. The Company determines the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognizes the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards.

The Company accounts for stock options and shares of restricted stock granted to non-employees also based on the fair value of the awards determined using the Black-Scholes option-pricing model. The fair value of the awards granted to non-employees is remeasured as the awards vest, and the resulting change in value, if any, is recognized in the statement of operations during the period the related services are rendered, which is generally the vesting period.

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

Reduction in Work Force

On December 7, 2009, the Company 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 for the year ending December 31, 2010.

As a result of this workforce reduction, the Company recorded a charge of \$119,000 related to employee severance and other benefits which was included as operating expenses in the statement of operations for the year ended December 31, 2009. As of December 31, 2009, the Company 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 nine months ended September 30, 2010, the Company paid the remaining \$89,000.

Net Loss per Share of Common Stock

The Company's basic net loss per share of common stock is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period. The weighted average number of shares of common stock used to calculate the Company's basic net loss per share of common stock excludes restricted stock held by the founders that are subject to repurchase as these shares are not deemed to be issued for accounting purposes until they vest. The diluted net loss per share of common stock is computed by giving effect to all potential common stock equivalents outstanding for the period determined using the treasury stock method. For purposes of this calculation, convertible preferred stock, options to purchase common stock, restricted stock subject to repurchase, warrants to purchase convertible preferred stock and warrants to purchase common stock are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share of common stock as their effect is antidilutive.

Unaudited Pro Forma Net Loss per Share of Common Stock

In contemplation of the Company's initial public offering, the Company has presented the unaudited pro forma basic and diluted net loss per share of common stock which has been computed to give effect to the automatic conversion of the convertible preferred stock into shares of common stock on a weighted average basis. Also, the numerator in the pro forma basic and diluted net loss per share calculation has been adjusted to remove gains and losses resulting from the remeasurement of the convertible preferred stock warrant liability as if the conversion had occurred as of the beginning of the period.

Recently Issued Accounting Pronouncements

In October 2009, the Financial Accounting Standards Board, or FASB, issued an accounting standards update that provides guidance on whether multiple deliverables exist, how the deliverables should be separated and how the consideration should be allocated to one or more units of accounting. This update establishes a selling price hierarchy for determining the selling price of a deliverable. The selling price used for each deliverable will be based on vendor specific objective evidence, if available, third party evidence if vendor-specific objective evidence is not available, or estimated selling price if neither vendor-specific nor third-party evidence is available. The Company will be required to apply this guidance prospectively for revenue arrangements entered into or materially modified after January 1, 2011. The

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

Company has not recognized any revenue since inception. Therefore, adoption of this guidance is not expected to have a material impact on the Company's financial statements.

In January 2010, the FASB issued an amendment to an accounting standard which requires new disclosures for fair value measurements and provides clarification for existing fair value disclosure requirements. The amendment will require an entity to disclose separately the amounts of significant transfers in and out of Levels I and II fair value measurements and to describe the reasons for the transfers; and to disclose information about purchases, sales, issuances and settlements separately in the reconciliation for fair value measurements using significant unobservable inputs, or Level III inputs. This amendment clarifies existing disclosure requirements for the level of disaggregation used for classes of assets and liabilities measured at fair value and require disclosures about the valuation techniques and inputs used to measure fair value for both recurring and nonrecurring fair value measurements using Level II and Level III inputs. This guidance is effective for interim and annual reporting periods beginning after December 15, 2009, except for certain Level III activity disclosure requirements that will be effective for reporting periods beginning after December 15, 2010. Accordingly, the Company adopted this amendment as of January 1, 2010, except for the additional Level III requirements which will be adopted during the year ending December 31, 2011.

In April 2010, the FASB issued an accounting standard update which provides guidance on the criteria to be followed in recognizing revenue under the milestone method. The milestone method allows a vendor who is involved with the provision of deliverables to recognize the full amount of a milestone payment upon achievement, if, at the inception of the revenue arrangement, the milestone is determined to be substantive as defined in the standard. The guidance is effective on a prospective basis for milestones achieved in fiscal years and interim periods within those fiscal years, beginning on or after June 15, 2010. The Company has not recognized any revenue since inception. Therefore, adoption of this guidance is not expected to have a material impact on the Company's financial statements.

Reverse Stock Split

In January 2011, the Company's board of directors and stockholders approved an amended and restated certificate of incorporation effecting a 1-for-4 reverse stock split of the Company's issued and outstanding shares of common stock and convertible preferred stock and on January 28, 2011, the Company filed an amended and restated certificate of incorporation effecting a 1-for-4 reverse stock split. The par value of the common and convertible preferred stock was not adjusted as a result of the reverse stock split. All issued and outstanding common stock, convertible preferred stock, warrants for common stock, warrants for convertible preferred stock, and per share amounts contained in the Company's financial statements have been retroactively adjusted to reflect this reverse stock split for all periods presented.

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

2. Cash, Cash Equivalents and Short-Term Investments

Cash, cash equivalents and short-term investments consist of the following (in thousands):

	<u>As of December 31, 2008</u>			<u>Fair Value</u>
	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	
Cash	\$ 397	\$ —	\$ —	\$ 397
Money market funds	678	—	—	678
U.S. government agency obligations	12,078	58	—	12,136
Corporate debt obligations	6,990	6	—	6,996
	<u>\$ 20,143</u>	<u>\$ 64</u>	<u>\$ —</u>	<u>\$ 20,207</u>

	<u>As of December 31, 2009</u>			<u>Fair Value</u>
	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	
Cash	\$ 960	\$ —	\$ —	\$ 960
Money market funds	6,190	—	—	6,190
U.S. government agency obligations	5,398	—	(2)	5,396
	<u>\$12,548</u>	<u>\$ —</u>	<u>\$ (2)</u>	<u>\$12,546</u>

	<u>As of September 30, 2010</u>			<u>Fair Value</u>
	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Gross Unrealized Losses</u>	
Cash	\$ 418	\$ —	\$ —	\$ 418
Money market funds	7,140	—	—	7,140
U.S. government agency obligations	522	2	—	524
	<u>\$ 8,080</u>	<u>\$ 2</u>	<u>\$ —</u>	<u>\$ 8,082</u>

As of December 31, 2008, 2009 and September 30, 2010, the contractual maturity of all investments held was less than one year.

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

3. Fair Value of Financial Instruments

The Company measures and reports its convertible preferred stock warrant liability and short-term investments at fair value. The following table sets forth the fair value of the Company's financial assets and liabilities by level within the fair value hierarchy (in thousands):

	As of December 31, 2008			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	\$ 678	\$ 678	\$ —	\$ —
U.S. government agency obligations	12,136	—	12,136	—
Corporate obligations	6,996	—	6,996	—
Total assets measured at fair value	<u>\$19,810</u>	<u>\$ 678</u>	<u>\$19,132</u>	<u>\$ —</u>
Liabilities				
Convertible preferred stock warrant liability	\$ 240	\$ —	\$ —	\$ 240
Total liabilities measured at fair value	<u>\$ 240</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 240</u>

	As of December 31, 2009			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	\$ 6,190	\$6,190	\$ —	\$ —
U.S. government agency obligations	5,396	—	5,396	—
Total assets measured at fair value	<u>\$11,586</u>	<u>\$6,190</u>	<u>\$5,396</u>	<u>\$ —</u>
Liabilities				
Convertible preferred stock warrant liability	\$ 169	\$ —	\$ —	\$ 169
Total liabilities measured at fair value	<u>\$ 169</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 169</u>

	As of September 30, 2010 (Unaudited)			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	\$ 7,140	\$7,140	\$ —	\$ —
U.S. government agency obligations	524	—	524	—
Total assets measured at fair value	<u>\$ 7,664</u>	<u>\$7,140</u>	<u>\$ 524</u>	<u>\$ —</u>
Liabilities				
Convertible preferred stock warrant liability	\$ 2,219	\$ —	\$ —	\$ 2,219
Call option liability	476	—	—	476
Total liabilities measured at fair value	<u>\$ 2,695</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$2,695</u>

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

The following table sets forth a summary of the changes in the fair value of the Company's Level III financial liabilities (in thousands):

	<u>Year Ended December 31,</u>			<u>Nine Months Ended</u>	
	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>2009</u>	<u>September 30,</u>
				(Unaudited)	
Fair value—beginning of period	\$ —	\$ 1	\$ 240	\$ 240	\$ 169
Issuance of warrants	1	162	—	—	1,223
Issuance of call option	—	—	—	—	476
Change in fair value of Level III liabilities	—	77	(71)	(168)	827
Fair value—end of period	<u>\$ 1</u>	<u>\$ 240</u>	<u>\$ 169</u>	<u>\$ 72</u>	<u>\$ 2,695</u>

The determination of the fair value of the convertible preferred stock warrants is discussed in Note 7.

4. Property and Equipment

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

	<u>December 31,</u>		<u>September 30,</u>
	<u>2008</u>	<u>2009</u>	<u>2010</u>
			(Unaudited)
Research equipment	\$ 675	\$ 1,003	\$ 1,009
Leasehold improvements	1,005	1,008	1,008
Computer equipment and software	227	248	246
Furniture and fixtures	110	107	108
Total property, plant and equipment	<u>2,017</u>	<u>2,366</u>	<u>2,371</u>
Less accumulated depreciation and amortization	<u>(605)</u>	<u>(1,086)</u>	<u>(1,445)</u>
	<u>\$ 1,412</u>	<u>\$ 1,280</u>	<u>\$ 926</u>

Depreciation and amortization expense was \$216,000, \$383,000, \$481,000, \$363,000, \$359,000, \$1.1 million and \$1.4 million for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

5. Long-Term Debt

Equipment Financing Obligation

In March 2007, the Company entered into an equipment financing agreement in which the Company could receive advances for an amount up to \$750,000. Advances under the agreement were repaid in 30 monthly installments of principal and interest and carried an average interest rate of 9.4% per annum. As of December 31, 2008, the Company had an outstanding balance of \$284,000 under the agreement. As of December 31, 2009, the Company had repaid all amounts outstanding under the agreement.

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(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

In connection with this agreement, the Company issued immediately exercisable and fully vested warrants to purchase 2,500 shares of its Series A convertible preferred stock, or Series A, at an exercise price of \$10.00 per share. The fair value of the Series A warrant on the date of issuance of \$1,000, as determined using the Black-Scholes option-pricing model, was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The deferred financing cost was amortized to interest expense over the draw down term. As of December 31, 2009 and September 30, 2010, the deferred financing cost had been fully amortized.

Loan and Security Agreement

In September 2008, the Company entered into a \$12.0 million loan and security agreement with Pinnacle Ventures L.L.C. In November 2008, the Company drew down all \$12.0 million of the loan facility. The loan is repayable over 36 months, carries an interest rate of 8.5% per annum and is collateralized by the Company's tangible assets and proceeds from intellectual property. An additional \$600,000 will be due as a final payment at the end of the loan term in November 2011, representing a 5.0% final payment fee. The final payment is being accreted on an effective interest basis over the term of the loan agreement. As of December 31, 2009 and September 30, 2010, the Company accrued \$311,000 and \$466,000 relating to this final payment, which is classified as a component of long-term debt in the balance sheet. As of December 31, 2008, 2009 and September 30, 2010, the Company had outstanding borrowings under the loan and security agreement of \$12.0 million, \$9.7 million and \$6.4 million.

In connection with the loan and security agreement, the Company issued immediately exercisable and fully vested warrants to purchase 56,250 shares of Series B convertible preferred stock, or Series B, with an exercise price of \$16.00 per share. Upon the closing of the Company's Series C convertible preferred stock, or Series C, financing during the year ended December 31, 2009, the warrants underlying the loan and security agreement became exercisable for 228,264 shares of Series C with an exercise price of \$3.94 per share.

As discussed in Note 7 "Warrants," the Company determined the fair value of the Series B and Series C warrants on the dates of issuance to be \$162,000, as determined using the Black-Scholes option-pricing model, which was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The deferred financing cost is being amortized to interest expense over the loan term. For the years ended December 31, 2008, 2009 and the nine months ended September 30, 2009 and 2010, amortization of the deferred financing cost to interest expense was \$110,000, \$19,000, \$14,000 and \$13,000. As of December 31, 2008, 2009 and September 30, 2010, deferred financing cost on the balance sheets related to this loan and security agreement was \$52,000, \$33,000 and \$20,000.

Scheduled principal payments for the Company's loan and security agreement as of December 31, 2009 are as follows (in thousands):

Year Ending December 31:	
2010	\$4,726
2011	<u>5,008</u>
Total long-term debt	<u>\$9,734</u>

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(A Development Stage Company)

Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

During the nine months ended September 30, 2010, the Company made regular payments on the loan and security agreement of \$3.4 million.

6. Convertible Notes

2006 Convertible Notes

In March and April 2006, the Company issued convertible notes, or 2006 Convertible Notes, to various individuals, including Company executives, in exchange for \$1.0 million in cash. These notes bore interest at 6.0% per annum and were due to be repaid on March 1, 2008. In August 2006, the 2006 Convertible Notes and related accrued interest totaling \$1.0 million automatically converted into 102,141 shares of Series A upon the closing of the Series A financing.

In conjunction with the issuance of the 2006 Convertible Notes during the year ended December 31, 2006, the Company issued warrants to purchase an aggregate of 25,534 shares of common stock with an exercise price of \$0.04 per share. As discussed in Note 7 “Warrants”, the Company calculated the fair value of the warrants on the date of issuance to be \$25,000, as determined using the Black-Scholes option-pricing model, which was amortized as interest expense during the year ended December 31, 2006. In addition, the Company also recognized a beneficial conversion feature on the 2006 Convertible Notes in the amount of \$25,000 as interest expense during the year ended December 31, 2006.

2010 Convertible Notes

On September 14, 2010, the Company sold convertible promissory notes, or 2010 Convertible Notes, to purchase shares of the Company’s equity securities to certain existing investors for an aggregate purchase price of \$8.0 million. The 2010 Convertible Notes cannot be prepaid without written consent of the holders, accrue interest at a rate of 4.0% per annum and have 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 Convertible Notes are automatically convertible (1) into the securities that are sold in the Company’s next equity financing prior to September 14, 2011, with total proceeds of not less than \$15.0 million, or Qualified Financing, at the price at which such securities are sold to other investors, (2) into securities that are sold in the Company’s initial public offering at a conversion price equal to 80% of the initial public offering price or (3) following September 14, 2011, with the consent of the holders of a majority of the principal amount of the 2010 Convertible Notes still outstanding, into shares of Series C at the Series C price of \$3.94 per share. In addition, holders of the 2010 Convertible Notes have the option to convert the 2010 Convertible Notes into shares of Series C in connection with a liquidation, sale of substantially all of the Company’s assets, or merger, if such liquidation, sale of substantially all of the Company’s assets, or merger occurs before the Qualified Financing or initial public offering.

Upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 Convertible Notes outstanding, the Company will sell an additional \$4.0 million of 2010 Convertible Notes. This additional \$4.0 million was determined to be a call option that has been recorded at its fair value of \$476,000 as a debt discount that will be amortized to interest expense over the one-year term of the 2010 Convertible Notes. The fair value of the call option was determined by evaluating multiple potential outcomes using a market approach and an income approach depending on the scenario and discounted these values back to September 30, 2010 while applying estimated probabilities to each scenario value. These scenarios include a potential initial public offering, merger or sale at different times during 2011 and 2012 as well as remaining private.

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In conjunction with the issuance of the 2010 Convertible Notes, the Company issued warrants that are 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 Series C at a price per share of the Series C. The aggregate number of shares exercisable under the warrants will equal 25% of the principal amount of the 2010 Convertible 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 of \$3.94 per share. As discussed in Note 7 “Warrants,” the Company calculated the fair value of the warrants to be \$1.2 million, which was recorded as a debt discount that will be amortized to interest expense over the one-year term of the 2010 Convertible Notes.

In addition, the Company also recognized a beneficial conversion feature related to these warrants and the call option discussed above in the aggregate amount of \$1.7 million as an additional debt discount that will also be amortized to interest expense over the one-year term of the 2010 Convertible Notes. In addition to these beneficial conversion features, the 2010 Convertible Notes have contingent beneficial conversion features related to the conversion options following the maturity of the 2010 Convertible Notes or in connection with a liquidation, sale or merger into Series C. The contingent beneficial features were determined on the date of the issuance of the 2010 Convertible Notes based on the intrinsic value of this feature in the amount of \$2.8 million. This beneficial conversion feature will be recorded if and when the related contingent event occurs.

Amortization expense for the debt discount from the issuance of the 2010 Convertible Notes on September 14, 2010 through the end of the reporting period on September 30, 2010 was insignificant.

7. Warrants

Series A Warrants

In March 2007, the Company entered into an equipment financing agreement in which the Company issued immediately exercisable and fully vested warrants to purchase 2,500 shares of its Series A with an exercise price of \$10.00 per share. The Series A warrants expire in March 2017. The fair value of the Series A warrant on the date of issuance was \$1,000, as determined using the Black-Scholes option-pricing model using the following assumptions: 10 year contractual term, 72% expected volatility, 4.1% risk-free interest rate and no expected dividend. This fair value was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The Company revalued the convertible preferred stock warrant liability related to the Series A warrants at the end of each reporting period using the Black-Scholes option-pricing model with the following assumptions:

	<u>Year Ended December 31,</u>			<u>Nine Months Ended</u> <u>September 30,</u>	
	<u>2007</u>	<u>2008</u>	<u>2009</u>	<u>2009</u>	<u>2010</u>
Expected term (in years)	9.2	8.2	7.2	7.5	6.5
Risk-free interest rate	4.1%	2.1%	3.1%	3.1%	1.9%
Expected volatility	72%	81%	74%	75%	82%
Expected dividend rate	0%	0%	0%	0%	0%

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The fair value of the liability related to the Series A warrants was estimated to be \$10,000, \$2,000 and \$10,000 as of December 31, 2008, 2009 and September 30, 2010. The change in the fair value of the Series A warrants resulted in a charge to other income (expense), net of \$9,000 and \$8,000 during the year ended December 31, 2008 and the nine months ended September 30, 2010 and a benefit to other income (expense), net of \$7,000 and \$8,000 and during the nine months ended September 30, 2009 and the year ended December 31, 2009. As of September 30, 2010, the Series A warrants had not been exercised and were still outstanding.

Series B and Series C Warrants

In September 2008, the Company entered into a \$12.0 million loan and security agreement with Pinnacle Ventures. In November 2008, the Company drew down all \$12.0 million of the loan facility. In connection with the loan and security agreement, the Company issued immediately exercisable and fully vested warrants to purchase 56,250 shares of Series B with an exercise price of \$16.00 per share. Upon the closing of the Series C financing during the year ended December 31, 2009, the warrants underlying the loan and security agreement became exercisable for 228,264 shares of Series C with an exercise price of \$3.94 per share. These warrants expire in September 2018.

The Company determined the fair value of the Series B and Series C warrants on the dates of issuance to be \$162,000, as determined using the Black-Scholes option-pricing model using the following assumptions: 10 year contractual term, 76% expected volatility, 3.4% risk-free interest rate and no expected dividend, which was recorded as a convertible preferred stock warrant liability and as a deferred financing cost in other assets. The Company revalued the convertible preferred stock warrant liability related to the Series B and Series C warrants at the end of each reporting period using the Black-Scholes option-pricing model with the following assumptions:

	<u>Year Ended December 31,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2008</u>	<u>2009</u>	<u>2009</u>	<u>2010</u>
			(Unaudited)	
Expected term (in years)	9.7	8.7	9.0	8.0
Risk-free interest rate	2.4%	3.4%	3.3%	2.2%
Expected volatility	87%	76%	80%	83%
Expected dividend rate	0%	0%	0%	0%

The fair value of the convertible preferred stock warrant liability related to these Series B and Series C warrants was estimated to be \$230,000, \$167,000 and \$986,000 as of December 31, 2008, 2009 and September 30, 2010. The change in the fair value of the warrants resulted in a charge to other income (expense), net of \$68,000 and \$819,000 during the year ended December 31, 2008 and the nine months ended September 30, 2010 and a benefit to other income (expense), net of \$161,000 and \$63,000 during the nine months ended September 30, 2009 and the year ended December 31, 2009. As of September 30, 2010, the Series C warrants had not been exercised and were still outstanding.

2010 Warrants

The Company issued warrants in connection with the 2010 Convertible Notes in September 2010, or the 2010 Warrants. The 2010 Warrants are exercisable into (1) shares of preferred stock sold in the next

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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 Series C at a price per share of the Series C (x) if the next equity financing with proceeds in excess of \$15.0 million does not occur prior to September 14, 2011, upon the election of holders of a majority of the aggregate principal amount of the 2010 Convertible Notes or (y) in the event of the initial public offering, a liquidation, sale of substantially all of the Company's assets, or merger. Each 2010 Warrant may be exercisable for a number of shares equal to the quotient obtained by dividing 25% of the principal amount of the 2010 Convertible Notes by the applicable per share price indicated above. The 2010 Warrants terminate if they are not exercised immediately prior to an initial public offering. The 2010 Warrants are exercisable upon issuance and allow for cashless exercises.

In order to determine a fair value for the 2010 Warrants upon issuance of the 2010 Convertible Notes, the Company evaluated multiple potential outcomes using the intrinsic value or Black-Scholes value depending on the scenario and discounted these values back to September 30, 2010 while applying estimated probabilities to each scenario value. These scenarios included a potential initial public offering or potential merger or sale at different times during 2011 and 2012 as well as remaining private with estimated future qualifying equity financings. Accordingly, the Company determined the fair value of the warrants to be \$1,223,000, which was recorded as a convertible preferred stock warrant liability and a debt discount. The Company will revalue the 2010 Warrants at the end of each reporting period; however, there was no adjustment to the convertible preferred stock warrant liability as of September 30, 2010 as there was no change in the fair value of the 2010 Warrants between the time of issuance on September 14, 2010 and the end of the period.

Common Stock Warrants

In March and April 2006, the Company issued the 2006 Convertible Notes to various individuals, including the Company executives. In conjunction with the issuance of the 2006 Convertible Notes, the Company issued warrants to purchase an aggregate of 25,534 shares of common stock with an exercise price of \$0.04 per share. The Company calculated the fair value of the warrants on the date of issuance to be \$25,000, as determined using the Black-Scholes option-pricing model using the following assumptions: three year contractual term, 72% expected volatility, 4.0% risk-free interest rate and no expected dividend, which was fully amortized as interest expense during the year ended December 31, 2006. These common stock warrants were exercised during the year ended December 31, 2006.

8. Commitments and Contingencies

Operating Leases

In January 2007, the Company entered into a non-cancelable lease agreement for office and laboratory facilities in Redwood City, California. The lease term commenced in April 2007 and expires in April 2012. Rental expense from the facility lease is recognized on a straight-line basis from the inception of the lease in January 2007, the early access date, through the end of the lease. Rent expense was \$284,000, \$158,000, \$158,000, \$118,000, \$118,000, \$659,000 and \$777,000 for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

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Future minimum payments under the lease agreement as of December 31, 2009 are as follows (in thousands):

Year Ending December 31:	
2010	\$ 338
2011	348
2012	97
Total minimum payments	<u>\$783</u>

During the nine months ended September 30, 2010, the Company made regular payments on the operating lease of \$253,000.

During 2007, the landlord provided a tenant improvement allowance of \$746,000 to the Company to complete the office and lab facility. The Company has recorded the tenant improvement allowance paid by the landlord as a leasehold improvement asset and a deferred rent liability on the balance sheet. The allowance is amortized as a credit to rent expense over the term of the lease, and the leasehold improvements are amortized as depreciation expense over the period from when the improvements were placed in service until the end of their useful life, which is the end of the lease term. As of December 31, 2008, 2009 and September 30, 2010, the Company has an unamortized tenant improvement allowance of \$596,000, \$425,000 and \$290,000.

Litigation

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

9. Stockholders' Equity

Common Stock

As of December 31, 2008, 2009 and September 30, 2010, the Company had reserved shares of common stock, on an as if converted basis, for issuance as follows:

	December 31,		September 30,
	2008	2009	2010
Issuances under stock option plan	717,000	2,071,445	2,060,490
Conversion of convertible preferred stock	4,779,185	8,536,438	8,555,713
Issuances upon exercise of convertible preferred stock warrants	231,678	231,678	231,678
	<u>5,727,863</u>	<u>10,839,561</u>	<u>10,847,881</u>

The above table does not include potential issuances of common stock related to the 2010 Convertible Notes or the 2010 Warrants.

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Convertible Preferred Stock

During the year ended December 31, 2006, the Company completed a private placement of an aggregate of 2,111,639 shares of Series A, which included 102,141 shares issued upon conversion of the 2006 Convertible Notes, at a price of \$10.00 per share, resulting in net cash proceeds of \$21.0 million.

During the year ended December 31, 2008, the Company issued 1,263,635 shares of Series B at \$16.00 per share, resulting in net cash proceeds of \$20.1 million.

During the year ended December 31, 2009, the Company issued 3,757,253 shares of Series C at \$3.94 per share, resulting in net cash proceeds of \$14.7 million. During the nine months ended September 30, 2010, the Company issued another 19,275 shares of Series C at \$3.94 per share, resulting in net cash proceeds of \$76,000.

	<u>As of December 31, 2008</u>		
	<u>Shares Authorized</u>	<u>Shares Issued and Outstanding</u>	<u>Aggregate Liquidation Preference</u>
Series A	8,456,581	2,111,639	\$21,116,000
Series B	5,279,544	1,263,635	20,218,000
Total	<u>13,736,125</u>	<u>3,375,274</u>	<u>\$ 41,334,000</u>

	<u>As of December 31, 2009</u>		
	<u>Shares Authorized</u>	<u>Shares Issued and Outstanding</u>	<u>Aggregate Liquidation Preference</u>
Series A	8,456,581	2,111,639	\$21,116,000
Series B	5,279,544	1,263,635	20,218,000
Series C	33,000,000	3,757,253	14,814,000
Total	<u>46,736,125</u>	<u>7,132,527</u>	<u>\$56,148,000</u>

	<u>As of September 30, 2010</u>		
	<u>Shares Authorized</u>	<u>Shares Issued and Outstanding</u> (Unaudited)	<u>Aggregate Liquidation Preference</u>
Series A	8,456,581	2,111,639	\$21,116,000
Series B	5,279,544	1,263,635	20,218,000
Series C	33,000,000	3,776,528	14,890,000
Total	<u>46,736,125</u>	<u>7,151,802</u>	<u>\$56,224,000</u>

The Company recorded the convertible preferred stock at fair value on the dates of issuance, net of issuance costs. The Company classifies the convertible preferred stock outside of stockholders' deficit because the shares contain redemption features that are not solely within the Company's control. For the

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years ended December 31, 2007, 2008 and 2009, the Company did not adjust the carrying values of the redeemable convertible preferred stock to the deemed redemption values of such shares since a liquidation event was not probable. Subsequent adjustments to increase the carrying values to the ultimate redemption values will be made only when it becomes probable that such a liquidation event will occur.

The rights, preferences and privileges of the convertible preferred stockholders are as follows:

Conversion Rights

Each share of convertible preferred stock is convertible at the option of the holder into the number of shares determined by dividing the original purchase price by the applicable conversion price. The original per share purchase price was \$10.00, \$16.00 and \$3.94 for Series A, Series B and Series C. At the current conversion prices, each share of Series A, Series B and Series C will convert into 1.37, 1.50 and 1.00 share(s) of common stock. The conversion price per share for convertible preferred stock shall be adjusted for certain recapitalizations, splits, combinations, common stock dividends, or similar events. The convertible preferred stock automatically converts into shares of common stock at the conversion price in effect upon the earlier of (1) the closing of an underwritten initial public offering at a public offering price of at least \$12.00 per share (adjusted for stock dividends, stock splits, recapitalizations, or similar events) with aggregate gross cash proceeds to the Company of at least \$30 million, or (2) when the holders of 60% of the outstanding shares of convertible preferred stock elect conversion.

Voting Rights

Each share of convertible preferred stock has a number of votes equal to the number of shares of common stock into which it is convertible. The Series A holders, as a class, are entitled to elect two members of the board of directors; the Series B holders, as a class, are entitled to elect one member of the board of directors; the common stock holders, as a class, are entitled to elect two members of the board of directors. The common stock holders and the holders of the convertible preferred stock voting together are entitled to elect the remaining members of the board of directors.

Liquidation Preferences

In the event of any liquidation of the Company, the holders of the Series A, Series B and Series C are entitled to liquidation preferences of \$10.00, \$16.00 and \$3.94 per share, plus any declared and unpaid dividends. Upon distribution of the liquidation preferences to the holders of the convertible preferred stock, if assets remain, holders of the common stock will receive all of the remaining assets on a pro rata basis.

Dividends Rights

The holders of the Series A, Series B and Series C are entitled to receive dividends, when and if declared by the board of directors, in the amount of \$0.80, \$1.28 and \$0.32 per share (adjusted for stock splits, stock dividends, recapitalizations or similar events), per annum on each outstanding share of convertible preferred stock. The dividends are payable in preference and priority to any dividend on common stock and are noncumulative. No dividends have been declared through September 30, 2010.

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Redemption Rights

The Series A, Series B and Series C are not redeemable.

10. Stock-Based Compensation

The Company recorded stock-based compensation expense for its stock-based awards as follows (in thousands):

	<u>Year Ended December 31,</u>			<u>Period from July 13, 2005 (Inception) Through December 31, 2009</u>	<u>Nine Months Ended September 30,</u>		<u>Period from July 13, 2005 (Inception) Through September 30, 2010 (Unaudited)</u>
	<u>2007</u>	<u>2008</u>	<u>2009</u>		<u>2009</u>	<u>2010</u>	
Employee stock options	\$ 29	\$ 126	\$ 282	\$ 437	\$ 171	\$ 983	\$ 1,420
Non-employee stock options	4	71	30	105	30	31	136
Restricted stock	95	259	151	547	116	93	640
Total	<u>\$128</u>	<u>\$ 456</u>	<u>\$ 463</u>	<u>\$ 1,089</u>	<u>\$ 317</u>	<u>\$1,107</u>	<u>\$ 2,196</u>

Stock Option Plan

As of December 31, 2008, 2009 and September 30, 2010, the Company had one stock-based compensation plan, the 2006 Stock Plan, or the Plan. In August 2006, the Company established the Plan in which 342,000 shares of common stock were originally reserved for the issuance of incentive stock options, or ISOs, and nonstatutory stock options, or NSOs, to employees, directors or consultants of the Company. In February 2008, an additional 375,000 shares of common stock were reserved for issuance under the Plan and, in November 2009, an additional 1,376,059 shares of common stock were reserved for issuance under the Plan. Per the Plan, the exercise price of ISOs and NSOs granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company shall be no less than 110% of the fair value per share of the underlying common stock on the date of grant.

The Company's stock options generally vest over four years at a rate of 25% on the first anniversary and 1/48th per month thereafter. The stock options generally expire ten years from the date of grant. However, in the case of an ISO issued to an optionee who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company, the term of the option will be no more than five years. Stock bonus awards and rights to immediately purchase stock may also be granted under the Plan, with terms, conditions and restrictions determined by the board of directors.

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The following table summarizes option activity under the Plan and related information:

	Number of Shares Available for Grant	Options Outstanding	
		Number of Shares Underlying Outstanding Options	Weighted Average Exercise Price Per Share
Balance as of January 1, 2007	342,000	—	—
Options granted	(290,625)	290,625	\$ 1.20
Options forfeited	1,250	(1,250)	1.20
Balance as of December 31, 2007	52,625	289,375	1.20
Additional options authorized	375,000	—	—
Options granted	(199,375)	199,375	4.00
Balance as of December 31, 2008	228,250	488,750	2.36
Additional options authorized	1,376,059	—	—
Options granted	(229,375)	229,375	5.52
Options forfeited	30,885	(30,885)	2.56
Options exercised	—	(21,614)	1.20
Balance as of December 31, 2009	1,405,819	665,626	3.48
Options granted (unaudited)	(1,316,610)	1,316,610	1.20
Options forfeited (unaudited)	78,421	(78,421)	3.98
Options exercised (unaudited)	—	(10,955)	1.89
Balance as of September 30, 2010 (unaudited)	167,630	1,892,860	1.88

Additional information regarding the Company's stock options outstanding and vested and exercisable as of December 31, 2009 is summarized below:

Exercise Prices	Options Outstanding			Options Vested and Exercisable	
	Number of Stock Options Outstanding	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price per Share	Shares Subject to Stock Options	Weighted Average Exercise Price per Share
\$1.20	208,125	7.5	\$ 1.20	141,867	1.20
\$1.32	43,750	7.3	1.32	33,723	1.32
\$4.00	181,875	8.6	4.00	85,151	4.00
\$5.52	231,876	9.3	5.52	48,114	5.52
	665,626	8.4	3.48	308,855	2.66

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Additional information regarding the Company's stock options outstanding and vested and exercisable as of September 30, 2010 is summarized below:

Exercise Prices	Options Outstanding			Options Vested and Exercisable	
	Number of Stock Options Outstanding	Weighted Average Remaining Contractual Life (Years) (Unaudited)	Weighted Average Exercise Price per Share	Shares Subject to Stock Options	Weighted Average Exercise Price per Share (Unaudited)
\$1.20	1,495,360	9.4	\$ 1.20	512,848	\$ 1.20
\$1.32	43,750	6.5	1.32	41,926	1.32
\$4.00	160,000	7.9	4.00	105,267	4.00
\$5.52	193,750	8.5	5.52	82,622	5.52
	<u>1,892,860</u>	9.1	1.88	<u>742,663</u>	2.08

The weighted average grant-date fair value of options granted for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010, was \$0.84, \$2.88, \$1.96, \$1.96, \$2.00, \$1.76 and \$1.92 per share. Total future stock-based compensation expense related to these unvested options based on grant date fair value estimates to be recorded subsequent to December 31, 2009 and September 30, 2010 was \$710,000 and \$2.3 million which is expected to be recognized over a weighted-average period of 2.7 years and 1.6 years. The total fair value of shares vested during the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010, was \$35,000, \$169,000, \$244,000, \$232,000, \$2.5 million, \$448,000 and \$3.0 million. The total intrinsic value of options exercised during the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010 was zero, zero, \$62,000, \$62,000, \$3,000, \$62,000 and \$65,000.

Determining Fair Value of Stock Options

The fair value of each grant of stock options was determined by the Company and its board of directors using the methods and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Valuation Method—The Company estimates the fair value of its stock options using the Black-Scholes option-pricing model.

Expected Term—The expected term represents the period that the stock-based awards are expected to be outstanding. For option grants that are considered to be “plain vanilla,” the Company used the simplified method to determine the expected term as provided by the Securities and Exchange Commission. The simplified method calculates the expected term as the average of the time-to-vesting and the contractual life of the options. For other option grants, the expected term is derived from the Company's historical data on employee exercises and post-vesting employment termination behavior taking into account the contractual life of the award.

AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)

Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

Expected Volatility—The expected volatility was based on the historical stock volatilities of several of the Company’s publicly listed peers over a period approximately equal to the expected terms of the options as the Company did not have a sufficient trading history to use the volatility of its own common stock.

Fair Value of Common Stock—The fair value of the common stock underlying the stock options has historically been determined by the Company’s board of directors. Because there has been no public market for the Company’s common stock, the board of directors has determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including valuations of comparable companies, sales of convertible preferred stock to unrelated third parties, operating and financial performance, lack of liquidity of capital stock and general and industry-specific economic outlook, amongst other factors. The fair value of the underlying common stock shall be determined by the board of directors until such time that the Company’s common stock is listed on an established stock exchange or national market system.

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

Expected Dividend—The expected dividend has been zero as the Company has never paid dividends and does not expect to pay dividends.

Forfeiture Rate—The Company estimates its forfeiture rate based on an analysis of its actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior, and other factors. The impact from a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from that estimated by the Company, the Company may be required to record adjustments to stock-based compensation expense in future periods.

Summary of Assumptions—The fair value of each employee stock option was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,			Period from July 13, 2005 (Inception) Through December 31, 2009	Nine Months Ended September 30,		Period from July 13, 2005 (Inception) Through September 30, 2010 (Unaudited)
	2007	2008	2009		2009	2010 (Unaudited)	
Expected term (in years)	6.25	6.25	6.25	6.25	6.25	5.75 - 6.25	5.75 - 6.25
Risk-free interest rate	3.6% - 4.6%	3.5%	3.0%	2.6% - 4.6%	3.0%	1.6% - 2.4%	1.6% - 4.6%
Expected volatility	72%	74%	73%	70% - 74%	73%	75%	70% - 75%
Expected dividend rate	0%	0%	0%	0%	0%	0%	0%

AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)

Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

Employee Stock-Based Compensation for Stock Options

The Company recorded compensation expense for options granted to employees as follows (in thousands):

	Year Ended December 31,			Period from July 13, 2005 (Inception) Through December 31, 2009	Nine Months Ended September 30,		Period from July 13, 2005 (Inception) Through September 30, 2010
	2007	2008	2009		2009	2010	
Research and development	\$ 25	\$ 66	\$ 167	\$ 258	\$ 74	\$ 539	\$ 797
General and administrative	4	60	115	179	97	444	623
Total	\$ 29	\$ 126	\$ 282	\$ 437	\$ 171	\$ 983	\$ 1,420

There were no capitalized stock-based compensation costs or recognized stock-based compensation tax benefits during the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, or the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

Non-Employee Stock-Based Compensation for Stock Options

During the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010, the Company granted 25,000, 37,500, zero, zero, zero, 62,500 and 62,500 stock options to non-employees of the Company. Also during the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010, certain employees of the Company transitioned to non-employees, therefore, zero, 19,791, 2,708, 71,956, 22,499 and 94,455 options became non-employee options during these periods. As of December 31, 2009 and September 30, 2010, the Company had non-employee stock options to purchase 32,395 and 70,802 shares of common stock outstanding with exercise prices ranging from \$1.20 to \$5.52 and contractual lives up to ten years. As of December 31, 2009 and September 30, 2010, 29,973 and 41,844 of these shares were vested, 3,124 and 5,601 of these options had been exercised and 15,885 and 75,280 of these options had been forfeited. The Company has recorded stock-based compensation expense for to these non-employee options of \$4,000, \$71,000, \$30,000, \$30,000, \$31,000, \$105,000 and \$136,000 for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

Restricted Stock

In January 2006, the Company issued 500,000 shares of its common stock, which consisted of 250,000 shares to each of the two founders, for \$0.004 per share. These shares were initially fully vested but were subject to the right of first refusal by the Company until such time as a public market existed for the common stock. In August 2006, as a condition of the closing of the Series A financing, the founders signed a vesting agreement which required that 50% of the shares purchased by each founder be subject to a right of repurchase by the Company which lapses at a rate of 1/48th per month over four years. Under the terms of the agreements, the repurchase price is the original exercise price. As such, the shares

AcelRx Pharmaceuticals, Inc.
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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

subject to vesting repurchase right are not deemed outstanding for accounting purposes until the shares vest and a liability has been included on the balance sheets for an amount equal to the purchase price of the invested founder shares. These amounts will be reclassified to stockholders' equity as the repurchase rights lapse. As of December 31, 2008 and 2009, 104,166 and 41,666 of the founders' shares are still subject to repurchase. All restricted shares were no longer subject to repurchase as of September 30, 2010.

During the year ended December 31, 2006, three employees purchased an aggregate of 85,000 shares of the Company's common stock for \$0.004 per share, and two employees purchased an aggregate of 47,500 shares of common stock for \$1.00 per share, the estimated fair value of the Company's common stock at the time of each purchase. These shares are subject to a right of repurchase by the Company, which lapses with respect to 25% of the shares one year from the purchase date and 1/48th per month thereafter if the holders remain employees of the Company. Under the terms of these agreements, the repurchase price is the original exercise price. As such, these shares are not deemed outstanding for accounting purposes until the repurchase rights lapse and a liability has been included on the balance sheets for an amount equal to the purchase price of the shares. These amounts will be reclassified to stockholders' equity as the repurchase rights lapse. In August 2008, the Company repurchased 18,750 of these restricted shares of common stock for \$0.004 per share. As of December 31, 2008 and 2009, 13,489 and 1,614 of these restricted shares are still subject to repurchase. These restricted shares were no longer subject to repurchase as of September 30, 2010.

The Company determined the aggregate fair value of these restricted shares on the grant dates to be \$362,000, as determined using the Black-Scholes option-pricing model. Stock-based compensation expense related to these shares was \$95,000, \$259,000, \$151,000, \$127,000, \$138,000, \$547,000 and \$685,000 for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010. These amounts are net of the amortization of the liability related to the restricted shares that are subject to repurchase of \$21,000, \$12,000, \$12,000, \$9,000, \$2,000, \$47,000 and \$49,000 for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

11. Net Loss per Share of Common Stock

The following table sets for the computation of the Company's basic and diluted net loss per share of common stock during the years ended December 31, 2007, 2008, 2009 and the nine months ended September 30, 2009 and 2010 (in thousands, except for share and per share amounts):

	Year Ended December 31,			Nine Months Ended September 30,	
	2007	2008	2009	2009 (Unaudited)	2010
Net loss	\$ (9,630)	\$ (20,662)	\$ (20,119)	\$ (16,422)	\$ (10,821)
Shares used in computing net loss per share of common stock, basic and diluted	364,039	472,914	576,021	564,571	650,774
Net loss per share of common stock, basic and diluted	\$ (26.45)	\$ (43.69)	\$ (34.93)	\$ (29.09)	\$ (16.63)

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net loss per share of common stock for the periods presented because including them would have been antidilutive:

	Year Ended December 31,			Nine Months Ended September 30,	
	2007	2008	2009	2009 (Unaudited)	2010
Convertible preferred stock	2,111,639	3,375,274	7,132,527	3,375,274	7,151,802
Stock options to purchase common stock	289,375	488,750	665,626	668,125	1,892,860
Restricted shares of common stock subject to repurchase	234,218	117,657	43,282	61,875	—
Convertible preferred stock warrants	2,500	58,750	230,764	58,750	230,764

The above table does not include common stock equivalents related to the 2010 Convertible Notes or the 2010 Warrants.

AcelRx Pharmaceuticals, Inc.
(A Development Stage Company)

Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

The following table sets forth the computation of the Company's pro forma basic and diluted net loss per share of common stock during the year ended December 31, 2009 and the nine months ended September 30, 2010 (in thousands, except for share and per share amounts):

	<u>Year Ended</u> <u>December 31, 2009</u>	<u>Nine Months Ended</u> <u>September 30,</u> <u>2010</u> <small>(Unaudited)</small>
Net loss	\$ (20,119)	\$ (10,821)
Change in fair value of convertible preferred stock warrant liabilities	(71)	827
Net loss used in computing pro forma net loss per share of common stock, basic and diluted	<u>\$ (20,190)</u>	<u>\$ (9,994)</u>
Shares used in computing net loss per share of common stock, basic and diluted	576,021	650,774
Pro forma adjustments to reflect assumed conversion of convertible preferred stock	<u>5,170,351</u>	<u>8,554,225</u>
Shares used in computing pro forma net loss per share of common stock, basic and diluted	5,746,372	9,204,999
Pro forma net loss per share of common stock, basic and diluted	<u>\$ (3.51)</u>	<u>\$ (1.09)</u>

12. 401(k) Plan

The Company sponsors a 401(k) plan that stipulates that eligible employees can elect to contribute to the 401(k) plan, subject to certain limitations. Pursuant to the 401(k) plan, the Company makes a discretionary safe harbor profit-sharing contribution equal to 3% of the related compensation. Eligible employees are 100% vested in this safe harbor profit-sharing contribution regardless of whether they make salary deferrals into the 401(k) plan. Contributions were \$33,000, \$93,000, \$133,000, \$97,000, \$78,000, \$259,000 and \$337,000 for the years ended December 31, 2007, 2008, 2009, the nine months ended September 30, 2009 and 2010, and the periods from July 13, 2005 (inception) through December 31, 2009 and September 30, 2010.

AcelRx Pharmaceuticals, Inc.
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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

13. Income Taxes

The Company did not record a provision for income taxes for the years ended December 31, 2007, 2008 and 2009. Net deferred tax assets as of December 31, 2008 and 2009 consist of the following (in thousands):

	December 31,	
	2008	2009
Deferred tax assets:		
Accruals and other	\$ 243	\$ 296
Research credits	773	1,283
Net operating loss carryforward	13,246	21,070
Total deferred tax assets	14,262	22,649
Deferred tax liabilities:		
Unrealized gains or losses on investments	(25)	—
Total deferred tax liabilities	(25)	—
Gross deferred tax assets	14,237	22,649
Valuation allowance	(14,237)	(22,649)
Net deferred tax assets	\$ —	\$ —

Reconciliations of the statutory federal income tax to the Company's effective tax for the years ended December 31, 2007, 2008 and 2009 are as follows (in thousands):

	Year Ended December 31,		
	2007	2008	2009
Tax at statutory federal rate	\$ (3,274)	\$ (7,034)	\$ (6,840)
State tax—net of federal benefit	(615)	(1,334)	(1,300)
Other	(70)	(263)	(272)
Change in valuation allowance	3,959	8,631	8,412
Provision (benefit) for income taxes	\$ —	\$ —	\$ —

A valuation allowance is provided when it is more likely than not that the deferred tax assets will not be realized. The Company has established a valuation allowance to offset net deferred tax assets as of December 31, 2008 and 2009 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets.

The valuation allowance increased by \$4.0 million, \$8.6 million and \$8.4 million during the years ended December 31, 2007, 2008 and 2009.

As of December 31, 2009, the Company has federal net operating loss carryforwards of \$52.9 million expiring beginning in 2025. As of December 31, 2009, the Company has state net operating loss carryforwards of \$52.8 million, expiring beginning in 2017.

AcelRx Pharmaceuticals, Inc.
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Notes to Financial Statements—(Continued)

(Information pertaining to September 30, 2010, the nine months ended September 30, 2009 and 2010 and for the period from July 13, 2005 (Inception) through September 30, 2010 is unaudited)

As of December 31, 2009, the Company has federal research credit carryovers of \$887,000 expiring beginning in 2026. As of December 31, 2009, the Company has state research credit carryovers of \$599,000 which will carryforward indefinitely.

Internal Revenue Code section 382 places a limitation, or the Section 382 Limitation, on the amount of taxable income that can be offset by net operating carryforwards after a change in control (generally greater than 50% change in ownership) of a loss corporation. California has similar rules. The Company's capitalization described herein resulted in such a change. Generally, after a control change, a loss corporation cannot deduct operating loss carryforwards in excess of the Section 382 Limitation. Management has determined the impact such limitation may have on the utilization of its operating loss carryforwards against taxable income in future periods.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2007, 2008 and 2009 is as follows (in thousands):

	Year Ended December 31.		
	2007	2008	2009
Unrecognized benefit—beginning of period	\$ 26	\$ 96	\$292
Gross increases—current period tax positions	70	196	203
Unrecognized benefit—end of period	<u>\$96</u>	<u>\$292</u>	<u>\$495</u>

The entire amount of the unrecognized tax benefits would not impact our effective tax rate if recognized.

Accrued interest and penalties related to unrecognized tax benefits are classified as income tax expense and were immaterial. The Company files income tax returns in the United States and in California. The tax years 2005 through 2008 remain open in both jurisdictions. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions.

14. Subsequent Events (unaudited)

Stock Option Modification

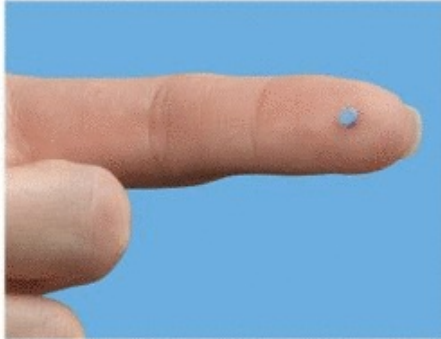
In December 2010, the Company's board of directors allowed all employees and non-employees to increase the exercise price of stock options granted to them on June 15, 2010 in light of the potential risk of adverse tax consequences under Internal Revenue Service Code Section 409A. Based on the elections by the optionees, 1,233,485 of the 1,316,610 options granted on June 15, 2010, including vested and unvested options, were modified 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.

2010 Convertible Notes Amendment

During the first quarter of the year ending December 31, 2011, the 2010 Convertible Notes were amended so that the note holders option to invest the second tranche of \$4.0 million expires upon the closing of an initial public offering by the Company.



Sufentanil NanoTab



ARX-01
Sufentanil NanoTab PCA System



ARX-02
Sufentanil NanoTab BTP Management System



ARX-03
Sufentanil/Triazolam NanoTab



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

5,770,000 Shares

ACELRX PHARMACEUTICALS, INC.

Common Stock



PROSPECTUS

Until and including _____, 2011, all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Sole Book-Running Manager

Piper Jaffray

Canaccord Genuity

Cowen and Company

JMP Securities

, 2011

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the fees and expenses, other than estimated underwriting discounts and commissions, payable in connection with the registration of the common stock hereunder. All amounts are estimates except the SEC registration fee, the FINRA filing fee and the NASDAQ Global Market listing fee.

SEC registration fee	\$ 6,921
FINRA filing fee	9,125
NASDAQ Global Market listing fee	125,000
Blue sky fees and expenses	15,000
Printing and engraving expenses	175,000
Legal fees and expenses	850,000
Accounting fees and expenses	850,000
Transfer agent and registrar fees	9,229
Miscellaneous expenses	—
Total	<u>\$ 2,040,275</u>

Item 14. Indemnification of Directors and Officers

Section 145 of the Delaware General Corporation Law permits a corporation to include in its charter documents, and in agreements between the corporation and its directors and officers, provisions expanding the scope of indemnification beyond that specifically provided by the current law.

The Registrant's amended and restated certificate of incorporation provides for the indemnification of directors to the fullest extent permissible under Delaware law.

The Registrant's amended and restated bylaws provide for the indemnification of officers, directors and third parties acting on the Registrant's behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to the Registrant's best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

The Registrant has entered into indemnification agreements with each of its directors and executive officers, in addition to the indemnification provisions provided for in its charter documents, and the Registrant intends to enter into indemnification agreements with any new directors and executive officers in the future.

The underwriting agreement (filed as Exhibit 1.1 hereto) will provide for indemnification by the underwriters of the Registrant, the Registrant's executive officers and directors, and indemnification of the underwriters by the Registrant for certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, in connection with matters specifically provided in writing by the underwriters for inclusion in the registration statement.

The Registrant intends to purchase and maintain insurance on behalf of any person who is or was a director or officer against any loss arising from any claim asserted against him or her and incurred by him or her in that capacity, subject to certain exclusions and limits of the amount of coverage.

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Item 15. Recent Sales of Unregistered Securities

Since November 1, 2007, the Registrant has issued and sold the following unregistered securities (share amounts and per share amounts have been retroactively adjusted to give effect to a 1-for-4 reverse stock split that became effective on January 28, 2011):

(a) Issuances of Capital Stock

1. In February 2008, the Registrant issued and sold an aggregate of 1,263,635 shares of the Registrant's Series B convertible preferred stock to twelve (12) purchasers at \$16.00 per share for an aggregate consideration of approximately \$20.2 million. Upon completion of this offering, these shares of Series B convertible preferred stock will convert into 1,895,099 shares of the Registrant's common stock.
2. In December 2008, the Registrant issued 2,500 shares of its common stock to one (1) service provider as consideration for services provided to the Registrant.
3. In November 2009, the Registrant issued 3,757,253 shares of the Registrant's Series C convertible preferred stock to eight (8) purchasers at approximately \$3.94 per share, for approximately \$14.8 million. Upon completion of this offering, these shares of Series C convertible preferred stock will convert into 3,757,253 shares of the Registrant's common stock.
4. In January 2010, the Registrant issued 19,275 shares of the Registrant's Series C convertible preferred stock to two (2) purchasers at approximately \$3.94 per share, for approximately \$76,000. Upon completion of this offering, these shares of Series C convertible preferred stock will convert into 19,275 shares of the Registrant's common stock.
5. Between November 1, 2007 and November 12, 2010, the Registrant issued and sold an aggregate of 32,569 shares of its common stock to the Registrant's employees, consultants and directors at prices ranging from \$1.20 to \$5.52 per share pursuant to exercises of options granted under the Registrant's 2006 Stock Plan.

(b) Stock Option Grants and Warrant Issuances

6. Between November 1, 2007 and January 31, 2011, the Registrant granted stock options to purchase an aggregate of 1,899,110 shares of the Registrant's common stock at exercise prices ranging from \$1.20 to \$5.52 per share to a total of 40 employees, consultants and directors of the Registrant under the Registrant's 2006 Stock Plan, of which options to purchase 119,619 shares were cancelled without being exercised. On December 27, 2010, the Registrant amended options to purchase an aggregate of 1,233,485 shares of the Registrant's common stock originally granted to 15 employees on June 15, 2010 to increase the exercise price of these options from \$1.20 per share to \$2.36 per share.
7. In September 2008, in connection with its borrowing under a \$12.0 million loan and security agreement, the Registrant issued a warrant to purchase up to an aggregate of 56,250 shares of the Registrant's Series B convertible preferred stock to the lender at an exercise price of \$16.00 per share. Upon the initial closing of the Registrant's Series C convertible preferred stock financing in November 2009, the warrant became exercisable for 228,264 shares of the Registrant's Series C convertible preferred stock at an exercise price of approximately \$3.94 per share. Upon completion of this offering, these warrants will become warrants to purchase 228,264 shares of the Registrant's common stock at an exercise price of approximately \$3.94 per share.
8. In September 2010, in connection with a bridge loan financing, the Registrant granted warrants to purchase an aggregate of \$2.0 million of its preferred stock to eight

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(8) purchasers. In connection with this offering, these warrants will become warrants to purchase 507,429 shares of the Registrant's Series C convertible preferred stock (convertible into 507,429 shares of the Registrant's common stock) at an exercise price of approximately \$3.94 per share. The warrants will be terminated in the event they are not exercised prior to the closing of this offering.

(c) Issuances of Convertible Promissory Notes

9. In September 2010, in connection with a bridge loan financing, the Registrant issued convertible promissory notes to eight (8) purchasers for an aggregate principal amount of \$8.0 million. Upon completion of this offering, these convertible promissory notes will convert into shares of the Registrant's common stock at a conversion price equal to eighty percent (80%) of the price per share of the Registrant's common stock sold by the Registrant in the offering.

The issuances of securities described above in paragraphs 1 through 5 and 7 through 9 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 the Registrant or had adequate access, through their relationship with the Registrant, to financial statement or non-financial statement information about the Registrant. The sale of these securities was made without general solicitation or advertising.

The issuance of securities described above in paragraph 6 was exempt from registration under the Securities Act, in reliance on Rule 701 of the Securities Act, pursuant to compensatory benefit plans or agreements approved by the Registrant's board of directors.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits.

<u>Exhibit Number</u>	<u>Description of the Document</u>
1.1#	Form of Underwriting Agreement.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, currently in effect.
3.2#	Form of Amended and Restated Certificate of Incorporation of the Registrant to be effective upon the closing of this offering.
3.3#	Bylaws of the Registrant, currently in effect.
3.4#	Form of Amended and Restated Bylaws of the Registrant to be effective upon the closing of this offering.
4.1	Reference is made to Exhibits 3.1 through 3.4.
4.2	Specimen Common Stock Certificate of the Registrant.
4.3#	Amended and Restated Investor's Rights Agreement, among the Registrant and certain of its security holders, dated as of November 23, 2009.

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<u>Exhibit Number</u>	<u>Description of the Document</u>
4.4#	Warrant to Purchase Stock of the Registrant, issued to Wells Fargo Bank, N.A., dated March 15, 2007.
4.5#	Warrant to Purchase Preferred Stock of the Registrant, issued to Pinnacle Ventures II Equity Holdings, L.L.C., dated September 16, 2008.
4.6#	Form of Convertible Promissory Note, dated September 14, 2010.
4.7#	Form of Warrant to Purchase Preferred Stock, dated September 14, 2010.
5.1#	Opinion of Cooley LLP.
10.1+#	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.
10.2+#	2006 Stock Plan, as amended.
10.3+#	Form of Notice of Stock Option and Stock Option Agreement under 2006 Stock Plan for executive officers.
10.4+#	2011 Equity Incentive Plan.
10.5+#	Forms of Stock Option Grant Notice, Stock Option Exercise Notice and Stock Option Agreement under 2011 Equity Incentive Plan.
10.6+#	Form of Restricted Stock Unit Award Agreement under 2011 Equity Incentive Plan.
10.7+#	2011 Employee Stock Purchase Plan.
10.8#	Lease Agreement, between Metropolitan Life Insurance Company and Registrant, dated January 2, 2007.
10.9#	Loan and Security Agreement between Registrant and Pinnacle Ventures, L.L.C., as agent for the Lenders (as defined therein) and the Lenders, dated September 16, 2008.
10.10	Note and Warrant Purchase Agreement between Registrant and the Purchasers defined therein, dated September 14, 2010, as amended.
10.11+#	Founder's Vesting Agreement between Registrant and Pamela Palmer, dated August 16, 2006.
10.12+#	Founder's Vesting Agreement between Registrant and Thomas Schreck, dated August 16, 2006.
10.13+#	Offer Letter between the Registrant and Thomas Schreck, dated August 15, 2006.
10.14+#	Amended and Restated Offer Letter between the Registrant and Larry Hamel, dated December 31, 2010.
10.15+#	Amended and Restated Offer Letter between the Registrant and Badri (Anil) Dasu, dated December 30, 2010.
10.16+#	Amended and Restated Offer Letter between the Registrant and Pamela Palmer, dated December 29, 2010.
10.17+#	Amended and Restated Offer Letter between the Registrant and Richard King, dated December 31, 2010.
10.18+#	Amended and Restated Offer Letter between the Registrant and James Welch, dated December 29, 2010.
10.19+#	Resignation Agreement, between the Registrant and Thomas Schreck, dated May 6, 2010.

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<u>Exhibit Number</u>	<u>Description of the Document</u>
23.1	Consent of Independent Registered Public Accounting Firm.
23.2#	Consent of Cooley LLP (included in Exhibit 5.1).
24.1#	Power of Attorney (included on signature page to this registration statement).

† To be filed by amendment.

+ Indicates management contract or compensatory plan.

Previously filed.

(b) Financial Statement Schedules

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the notes thereto.

Item 17. Undertakings

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933, as amended, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933, as amended, and will be governed by the final adjudication of such issue.

The Registrant hereby undertakes that:

- (a) The Registrant will provide to the underwriters at the closing as specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.
- (b) For purposes of determining any liability under the Securities Act of 1933, as amended, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933, as amended, shall be deemed to be part of this registration statement as of the time it was declared effective.
- (c) For the purpose of determining any liability under the Securities Act of 1933, as amended, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Description of the Document</u>
1.1#	Form of Underwriting Agreement.
3.1	Amended and Restated Certificate of Incorporation of the Registrant, currently in effect.
3.2#	Form of Amended and Restated Certificate of Incorporation of the Registrant to be effective upon the closing of this offering.
3.3#	Bylaws of the Registrant, currently in effect.
3.4#	Form of Amended and Restated Bylaws of the Registrant to be effective upon the closing of this offering.
4.1	Reference is made to Exhibits 3.1 through 3.4.
4.2	Specimen Common Stock Certificate of the Registrant.
4.3#	Amended and Restated Investor's Rights Agreement, among the Registrant and certain of its security holders, dated as of November 23, 2009.
4.4#	Warrant to Purchase Stock of the Registrant, issued to Wells Fargo Bank, N.A., dated March 15, 2007.
4.5#	Warrant to Purchase Preferred Stock of the Registrant, issued to Pinnacle Ventures II Equity Holdings, L.L.C., dated September 16, 2008.
4.6#	Form of Convertible Promissory Note, dated September 14, 2010.
4.7#	Form of Warrant to Purchase Preferred Stock, dated September 14, 2010.
5.1#	Opinion of Cooley LLP.
10.1+#	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.
10.2+#	2006 Stock Plan, as amended.
10.3+#	Form of Notice of Stock Option and Stock Option Agreement under 2006 Stock Plan for executive officers.
10.4+#	2011 Equity Incentive Plan.
10.5+#	Forms of Stock Option Grant Notice, Stock Option Exercise Notice and Stock Option Agreement under 2011 Equity Incentive Plan.
10.6+#	Form of Restricted Stock Unit Award Agreement under 2011 Equity Incentive Plan.
10.7+#	2011 Employee Stock Purchase Plan.
10.8#	Lease Agreement, between Metropolitan Life Insurance Company and Registrant, dated January 2, 2007.
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24.1#	Power of Attorney (included on signature page to this registration statement).

† To be filed by amendment.

+ Indicates management contract or compensatory plan.

Previously filed.

**AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
ACELRX PHARMACEUTICALS, INC.**

The undersigned, Richard King, hereby certifies that:

1. He is the duly elected and acting President and Chief Executive Officer of AcelRx Pharmaceuticals, Inc., a Delaware corporation.
2. The Certificate of Incorporation of this corporation was originally filed with the Secretary of State of Delaware on July 13, 2005. The corporation was originally incorporated under the name of SuRx., Inc.
3. The Certificate of Incorporation of this corporation shall be amended and restated to read in full as follows:

ARTICLE I

The name of this corporation is AcelRx Pharmaceuticals, Inc. (the “Corporation”).

ARTICLE II

The address of the Corporation’s registered office in the State of Delaware is 3500 South Dupont Highway, Dover, County of Kent. The name of its registered agent at such address is Incorporating Services, Ltd.

ARTICLE III

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the Delaware General Corporation Law.

ARTICLE IV

(A) **Classes of Stock.** The Corporation is authorized to issue two classes of stock to be designated, respectively, “Common Stock” and “Preferred Stock.” The total number of shares which the Corporation is authorized to issue is 117,736,125 shares, each with a par value of \$0.001 per share. 71,000,000 shares shall be Common Stock, 46,736,125 shares shall be Preferred Stock.

(B) **Rights, Preferences and Restrictions of Preferred Stock.** The Preferred Stock authorized by this Amended and Restated Certificate of Incorporation (this “Restated Certificate”) may be issued from time to time in one or more series. The first series of Preferred Stock shall be designated “Series A Preferred Stock” and shall consist of 8,456,581 shares. The

second series of Preferred Stock shall be designated “Series B Preferred Stock” and shall consist of 5,279,544 shares. The third series of Preferred Stock shall be designated “Series C Preferred Stock” and shall consist of 33,000,000 shares. The rights, preferences, privileges, and restrictions granted to and imposed on the Preferred Stock are as set forth below in this Article IV(B).

1. **Dividend Provisions.** The holders of shares of Preferred Stock shall be entitled to receive, on a pari passu basis, non-cumulative dividends, out of any assets legally available therefor, prior and in preference to any declaration or payment of any dividend (payable other than in Common Stock or other securities and rights convertible into or entitling the holder thereof to receive, directly or indirectly, additional shares of Common Stock of the Corporation, provided that an adjustment to the respective Conversion Price (as defined below) of such other securities or rights has been made in accordance with Section 4(d)(ii) below) on the Common Stock of the Corporation, at the rate of \$0.80 per share (as adjusted for stock splits, stock dividends, reclassification and the like) per annum on each outstanding share of Series A Preferred Stock, at the rate of \$1.28 per share (as adjusted for stock splits, stock dividends, reclassification and the like) per annum on each outstanding share of Series B Preferred Stock and at a rate of \$0.315424 per share (as adjusted for stock splits, stock dividends, reclassification and the like) per annum on each share of Series C Preferred Stock, payable quarterly when, as and if declared by the Board of Directors of the Corporation (the “Board of Directors”). After payment of such dividends, any additional dividends shall be distributed among the holders of Preferred Stock and Common Stock pro rata based on the number of shares of Common Stock then held by each holder (assuming conversion of all such Preferred Stock into Common Stock).

2. **Liquidation.**

(a) **Preference.** In the event of a Liquidation Transaction (as defined in Section 2(c)(i)), either voluntary or involuntary, the holders of the Preferred Stock shall be entitled to receive, on a pari passu basis, prior and in preference to, any distribution of any of the assets of the Corporation to the holders of Common Stock by reason of their ownership thereof, (i) for the Series A Preferred Stock, an amount per share equal to \$10.00 per share (as adjusted for stock splits, stock dividends, reclassification and the like) for each share of Series A Preferred Stock then held, plus declared but unpaid dividends, (ii) for the Series B Preferred Stock, an amount per share equal to \$16.00 per share (as adjusted for stock splits, stock dividends, reclassification and the like) for each share of Series B Preferred Stock then held, plus declared but unpaid dividends and (iii) for the Series C Preferred Stock, an amount per share equal to \$3.9428 per share (as adjusted for stock splits, stock dividends, reclassification and the like) for each share of Series C Preferred Stock then held, plus declared but unpaid dividends. If, upon the occurrence of such event, the assets and funds thus distributed among the holders of the Preferred Stock shall be insufficient to permit the payment to such holders of the full aforesaid preferential amounts, then the entire assets and funds of the Corporation legally available for distribution shall be distributed ratably among the holders of the Preferred Stock in proportion to the preferential amount each such holder is otherwise entitled to receive.

(b) **Remaining Assets.** Upon the completion of the distribution required by Section 2(a) above, if assets remain in the Corporation, the holders of the Common

Stock of the Corporation shall ratably receive all of the remaining assets of the Corporation based on the number of shares of Common Stock held by each.

(c) **Escrow and Contingency Payments.** In the event of a Liquidation Transaction, if any portion of the consideration payable to the stockholders of the Corporation is placed into escrow and/or is payable to the stockholders of the Corporation subject to contingencies, the transaction documents shall provide that (i) the portion of such consideration that is not placed in escrow and not subject to any contingencies (the “Initial Consideration”) shall be allocated among the holders of capital stock of the Corporation in accordance with Sections 2(a) and 2(b) as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event and (ii) any additional consideration which becomes payable to the stockholders of the Corporation upon release from escrow or satisfaction of contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Sections 2(a) and 2(b) after taking into account the previous payment of the Initial Consideration as part of the same transaction.

(d) **Certain Acquisitions.**

(i) **Deemed Liquidation.** For purposes of this Section 2, a “Liquidation Transaction” shall (A) mean any liquidation, dissolution, or winding up of the Corporation, or (B) be deemed to occur if the Corporation shall sell, convey, exclusively license or otherwise dispose of all or substantially all of its property or business or merge with or into or consolidate with any other corporation, limited liability company or other entity (other than a wholly-owned subsidiary of the Corporation) (the latter Liquidation Transaction, a “Deemed Liquidation”), provided, however, that none of the following shall be considered a Liquidation Transaction: (1) a merger effected exclusively for the purpose of changing the domicile of the Corporation, (2) an equity financing in which the Corporation is the surviving corporation, or (3) a transaction in which the stockholders of the Corporation immediately prior to the transaction own 50% or more of the voting stock of the surviving corporation following the transaction (taking into account only stock of the Corporation held by such stockholders prior to the transaction).

(ii) **Valuation of Consideration.** In the event of a Deemed Liquidation, if the consideration received by the Corporation is other than cash, its value will be deemed its fair market value. Any securities shall be valued as follows:

(A) Securities not subject to investment letter or other similar restrictions on free marketability:

(1) If traded on a securities exchange or The Nasdaq Stock Market (“Nasdaq”), the value shall be based on the formula specified in the definitive agreements for the Liquidation Transaction or, if no such formula exists, then the value of such securities shall be based on a formula approved by the Board of Directors and derived from the closing prices of the securities on such exchange or Nasdaq over a specified time period;

(2) If actively traded over-the-counter, the value shall be based on the formula specified in the definitive agreements for the Liquidation Transaction or, if no such formula exists, then the value of such securities shall be based on a formula approved by the Board of Directors and derived from the closing bid or sales prices (whichever is applicable) of such securities over a specified time period; and

(3) If there is no active public market, the value shall be the fair market value thereof, as determined in good faith by the Board of Directors.

(B) The method of valuation of securities subject to investment letter or other restrictions on free marketability (other than restrictions arising solely by virtue of a stockholder's status as an affiliate or former affiliate) shall be to make an appropriate discount from the market value determined as specified above in Section 2(d)(ii)(A) to reflect the approximate fair market value thereof, as determined in good faith by the Board of Directors.

(iii) **Notice of Liquidation Transaction.** The Corporation shall give each holder of record of Preferred Stock written notice of any impending Liquidation Transaction not later than 10 days prior to the stockholders' meeting called to approve such Liquidation Transaction, or 10 days prior to the closing of such Liquidation Transaction, whichever is earlier, and shall also notify such holders in writing of the final approval of such Liquidation Transaction. The first of such notices shall describe the material terms and conditions of the impending Liquidation Transaction and the provisions of this Section 2, and the Corporation shall thereafter give such holders prompt notice of any material changes. Unless such notice requirements are waived, the Liquidation Transaction shall not take place sooner than 20 days after the Corporation has given the first notice provided for herein or sooner than 20 days after the Corporation has given notice of any material changes provided for herein. Notwithstanding the other provisions of this Restated Certificate, all notice periods or requirements in this Restated Certificate may be shortened or waived, either before or after the action for which notice is required, upon the written consent of the holders of at least sixty percent (60%) of the Preferred Stock that are entitled to such notice rights, voting together as a single class.

(iv) **Effect of Noncompliance.** In the event the requirements of this Section 2(d) are not complied with, the Corporation shall forthwith either cause the closing of the Liquidation Transaction to be postponed until the requirements of this Section 2 have been complied with, or cancel such Liquidation Transaction, in which event the rights, preferences, privileges and restrictions of the holders of Preferred Stock shall revert to and be the same as such rights, preferences, privileges and restrictions existing immediately prior to the date of the first notice referred to in Section 2(d)(iii).

3. **Redemption.** The Preferred Stock is not redeemable at the option of the holder thereof.

4. **Conversion.** The holders of the Preferred Stock shall have conversion rights as follows (the "Conversion Rights"):

(a) **Right to Convert.**

(i) Subject to Section 4(c), each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time after the date of issuance of such share, at the office of the Corporation or any transfer agent for such stock, into such number of fully paid and nonassessable shares of Common Stock as is determined by (i) for the Series A Preferred Stock, dividing \$10.00 by the Conversion Price applicable to such share, determined as hereafter provided, in effect on the date the certificate is surrendered for conversion, (ii) for the Series B Preferred Stock, dividing \$16.00 by the Conversion Price applicable to such share, determined as hereafter provided, in effect on the date the certificate is surrendered for conversion and (iii) for the Series C Preferred Stock, dividing \$3.9428 by the Conversion Price applicable to such share, determined as hereafter provided, in effect on the date the certificate is surrendered for conversion. The initial Conversion Price per share of Series A Preferred Stock shall be \$10.00 (which conversion price shall be adjusted due to the sale of Series C Preferred Stock pursuant to the Series C Preferred Stock Purchase Agreement dated November 23, 2009 (the "Series C Purchase Agreement")). The initial Conversion Price per share of Series B Preferred Stock shall be \$16.00 (which conversion price shall be adjusted due to the sale of Series C Preferred Stock pursuant to the Series C Purchase Agreement). The initial Conversion Price per share of Series C Preferred Stock shall be \$3.9428. All such initial Conversion Prices shall be subject to adjustment as set forth in Section 4(d).

(ii) In connection with a future equity financing event or events in which the Corporation issues and sells equity securities at an original issue price of less than \$3.9428 per share (a "Qualified Financing"), each share of Series C Preferred Stock shall be convertible, at the election of the holders of at least sixty percent (60%) of the then outstanding shares of Series C Preferred Stock (the "Requisite Series C Holders"), into shares of the equity securities issued and sold by the Corporation in the Qualified Financing (the "Next Round Stock") at a conversion ratio of one share of Series C Preferred Stock converting into the number of shares of Next Round Stock equal to \$3.9428 divided by the price per share of the Next Round Stock. The conversion shall be effective at the closing of such Qualified Financing if such conversion has been so elected. The election to convert shares of Series C Preferred Stock into shares of the Next Round Stock shall be made in accordance with, and subject to, the provisions set forth in Section 4(c)(ii). The conversion right of the Series C Preferred Stock under this Section 4(a)(ii) shall terminate at the point when the Corporation has raised gross proceeds in future equity financing events (excluding the first \$15,370,864.84 but including any additional amounts raised pursuant to the Series C Purchase Agreement) in an amount equal to at least \$15,000,000 (the "Gross Raise Amount"). For the avoidance of doubt, in the event that there are multiple Qualified Financings prior to the Corporation raising the Gross Raise Amount, then upon the initial closing of each Qualified Financing, if the Requisite Series C Holders have not yet elected to convert into the Next Round Stock, the Requisite Series C Holders may elect to do so, provided that the Requisite Series C Holders are only entitled to one election pursuant to this Section 4(a)(ii). Upon the election and conversion of the Series C Preferred Stock into the Next Round Stock, the option to convert any shares into Next Round Stock pursuant to this Section 4(a)(ii) shall cease.

(b) **Automatic Conversion.** Each share of Preferred Stock shall automatically be converted into shares of Common Stock at the Conversion Price at the time in effect for such share immediately upon the earlier of (i) except as provided below in Section 4(c), immediately prior to and in connection with the closing of the Corporation's sale of its Common Stock in a firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "Securities Act"), the public offering price of which is not less than \$12.00 (as adjusted for stock splits, stock dividends, reclassification and the like) and which results in aggregate gross cash proceeds to the Corporation of not less than \$30,000,000 (before deduction of underwriting discounts and commissions), or (ii) the date specified by written consent or agreement of the holders of at least 60% of the then outstanding shares of Preferred Stock, voting together as a single class.

(c) **Mechanics of Conversion.**

(i) **Conversion to Common Stock.** Before any holder of Preferred Stock shall be entitled to convert such Preferred Stock into shares of Common Stock, the holder shall surrender the certificate or certificates therefor, duly endorsed (or a reasonably acceptable affidavit and indemnity undertaking in the case of a lost, stolen or destroyed certificate), at the office of the Corporation or of any transfer agent for such series of Preferred Stock, and shall give written notice to the Corporation at its principal corporate office, of the election to convert the same and shall state therein the name or names in which the certificate or certificates for shares of Common Stock are to be issued. The Corporation shall, as soon as practicable thereafter, issue and deliver at such office to such holder of Preferred Stock, or to the nominee or nominees of such holder, a certificate or certificates for the number of shares of Common Stock to which such holder shall be entitled as aforesaid and a certificate for the remaining number of shares of Preferred Stock, as the case may be, if less than all of the Preferred Stock, as the case may be, evidenced by the certificate were surrendered. Such conversion shall be deemed to have been made immediately prior to the close of business on (i) the date of such surrender of the shares of Preferred Stock to be converted or (ii) if applicable, the date of automatic conversion specified in Section 4(b) above, and the person or persons entitled to receive the shares of Common Stock issuable upon such conversion shall be treated for all purposes as the record holder or holders of such shares of public Common Stock as of such date. If the conversion is in connection with an underwritten public offering of securities registered pursuant to the Securities Act the conversion may, at the option of any holder tendering such Preferred Stock for conversion, be conditioned upon the closing with the underwriters of the sale of securities pursuant to such offering, in which event any persons entitled to receive Common Stock upon conversion of such Preferred Stock shall not be deemed to have converted such Preferred Stock until immediately prior to the closing of such sale of securities.

(ii) **Conversion to Next Round Stock.** Unless such notice period is waived by at least sixty percent (60%) of the holders of the Series C Preferred Stock, at least ten (10) business days prior to each initial closing of a Qualified Financing, the Corporation shall provide all holders of Series C Preferred Stock written notice of the Qualified Financing. In order to be eligible to convert shares of Series C Preferred Stock into shares of the Next Round Stock pursuant to Section 4(a)(ii) above, at least five (5) business days prior to such closing of

the Qualified Financing, holders representing at least sixty percent (60%) of the Series C Preferred Stock shall provide written notice to the Corporation and to all other holders of Series C Preferred Stock of the election to convert all shares of Series C Preferred Stock into shares of the Next Round Stock pursuant to Section 4(a)(ii). Each holder of Series C Preferred Stock shall surrender the certificate or certificates therefor, duly endorsed (or a reasonably acceptable affidavit and indemnity undertaking in the case of a lost, stolen or destroyed certificate), at the office of the Corporation or of any transfer agent for such series of Series C Preferred Stock, and provide the Corporation notice of the name or names in which the certificate or certificates for shares of the Next Round Stock are to be issued. Moreover, each holder shall also become a party and subject to all of the agreements and other terms of the Qualified Financing and otherwise agree to execute and deliver such other documents and certificates as are generally requested and provided by other purchasers of Next Round Stock. The Corporation shall, as soon as practicable thereafter and upon compliance of such holder with the requirements of this Section 4(c)(ii), issue and deliver at such office to such holder of such Series C Preferred Stock, or to the nominee or nominees of such holder, a certificate or certificates for the number of shares of the Next Round Stock equal to the number of shares of Series C Preferred Stock as determined pursuant to Section 4(a)(ii) above. Such conversion shall be deemed to have been made immediately prior to the close of business on the later of (i) the date of such surrender of the shares of the Series C Preferred Stock to be converted or (ii) the effective date of conversion specified in Section 4(a)(ii) above, and the person or persons entitled to receive the shares of the Next Round Stock issuable upon such conversion shall be treated for all purposes as the record holder or holders of such shares of the Next Round Stock as of such date. Regardless of whether the holder of Series C Preferred Stock has duly endorsed and surrendered the certificate of certificates therefore, and become a party and subject to all of the agreements and other terms of the Qualified Financing, such holder shall thereafter forfeit any rights associated with such shares of Series C Preferred Stock, including but not limited to conversion rights, liquidation rights and dividend rights, and the sole rights of such holder in connection with such shares of Series C Preferred Stock previously held shall instead be the rights associated with the Next Round Stock.

(d) **Conversion Price Adjustments of Preferred Stock for Certain Dilutive Issuances, Splits and Combinations.** The Conversion Price of the Preferred Stock shall be subject to adjustment from time to time as follows:

(i) **Issuance of Additional Stock below Purchase Price.**

(A) **Adjustment for Series A Preferred Stock or Series B Preferred Stock.**

(1) If the Corporation should issue, at any time after the date upon which any shares of Series C Preferred Stock were first issued (the "Purchase Date"), any Additional Stock (as defined below) without consideration or for a consideration per share less than Conversion Price of the Series A Preferred Stock or Series B Preferred Stock, respectively, in effect immediately prior to the issuance of such Additional Stock, the Conversion Price applicable to Series A Preferred Stock or Series B Preferred Stock in effect immediately prior to each such issuance shall automatically be adjusted as set forth in this Section 4(d)(i)(A), unless otherwise provided in this Section 4(d)(i).

(2) Whenever the Conversion Price of the Series A Preferred Stock or Series B Preferred Stock is adjusted pursuant to this Section 4(d)(i)(A), the new Conversion Price for such series shall be determined by multiplying the Conversion Price then in effect for such series by a fraction, (x) the numerator of which shall be the number of shares of Common Stock outstanding immediately prior to such issuance (the “Outstanding Common”) plus the number of shares of Common Stock that the aggregate consideration received by the Corporation for such issuance would purchase at such applicable Conversion Price; and (y) the denominator of which shall be the number of shares of Outstanding Common plus the number of shares of such Additional Stock. For purposes of the foregoing calculation, the term “Outstanding Common” shall include shares of Common Stock deemed issued pursuant to Section 4(d)(i)(F) below.

(B) **Adjustment for Series C Preferred Stock.**

(1) Until such time as the Corporation has raised the Gross Raise Amount, any issuances or deemed issuances of Additional Stock, after the Purchase Date, for consideration per share less than the Conversion Price of the Series C Preferred Stock in effect on the date and immediately prior to such issuance, shall cause the then existing Conversion Price of the Series C Preferred Stock to forthwith be adjusted to equal the Effective Price (as hereinafter defined).

(2) At any time or from time to time after the Corporation has raised the Gross Raise Amount, any issuances or deemed issuances of Additional Stock, after the Purchase Date, for no consideration or a consideration per share less than the then existing Conversion Price of the Series C Preferred Stock, the new Conversion Price for such series shall be determined by multiplying the Conversion Price then in effect for such series by a fraction, (x) the numerator of which shall be the number of shares of Outstanding Common plus the number of shares of Common Stock that the aggregate consideration received by the Corporation for such issuance would purchase at such Conversion Price; and (y) the denominator of which shall be the number of shares of Outstanding Common plus the number of shares of such Additional Stock. For purposes of the foregoing calculation, the term “Outstanding Common” shall include shares of Common Stock deemed issued pursuant to Section 4(d)(i)(F) below.

(3) The “Effective Price” of Additional Stock for purposes of this Section 4(d)(i)(B) shall mean the quotient determined by dividing the total number of Additional Stock issued or sold, or deemed to have been issued or sold by the Corporation under this Section 4(d)(i), into the Aggregate Consideration (as such term is defined below) received, or deemed to have been received by the Corporation for such Additional Stock. In the event that the number of shares of Additional Stock or the Effective Price cannot be ascertained at the time of issuance, such Additional Stock shall be deemed issued immediately upon the occurrence of the first event that makes such number of shares or the Effective Price, as applicable, ascertainable.

(4) For the purpose of making any adjustment required under this Section 4(d)(i)(B), the aggregate consideration received by the Corporation

for any issue or sale of securities (the “Aggregate Consideration”) shall be defined as: (A) to the extent it consists of cash, be computed at the gross amount of cash received by the Corporation before deduction of any underwriting or similar commissions, compensation or concessions paid or allowed by the Corporation in connection with such issue or sale and without deduction of any expenses payable by the Corporation, (B) to the extent it consists of property other than cash, be computed at the fair value of that property as determined in good faith by the Board of Directors, including at least two of the Preferred Director Representatives then in office, and (C) if (x) Additional Stock, (y) Preferred Stock or other stock, options, warrants, purchase rights or other securities convertible into, Additional Stock (“Convertible Securities”) or (z) rights or options to purchase either Additional Stock or Convertible Securities are issued or sold together with other stock or securities or other assets of the Corporation for a consideration which covers both, be computed as the portion of the consideration so received that may be reasonably determined in good faith by the Board of Directors to be allocable to such Additional Stock, Convertible Securities or rights or options.

(C) **Definition of “Additional Stock”.** For purposes of this Section 4(d)(i), “Additional Stock” shall mean any shares of Common Stock issued (or deemed to have been issued pursuant to Section 4(d)(i)(F)) by the Corporation after the Purchase Date) other than;

(1) Common Stock issued pursuant to stock dividends, stock splits or similar transactions, as described in Section 4(d)(ii) hereof;

(2) Common Stock issued or issuable to employees, officers, consultants or directors of the Corporation or other persons performing services for the Corporation, pursuant to any stock option plan or agreement or other stock incentive program or agreement of the Corporation as may be approved by the Board of Directors, including at least two of the Preferred Director Representatives then in office;

(3) Capital stock, or options or warrants to purchase capital stock, issued to financial institutions or lessors in connection with commercial credit arrangements, equipment financings, commercial property lease transactions or similar transactions, provided such issuances are for other than primarily equity financing purposes and provided further that the terms of which are approved by the Board of Directors, including at least two of the Preferred Director Representatives then in office;

(4) Common Stock or Preferred Stock issuable upon exercise of warrants, notes, or other convertible securities outstanding as of the date of this Restated Certificate;

(5) Common Stock issued upon conversion of the Preferred Stock;

(6) Common Stock issued or issuable in a public offering prior to or in connection with which all outstanding shares of Preferred Stock will be converted to Common Stock; and

(7) Capital stock issued or issuable to an entity as a component of any business relationship with such entity for the purpose of (A) joint venture, technology licensing or development activities, (B) distribution, supply or manufacture of the Corporation's products or services, (C) any equipment loan or leasing arrangement, real property leasing arrangement or debt financing, or (D) a merger or asset purchase with such entity, provided in each case that the terms of such business relationship with such entity are approved by the Board of Directors, including at least two of the Preferred Director Representatives then in office.

(D) **No Fractional Adjustments.** No adjustment of the Conversion Price for the Preferred Stock shall be made in an amount less than one cent per share, provided that any adjustments which are not required to be made by reason of this sentence shall be carried forward and shall be either taken into account in any subsequent adjustment made prior to three years from the date of the event giving rise to the adjustment being carried forward, or shall be made at the end of three years from the date of the event giving rise to the adjustment being carried forward.

(E) **Determination of Consideration.** In the case of the issuance of Common Stock for cash, the consideration shall be deemed to be the amount of cash paid therefor before deducting any reasonable discounts, commissions or other expenses allowed, paid or incurred by the Corporation for any underwriting or otherwise in connection with the issuance and sale thereof. In the case of the issuance of the Common Stock for a consideration in whole or in part other than cash, the consideration other than cash shall be deemed to be the fair value thereof as determined by the Board of Directors irrespective of any accounting treatment.

(F) **Deemed Issuances of Common Stock.** In the case of the issuance (whether before, on or after the applicable Purchase Date) of securities or rights convertible into, or entitling the holder thereof to receive directly or indirectly, additional shares of Common Stock (the "Common Stock Equivalents"), the following provisions shall apply for all purposes of this Section 4(d)(i):

(1) The aggregate maximum number of shares of Common Stock deliverable upon conversion, exchange or exercise (assuming the satisfaction of any conditions to convertibility, exchangeability or exercisability, including, without limitation, the passage of time, but without taking into account potential antidilution adjustments) of any Common Stock Equivalents and subsequent conversion, exchange or exercise thereof shall be deemed to have been issued at the time such securities were issued or such Common Stock Equivalents were issued and for a consideration equal to the consideration, if any, received by the Corporation for any such securities and related Common Stock Equivalents (excluding any cash received on account of accrued interest or accrued dividends), plus the minimum additional consideration, if any, to be received by the Corporation (without taking into account potential antidilution adjustments) upon the conversion, exchange or exercise of any Common Stock Equivalents (the consideration in each case to be determined in the manner provided in Section 4(d)(i)(F)).

(2) In the event of any change in the number of shares of Common Stock deliverable or in the consideration payable to the Corporation upon conversion, exchange or exercise of any Common Stock Equivalents, other than a change resulting from the antidilution provisions thereof, the Conversion Price of the Preferred Stock, to the extent in any way affected by or computed using such Common Stock Equivalents, shall be recomputed to reflect such change, but no further adjustment shall be made for the actual issuance of Common Stock or any payment of such consideration upon the conversion, exchange or exercise of such Common Stock Equivalents.

(3) Upon the termination or expiration of the convertibility, exchangeability or exercisability of any Common Stock Equivalents, the Conversion Price of the Preferred Stock, to the extent in any way affected by or computed using such Common Stock Equivalents, shall be recomputed to reflect the issuance of only the number of shares of Common Stock (and Common Stock Equivalents that remain convertible, exchangeable or exercisable) actually issued upon the conversion, exchange or exercise of such Common Stock Equivalents.

(4) The number of shares of Common Stock deemed issued and the consideration deemed paid therefor pursuant to Section 4(d)(i)(F)(1) shall be appropriately adjusted to reflect any change, termination or expiration of the type described in either Section 4(d)(i)(F)(2) or 4(d)(i)(F)(3).

(G) **No Increased Conversion Price.** Notwithstanding any other provisions of this Section 4(d)(i), except to the limited extent provided for in Sections 4(d)(i)(F)(2) and 4(d)(i)(F)(3), no adjustment of the Conversion Price pursuant to this Section 4(d)(i) shall have the effect of increasing the Conversion Price above the Conversion Price in effect immediately prior to such adjustment.

(ii) **Stock Splits and Dividends.** In the event the Corporation should at any time after the Purchase Date fix a record date for the effectuation of a split or subdivision of the outstanding shares of Common Stock or the determination of holders of Common Stock entitled to receive a dividend or other distribution payable in additional shares of Common Stock or Common Stock Equivalents without payment of any consideration by such holder for the additional shares of Common Stock or the Common Stock Equivalents (including the additional shares of Common Stock issuable upon conversion or exercise thereof), then, as of such record date (or the date of such dividend distribution, split or subdivision if no record date is fixed), the Conversion Price of the Preferred Stock shall be appropriately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase of the aggregate of shares of Common Stock outstanding and those issuable with respect to such Common Stock Equivalents with the number of shares issuable with respect to Common Stock Equivalents determined from time to time in the manner provided for deemed issuances in Section 4(d)(i)(F).

(iii) **Reverse Stock Splits.** If the number of shares of Common Stock outstanding at any time after the Purchase Date is decreased by a combination of the outstanding shares of Common Stock, then, following the record date of such combination, the

Conversion Price of the Preferred Stock shall be appropriately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in outstanding shares.

(e) **Other Distributions.** In the event the Corporation shall declare a distribution (other than a subdivision, combination or merger or sale of assets transaction provided for elsewhere in this Section 4 or in Section 2 of this Article IV(B)) payable in securities of other persons, evidences of indebtedness issued by the Corporation or other persons, assets (excluding cash dividends) or options or rights not referred to in Section 4(d)(i) or 4(d)(ii), then, in each such case for the purpose of this Section 4(e), the holders of the Preferred Stock shall be entitled to a proportionate share of any such distribution as though they were the holders of the number of shares of Common Stock of the Corporation into which their shares of Preferred Stock are convertible as of the record date fixed for the determination of the holders of Common Stock of the Corporation entitled to receive such distribution.

(f) **Recapitalizations.** If at any time or from time to time there shall be a recapitalization of the Common Stock (other than a subdivision, combination or merger or sale of assets transaction provided for elsewhere in this Section 4 or in Section 2 of this Article IV(B)) provision shall be made so that the holders of the Preferred Stock shall thereafter be entitled to receive upon conversion of such Preferred Stock the number of shares of stock or other securities or property of the Corporation or otherwise, to which a holder of Common Stock deliverable upon conversion would have been entitled on such recapitalization. In any such case, appropriate adjustment shall be made in the application of the provisions of this Section 4 with respect to the rights of the holders of such Preferred Stock after the recapitalization to the end that the provisions of this Section 4 (including adjustment of the Conversion Price then in effect and the number of shares purchasable upon conversion of such Preferred Stock) shall be applicable after that event and be as nearly equivalent as practicable.

(g) **No Impairment.** The Corporation will not, through any reorganization, recapitalization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Corporation, but will at all times in good faith assist in the carrying out of all the provisions of this Section 4 and in the taking of all such action as may be necessary or appropriate in order to protect the Conversion Rights of the holders of Preferred Stock against impairment.

(h) **No Fractional Shares and Certificate as to Adjustments.**

(i) No fractional shares shall be issued upon the conversion of any share or shares of the Preferred Stock, and the number of shares of Common Stock to be issued shall be rounded down to the nearest whole share. The number of shares issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the number of shares of Common Stock issuable upon such aggregate conversion. If the conversion would result in any fractional share, the Corporation shall, in lieu of issuing any such fractional share, pay the holder thereof an

amount in cash equal to the fair market value of such fractional share on the date of conversion, as determined in good faith by the Board of Directors.

(ii) Upon the occurrence of each adjustment or readjustment of the Conversion Price of the Preferred Stock pursuant to this Section 4, the Corporation, at its expense, shall promptly compute such adjustment or readjustment in accordance with the terms hereof and prepare and furnish to each holder of such Preferred Stock a certificate setting forth such adjustment or readjustment and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, upon the written request at any time of any holder of Preferred Stock, furnish or cause to be furnished to such holder a like certificate setting forth (A) such adjustment and readjustment, (B) the Conversion Price for the Series A Preferred Stock, the Series B Preferred Stock or the Series C Preferred Stock, as the case may be, at the time in effect, and (C) the number of shares of Common Stock and the amount, if any, of other property which at the time would be received upon the conversion of a share of the Series A Preferred Stock, the Series B Preferred Stock or the Series C Preferred Stock, as the case may be.

(i) **Notices of Record Date.** In the event of any taking by the Corporation of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend (other than a cash dividend) or other distribution, any right to subscribe for, purchase or otherwise acquire any shares of stock of any class or any other securities or property, or to receive any other right, the Corporation shall mail to each holder of Preferred Stock, at least 10 days prior to the date specified therein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend, distribution or right, and the amount and character of such dividend, distribution or right.

(j) **Reservation of Stock Issuable Upon Conversion.** The Corporation shall at all times reserve and keep available out of its authorized but unissued shares of Common Stock, solely for the purpose of effecting the conversion of the shares of the Series A Preferred Stock, the Series B Preferred Stock and the Series C Preferred Stock, such number of its shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding shares of such series of Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of such series of Preferred Stock, in addition to such other remedies as shall be available to the holder of such Preferred Stock, the Corporation will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to this Restated Certificate.

(k) **Notices.** Any notice required by the provisions of this Section 4 to be given to the holders of shares of Preferred Stock shall be deemed given if deposited in the United States mail, postage prepaid, and addressed to each holder of record at his address appearing on the books of the Corporation.

(l) **Waiver of Adjustment to Conversion Price.** Notwithstanding anything herein to the contrary, any downward adjustment of the Conversion Price of any series

of Preferred Stock may be waived, either prospectively or retroactively and either generally or in a particular instance, by the consent or vote of the holders of at least sixty percent (60%) of the outstanding shares of Preferred Stock. Any such waiver shall bind all future holders of shares of such series of Preferred Stock.

5. **Voting Rights.**

(a) Except as expressly provided by this Restated Certificate or as provided by law, the holders of Preferred Stock shall have the same voting rights as the holders of Common Stock and shall be entitled to notice of any stockholders' meeting in accordance with the Bylaws of the Corporation, and the holders of Common Stock and the Preferred Stock shall vote together as a single class on all matters. Each holder of Common Stock shall be entitled to one vote for each share of Common Stock held, and each holder of Preferred Stock shall be entitled to the number of votes equal to the number of shares of Common Stock into which such shares of Preferred Stock could be converted. Fractional votes shall not, however, be permitted and any fractional voting rights available on an as-converted basis (after aggregating all shares into which shares of Preferred Stock held by each holder could be converted) shall be rounded to the nearest whole number (with one-half being rounded upward).

(b) At each meeting of stockholders at which members of the Board of Directors are to be elected, or whenever members of the Board of Directors are to be elected by written consent of the stockholders, (i) the holders of Series A Preferred Stock shall have a right to elect two members of the Board of Directors (the "Series A Director Representatives"); (ii) the holders of Series B Preferred Stock shall have a right to elect one member of the Board of Directors (the "Series B Director Representative") (iii) the holders of a majority of the then outstanding shares of Common Stock, voting as a single class, shall have the right to elect two members of the Board of Directors; and (iv) the holders of a majority of the then outstanding shares of Common Stock, voting as a single class, and the holders of at least sixty percent (60%) of the then outstanding shares of Preferred Stock, voting together as a single class on an as-converted basis, shall have the right to elect the remaining members of the Board of Directors. The Series A Director Representatives and the Series B Director Representative are collectively referred to herein as the "Preferred Director Representatives."

(c) In the case of any vacancy on the Board of Directors occurring because of the death, resignation or removal of a director a successor shall be elected to serve for the unexpired term of the director whose office is vacant by the vote or written consent of the holders of the class or series of shares entitled to elect such director in accordance with the provisions of Section 5(b) above.

6. **Protective Provisions.** So long as at least 125,000 shares of Preferred Stock (subject to adjustment for stock splits, stock dividends, combinations, reclassifications or the like) are outstanding, the Corporation shall not (by amendment, merger, consolidation or otherwise) without first obtaining the approval (by vote or written consent, as provided by law) of the holders of at least at least sixty percent (60%) of the then outstanding shares of Preferred Stock, voting together as a single class on an as converted basis:

-
- (a) amend or waive any provision of the Corporation's Restated Certificate or Bylaws so as to either (i) alter or change the rights, preferences or privileges of the shares of Preferred Stock or (ii) materially and adversely affect the Preferred Stock;
- (b) increase or decrease the total number of authorized shares of the Corporation's Common Stock or Preferred Stock;
- (c) authorize or issue, or obligate itself to issue, any other equity security, including any security (other than Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock) convertible into or exercisable for any equity security, having a preference over, or being on a parity with, the Series C Preferred Stock, with respect to voting (other than the pari passu voting rights of Common Stock), dividends, redemption, conversion or upon liquidation;
- (d) redeem, purchase or otherwise acquire (or pay into or set funds aside for a sinking fund for such purpose) any share or shares of Common Stock; provided, however, that this restriction shall not apply to the repurchase of shares of Common Stock (i) from employees, officers, directors, consultants or other persons performing services for the Corporation or any subsidiary pursuant to agreements under which the Corporation has the option to repurchase such shares at no greater than cost upon the occurrence of certain events, such as the termination of employment, or (ii) through the exercise of any right of first refusal contained in an agreement approved by the Board of Directors;
- (e) effect a Liquidation Transaction;
- (f) change the number of authorized directors; or
- (g) declare or pay a dividend on the Common Stock or the Preferred Stock.

7. **Status of Converted Stock.** In the event any shares of Preferred Stock shall be converted pursuant to Section 4 hereof, the shares so converted shall be cancelled and shall not be issuable by the Corporation. This Restated Certificate shall be appropriately amended to effect the corresponding reduction in the Corporation's authorized capital stock.

(C) **Common Stock.**

1. **Dividend Rights.** Subject to the prior rights of holders of all classes of stock at the time outstanding having prior rights as to dividends, the holders of the Common Stock shall be entitled to receive, when and as declared by the Board of Directors, out of any assets of the Corporation legally available therefor, such dividends as may be declared from time to time by the Board of Directors, subject to a vote by the holders of at least sixty percent (60%) of the outstanding shares of Preferred Stock, voting together as a single class on an as converted basis, to approve such dividends.

2. **Liquidation Rights.** Upon the occurrence of a Liquidation Transaction, the assets of the Corporation shall be distributed as provided in Section 2 of Article IV(B).

3. **Redemption.** The Common Stock is not redeemable at the option of the holder thereof.

4. **Voting Rights.** Each holder of Common Stock shall have the right to one vote per share of Common Stock, and shall be entitled to notice of any stockholders' meeting in accordance with the Bylaws of the Corporation, and shall be entitled to vote upon such matters and in such manner as may be provided by law. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of shares of stock representing a majority of the votes represented by all outstanding shares of stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the Delaware General Corporation Law.

(D) **Reverse Stock Split.** Effective immediately, (i) each four (4) outstanding shares of the Corporation's Common Stock shall be combined and reconstituted as one (1) share of the Corporation's outstanding Common Stock, (ii) each four (4) outstanding shares of the Corporation's Series A Preferred Stock shall be combined and reconstituted as one (1) share of the Corporation's outstanding Series A Preferred Stock, (iii) each four (4) outstanding shares of the Corporation's Series B Preferred Stock shall be combined and reconstituted as one (1) share of the Corporation's outstanding Series B Preferred Stock and (iv) each four (4) outstanding shares of the Corporation's Series C Preferred Stock shall be combined and reconstituted as one (1) share of the Corporation's outstanding Series C Preferred Stock, (collectively, the "**Reverse Stock Split**"); provided, that all shares of Common Stock held by each holder shall be aggregated immediately prior to the effectiveness of the Reverse Stock Split; provided further, that all shares of a series of Preferred Stock held by each holder shall be aggregated immediately prior to the effectiveness of the Reverse Stock Split; provided further, that if the Reverse Stock Split would result in any fractional share, the Corporation shall, in lieu of issuing any such fractional share, pay the holder thereof an amount in cash equal to the fair market value of such fractional share on the effective date of the Reverse Stock Split as determined in good faith by the Corporation's Board of Directors. The Reverse Stock Split shall occur whether or not the certificates representing such shares of Common Stock or Preferred Stock are surrendered to the Corporation or its transfer agent; provided however, that the Corporation shall not be obligated to issue certificates evidencing the shares resulting from the Reverse Stock Split unless either the certificates evidencing such shares of Common Stock or Preferred Stock are delivered to the Corporation or its transfer agent as provided above, or the holder notifies the Corporation or its transfer agent that such certificates have been lost, stolen or destroyed and executes an agreement satisfactory to the Corporation to indemnify the Corporation from any loss incurred by it in connection with such certificates. Notwithstanding the foregoing, the par value of each share of the Corporation's outstanding Common Stock and Preferred Stock will not be adjusted in connection with the Reverse Stock Split. All share amounts, dollar amounts and other provisions in this Amended and Restated Certificate of Incorporation have been appropriately adjusted to reflect the Reverse Stock Split, and no further adjustments shall be made to the share amounts, dollar amounts and other provisions, except in the case of any stock splits, reverse splits, recapitalization and the like occurring after the effective time of the Reverse Stock Split.

ARTICLE V

The Board of Directors of the Corporation is expressly authorized to make, alter or repeal Bylaws of the Corporation.

ARTICLE VI

Elections of directors need not be by written ballot unless otherwise provided in the Bylaws of the Corporation.

ARTICLE VII

(A) To the fullest extent permitted by the Delaware General Corporation Law, as the same exists or as may hereafter be amended, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director.

(B) The Corporation shall indemnify to the fullest extent permitted by law any person made or threatened to be made a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact that he, his testator or intestate is or was a director or officer of the Corporation or any predecessor of the Corporation, or serves or served at any other enterprise as a director or officer at the request of the Corporation or any predecessor to the Corporation.

(C) Neither any amendment nor repeal of this Article VII, nor the adoption of any provision of the Corporation's Certificate of Incorporation inconsistent with this Article VII, shall eliminate or reduce the effect of this Article VII in respect of any matter occurring, or any action or proceeding accruing or arising or that, but for this Article VII, would accrue or arise, prior to such amendment, repeal or adoption of an inconsistent provision."

* * *

The foregoing Amended and Restated Certificate of Incorporation has been duly adopted by this corporation's Board of Directors and stockholders in accordance with the applicable provisions of Sections 228, 242 and 245 of the Delaware General Corporation Law.

Executed at Palo Alto, California, on January 28, 2011.

/s/ Richard King
Richard King
President and Chief Executive Officer

AcelRx
Pharmaceuticals, Inc.
AcelRx Pharmaceuticals, Inc.
INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

MR. SAMPLE & MRS. SAMPLE & MRS. SAMPLE

***** ZERO HUNDRED THOUSAND ZERO HUNDRED AND ZERO *****

FULLY-PAID AND NON-ASSESSABLE SHARES OF THE COMMON STOCK OF
AcelRx Pharmaceuticals, Inc. (hereinafter called the "Company"), transferable on the books of the Company in person or by duly authorized attorney, upon surrender of this Certificate properly endorsed. This Certificate and the shares represented hereby, are issued and shall be held subject to all of the provisions of the Certificate of Incorporation, as amended, and the By-Laws, as amended, of the Company (copies of which are on file with the Company and with the Transfer Agent), to all of which each holder, by acceptance hereof, assents. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

Witness the facsimile seal of the Company and the facsimile signatures of its duly authorized officers.

FACSIMILE SIGNATURE TO COME
President and Chief Executive Officer

FACSIMILE SIGNATURE TO COME
Chief Financial Officer

DATED *<Subject Only>*
COUNTERSIGNED AND REGISTERED BY:
COMPUTERSHARE TRUST COMPANY, N.A.
TRANSFER AGENT AND REGISTRAR

BY: _____
AUTHORIZED SIGNATURE

SEAL
ACELRX PHARMACEUTICALS, INC.
AND AREA
DELAWARE

SECURITY INSTRUCTIONS ON REVERSE

COMMON STOCK
PAR VALUE \$0.001

COMMON STOCK
THIS CERTIFICATE IS TRANSFERABLE IN ANY STATE OF NEW YORK, NY

Certificate Number
ZQ 000000

Shares
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CUSIP: 00441F 10-0
SEE REVERSE FOR CERTAIN DEFINITIONS

016570J 003590127C;RESTRICTED;4057-423

1234567

AcelRx
Pharmaceuticals, Inc.

PO BOX 43004, Providence, RI 02940-3004

MR A SAMPLE
DESIGNATION (IF ANY)
ADD 1
ADD 2
ADD 3
ADD 4



CUSIP	XXXXXXXX XX X
Holder ID	XXXXXXXXXXXX
Insurance Value	1,000,000.00
Number of Shares	123456
DTC	12345678 123456789012345
Certificate Numbers	Num/No. Denom. Total
1234567890/1234567890	1 1 1
1234567890/1234567890	2 2 2
1234567890/1234567890	3 3 3
1234567890/1234567890	4 4 4
1234567890/1234567890	5 5 5
1234567890/1234567890	6 6 6
Total Transaction	7

AcelRx Pharmaceuticals, Inc.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS, A SUMMARY OF THE POWERS, DESIGNATIONS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OF THE COMPANY AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND RIGHTS, AND THE VARIATIONS IN RIGHTS, PREFERENCES AND LIMITATIONS DETERMINED FOR EACH SERIES, WHICH ARE FIXED BY THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED, THE RESOLUTIONS OF THE BOARD OF DIRECTORS OF THE COMPANY AND THE AUTHORITY OF THE BOARD OF DIRECTORS TO DETERMINE VARIATIONS FOR FUTURE SERIES. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:			
TEN COM	- as tenants in common	UNIF GIFT MIN ACT - Custodian (Cust) (Minor)
TEN ENT	- as tenants by the entireties		under Uniform Gifts to Minors Act (State)
JT TEN	- as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT - Custodian (until age (Cust) (Minor) under Uniform Transfers to Minors Act (State)
Additional abbreviations may also be used though not in the above list.			

For value received, _____ hereby sell, assign and transfer unto _____
 PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____ Shares
 of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Attorney
 to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20 _____
 Signature: _____
 Signature: _____
 Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp
 THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17Ad-15.

The IRS requires that we report the cost basis of certain shares acquired after January 1, 2011. If your shares were covered by the legislation and you have sold or transferred the shares and requested a specific cost basis calculation method, we have processed as requested. If you did not specify a cost basis calculation method, we have defaulted to the first in, first out (FIFO) method. Please visit our website or consult your tax advisor if you need additional information about cost basis.
 If you do not keep in contact with us or do not have any activity in your account for the time periods specified by state law, your property could become subject to state unclaimed property laws and transferred to the appropriate state.

SECURITY INSTRUCTIONS
 THIS IS WATERMARKED PAPER. DO NOT ACCEPT WITHOUT NOTING WATERMARK. HOLD TO LIGHT TO VERIFY WATERMARK.



1534201

ACELRX PHARMACEUTICALS, INC.

NOTE AND WARRANT PURCHASE AGREEMENT

THIS NOTE AND WARRANT PURCHASE AGREEMENT (the "*Agreement*") is made as of the 14th day of September, 2010 (the "*Effective Date*") by and among ACELRX PHARMACEUTICALS, INC., a Delaware corporation (the "*Company*"), and the persons and entities named on the Schedule of Purchasers attached hereto as EXHIBIT A (individually, a "*Purchaser*" and collectively, the "*Purchasers*").

RECITAL

WHEREAS, to provide the Company with additional resources to conduct its business, the Purchasers are willing to loan to the Company up to an aggregate amount of up to twelve million dollars (\$12,000,000), subject to the conditions specified herein.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing, and the representations, warranties, covenants and conditions set forth below, the Company and each Purchaser, intending to be legally bound, hereby agree as follows:

1. AMOUNT AND TERMS OF THE LOAN(S); ISSUANCE OF WARRANTS

1.1 The Loan(s). Subject to the terms of this Agreement, each Purchaser agrees to lend to the Company the amount set forth opposite each such Purchaser's name on EXHIBIT A hereto (each, a "*Loan Amount*" and collectively the "*Total Loan Amount*" or "*Loan*") against the issuance and delivery by the Company of a convertible promissory note or notes for such amount(s), in substantially the form attached hereto as EXHIBIT B (each, a "*Note*" and collectively, the "*Notes*"). Each Note shall be convertible into shares of Equity Securities as provided in such Note.

1.2 Issuance of Warrants. At each Closing (as defined below), the Company shall issue and sell to each Purchaser, and each Purchaser shall purchase from the Company, a warrant in substantially the form attached hereto as EXHIBIT C (each, a "*Warrant*" and collectively the "*Warrants*") for a purchase price equal to one hundredth of one percent (0.01%) of the principal amount of the Note issued at such Closing (the "*Warrant Purchase Price*"). Each Warrant will be exercisable for the number of shares of preferred stock (rounded to the nearest whole share) at the exercise price as provided for in such Warrant. The shares of preferred stock issuable upon exercise of the Warrants are hereinafter referred to as the "*Warrant Shares*".

1.3 The Company and the Purchasers, as a result of arm's length bargaining, agree that:

- (a) Neither the Purchasers nor any affiliated company has rendered any services to the Company in connection with this Agreement;
- (b) The Warrants are not being issued as compensation;
- (c) The aggregate fair market value of the Notes, if issued apart from the Warrants, is equal to the Total Loan Amount; and the aggregate fair market value of the Warrants, if issued apart from the Notes, is equal to the aggregate Warrant Purchase Price for all Warrants issued in accordance with the terms of this Agreement; and

(d) All tax returns and other information return of each party relative to this Agreement and the Notes and Warrants issued pursuant hereto shall consistently reflect the matters agreed to in (a) through (c) above.

2. THE CLOSING(S)

2.1 Closing Date(s). The initial closing of the sale and purchase of the Notes and Warrants (the “*Initial Closing*”) shall be held on the Effective Date, or at such other time as the Company and a majority in interest of the Purchasers shall agree. The portion of the Loan Amount to be funded by each Purchaser at the Initial Closing is set forth on the Schedule of Purchasers hereto.

2.2 Second Closing. At any time on or before one hundred eighty (180) days following the Initial Closing or at such later time as the Requisite Holders (as hereinafter defined) may mutually agree, and upon receipt of the written election of the Requisite Holders, the Company shall issue up to the balance of the authorized Notes and Warrants not sold at the Initial Closing pursuant to this Agreement to Purchasers in their respective amounts as indicated in the Schedule of Purchasers under the heading “Second Closing” (the “*Second Closing*,” together with the Initial Closing, the “*Closings*” and each a “*Closing*”). Notwithstanding the above, in the event that the Company is contemplating a Deemed Liquidation (as such term is defined in the Company’s Amended and Restated Certificate of Incorporation) of the Company, the consent of the Company must also be obtained in order for the Second Closing to occur. For all sales made at the Second Closing (i) such sales shall be made on the terms and conditions set forth in this Agreement, (ii) the representations and warranties of the Company set forth in Section 3 hereof shall speak as of the Second Closing, except for the representations and warranties contained in Section 3.6, which shall speak only as of the Initial Closing, and (iii) the representations and warranties of the Purchasers in Section 4 hereof shall speak as of such Second Closing.

2.3 Delivery. At each Closing (i) each Purchaser shall deliver to the Company a check or wire transfer funds in the amount of such Purchaser’s portion of the Loan Amount funded at such Closing plus the applicable Warrant Purchase Price and (ii) the Company shall issue and deliver to each Purchaser (a) a Note in favor of such Purchaser payable in the principal amount of such Purchaser’s portion of the Loan Amount funded at such Closing and (b) a corresponding Warrant, as specified in Section 1.2.

3. REPRESENTATIONS, WARRANTIES AND COVENANTS OF THE COMPANY

The Company hereby represents and warrants to each Purchaser as follows:

3.1 Organization, Good Standing and Qualification . The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware. The Company has the requisite corporate power to own and operate its properties and assets and to carry on its business as now conducted and as proposed to be conducted. The Company is duly qualified and is authorized to do business and is in good standing as a foreign corporation in all jurisdictions in which the nature of its activities and of its properties (both owned and leased) makes such qualification necessary, except for those jurisdictions in which failure to do so would not have a material adverse effect on the Company or its business.

3.2 Corporate Power. The Company has all requisite corporate power to execute and deliver this Agreement, to issue each Note, to issue each Warrant (collectively, the “*Loan Documents*”) and to carry out and perform its obligations under the terms of this Agreement and under the terms of each Note and each Warrant. The Company’s Board of Directors has approved the Loan Documents

based upon a reasonable belief that the Loan is appropriate for the Company after reasonable inquiry concerning the Company's financing objectives and financial situation.

3.3 Authorization. All corporate action on the part of the Company, its directors and its stockholders necessary for the authorization, execution, delivery and performance of this Agreement by the Company and the performance of the Company's obligations hereunder, including the issuance and delivery of the Notes and Warrants and the reservation of the equity securities issuable upon conversion of the Notes and exercise of the Warrants (collectively, the "**Conversion Securities**") has been taken or will be taken prior to the issuance of such Conversion Securities. This Agreement, the Notes and the Warrants, when executed and delivered by the Company, shall constitute valid and binding obligations of the Company enforceable in accordance with their terms, subject to laws of general application relating to bankruptcy, insolvency, the relief of debtors and, with respect to rights to indemnity, subject to federal and state securities laws. The Conversion Securities, when issued in compliance with the provisions of this Agreement, the Notes and the Warrants will be validly issued, fully paid and nonassessable and free of any liens or encumbrances and issued in compliance with all applicable federal and securities laws.

3.4 Governmental Consents. All consents, approvals, orders, or authorizations of, or registrations, qualifications, designations, declarations, or filings with, any governmental authority, required on the part of the Company in connection with the valid execution and delivery of this Agreement, the offer, sale or issuance of the Notes, the Warrants and the Conversion Securities issuable upon conversion of the Notes, the exercise of the Warrants or the consummation of any other transaction contemplated hereby shall have been obtained and will be effective at the Closing.

3.5 Compliance with Laws. To its knowledge, the Company is not in violation of any applicable statute, rule, regulation, order or restriction of any domestic or foreign government or any instrumentality or agency thereof in respect of the conduct of its business or the ownership of its properties, which violation of which would materially and adversely affect the business, assets, liabilities, financial condition, operations or prospects of the Company.

3.6 Compliance with Other Instruments. The Company is not in violation or default of any term of its certificate of incorporation or bylaws, or of any provision of any mortgage, indenture or contract to which it is a party and by which it is bound or of any judgment, decree, order or writ, other than such violation(s) that would not have a material adverse effect on the Company. The execution, delivery and performance of this Agreement, the Notes and the Warrants, and the consummation of the transactions contemplated hereby or thereby will not result in any such violation or be in conflict with, or constitute, with or without the passage of time and giving of notice, either a default under any such provision, instrument, judgment, decree, order or writ or an event that results in the creation of any lien, charge or encumbrance upon any assets of the Company or the suspension, revocation, impairment, forfeiture, or nonrenewal of any material permit, license, authorization or approval applicable to the Company, its business or operations or any of its assets or properties. Without limiting the foregoing, the Company has obtained all waivers reasonably necessary with respect to any preemptive rights, rights of first refusal or similar rights, including any notice or offering periods provided for as part of any such rights, in order for the Company to consummate the transactions contemplated hereunder without any third party obtaining any rights to cause the Company to offer or issue any securities of the Company as a result of the consummation of the transactions contemplated hereunder.

3.7 Offering. Assuming the accuracy of the representations and warranties of the Purchasers contained in Section 4 hereof, the offer, issue, and sale of the Notes and the Warrants and the Conversion Securities are and will be exempt from the registration and prospectus delivery requirements of the Securities Act of 1933, as amended (the "**Securities Act**"), and have been registered or qualified (or are

exempt from registration and qualification) under the registration, permit, or qualification requirements of all applicable state securities laws.

4. REPRESENTATIONS AND WARRANTIES OF THE PURCHASERS

4.1 Purchase for Own Account. Each Purchaser represents that it is acquiring the Notes, the Warrants and the Conversion Securities (collectively, the “*Securities*”) solely for its own account and beneficial interest for investment and not for sale or with a view to distribution of the Securities or any part thereof, has no present intention of selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the same, and does not presently have reason to anticipate a change in such intention.

4.2 Information and Sophistication. Without lessening or obviating the representations and warranties of the Company set forth in Section 3, each Purchaser hereby: (i) acknowledges that it has received all the information it has requested from the Company and it considers necessary or appropriate for deciding whether to acquire the Securities, (ii) represents that it has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of the Securities and to obtain any additional information necessary to verify the accuracy of the information given the Purchaser and (iii) further represents that it has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risk of this investment.

4.3 Ability to Bear Economic Risk. Each Purchaser acknowledges that investment in the Securities involves a high degree of risk, and represents that it is able, without materially impairing its financial condition, to hold the Securities for an indefinite period of time and to suffer a complete loss of its investment.

4.4 Further Limitations on Disposition. Without in any way limiting the representations set forth above, each Purchaser further agrees not to make any disposition of all or any portion of the Securities unless and until:

(a) There is then in effect a Registration Statement under the Securities Act covering such proposed disposition and such disposition is made in accordance with such Registration Statement; or

(b) The Purchaser shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and if reasonably requested by the Company, such Purchaser shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, that such disposition will not require registration under the Securities Act or any applicable state securities laws, provided that no such opinion shall be required for dispositions in compliance with Rule 144 promulgated under the Securities Act, except in unusual circumstances.

(c) Notwithstanding the provisions of paragraphs (a) and (b) above, no such registration statement or opinion of counsel shall be necessary for a transfer by such Purchaser to a partner (or retired partner) or member (or retired member) of such Purchaser in accordance with partnership or limited liability company interests, or transfers by gift, will or intestate succession to any spouse or lineal descendants or ancestors, if all transferees agree in writing to be subject to the terms hereof to the same extent as if they were Purchasers hereunder.

4.5 Accredited Investor Status. Each Purchaser is an “accredited investor” as such term is defined in Rule 501 under the Securities Act.

4.6 Foreign Investor. If the Purchaser is not a United States person (as defined by Section 7701(a)(30) of the Internal Revenue Code of 1986, as amended), the Purchaser hereby represents that it has satisfied itself as to the full observance of the laws of its jurisdiction in connection with any invitation to subscribe for the Securities or any use of this Agreement, including (i) the legal requirements within its jurisdiction for the purchase of the Securities, (ii) any foreign exchange restrictions applicable to such purchase, (iii) any governmental or other consents that may need to be obtained, and (iv) the income tax and other tax consequences, if any, that may be relevant to the purchase, holding, redemption, sale, or transfer of the Securities. The Purchaser's subscription and payment for and continued beneficial ownership of the Securities will not violate any applicable securities or other laws of the Purchaser's jurisdiction.

4.7 Further Assurances. Each Purchaser agrees and covenants that at any time and from time to time it will promptly execute and deliver to the Company such further instruments and documents and take such further action as the Company may reasonably require in order to carry out the full intent and purpose of this Agreement and to comply with state or federal securities laws or other regulatory approvals.

5. MARKET STANDOFF AGREEMENT

Each Purchaser hereby agrees that such Purchaser shall not sell, transfer, make any short sale of, grant any option for the purchase of, or enter into any hedging or similar transaction with the same economic effect as a sale, any common stock (or other securities) of the Company held by such Purchaser (other than those included in the registration) for a period specified by the representative of the underwriters of common stock (or other securities) of the Company not to exceed one hundred eighty (180) days following the effective date of a registration statement of the Company filed under the Securities Act (or such longer period, not to exceed eighteen (18) days after the expiration of the one hundred eighty (180) day period, as the underwriters or the Company shall request in order to facilitate compliance with FINRA Rule 2711); *provided that*:

(a) such agreement shall apply only to the Company's first firm commitment underwritten public offering of its common stock registered under the Securities Act; and

(b) all officers and directors of the Company enter into similar agreements.

The Company agrees to use all reasonable efforts to ensure that the "lock-up" obligation of the Purchasers under this Section 5, and any agreement entered into by the Purchasers as a result of their obligations under this Section 5, shall provide that all Purchasers will participate on a pro-rata basis in any early release of portions of the securities of any stockholder subject to such "lock-up" obligations.

6. MISCELLANEOUS

6.1 Binding Agreement. The terms and conditions of this Agreement shall inure to the benefit of and be binding upon the respective successors and assigns of the parties. Nothing in this Agreement, expressed or implied, is intended to confer upon any third party any rights, remedies, obligations, or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement.

6.2 Governing Law. This Agreement shall be governed by and construed under the laws of the State of California as applied to agreements among California residents, made and to be performed entirely within the State of California, without giving effect to conflicts of laws principles.

6.3 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

6.4 Titles and Subtitles. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

6.5 Notices. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed telex, electronic mail or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the Company at the address set forth on the signature page hereto, and to Purchaser at the address(es) set forth on the Schedule of Purchasers attached hereto or at such other address(es) as the Company or Purchaser may designate by ten (10) days advance written notice to the other parties hereto.

6.6 Modification; Waiver. No modification or waiver of any provision of this Agreement or consent to departure therefrom shall be effective unless in writing and approved by the Company and the holders of a majority of the aggregate principal amount payable under all the Notes outstanding (such holders being the “*Requisite Holders*”). Any provision of the Notes or Warrants may be amended or waived by the written consent of the Company and Requisite Holders.

6.7 Expenses. The Company and each Purchaser shall each bear its respective expenses and legal fees incurred with respect to this Agreement and the transactions contemplated herein, except that, the Company shall pay the reasonable, documented legal fees and expenses incurred by (a) Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP in its capacity as counsel for certain of the Purchasers, not to exceed seventeen thousand dollars (\$17,000) and (b) special counsel to Kaiser Permanente Ventures, not to exceed three thousand dollars (\$3,000).

6.8 Waiver of Conflicts. Each party to this Agreement acknowledges that Cooley LLP (“*Cooley*”), outside general counsel to the Company, has in the past performed and is or may now or in the future represent one or more Purchasers or their affiliates in matters unrelated to the transactions contemplated by this Agreement (the “*Bridge Financing*”), including representation of such Purchasers or their affiliates in matters of a similar nature to the Bridge Financing. The applicable rules of professional conduct require that Cooley inform the parties hereunder of this representation and obtain their consent. Cooley has served as outside general counsel to the Company and has negotiated the terms of the Bridge Financing solely on behalf of the Company. The Company and each Purchaser hereby (a) acknowledge that they have had an opportunity to ask for and have obtained information relevant to such representation, including disclosure of the reasonably foreseeable adverse consequences of such representation; (b) acknowledge that with respect to the Bridge Financing, Cooley has represented solely the Company, and not any Purchaser or any stockholder, director or employee of the Company or any Purchaser; and (c) gives its informed consent to Cooley’s representation of the Company in the Bridge Financing.

6.9 Delays or Omissions. It is agreed that no delay or omission to exercise any right, power or remedy accruing to each Purchaser, upon any breach or default of the Company under this Agreement or any Note, or Warrant shall impair any such right, power or remedy, nor shall it be construed to be a waiver of any such breach or default, or any acquiescence therein, or of or in any similar breach or default thereafter occurring; nor shall any waiver of any single breach or default be deemed a waiver of any other breach or default theretofore or thereafter occurring. It is further agreed that any waiver, permit, consent or approval of any kind or character by Purchaser of any breach or default under this Agreement, or any

waiver by any Purchaser of any provisions or conditions of this Agreement must be in writing and shall be effective only to the extent specifically set forth in writing and that all remedies, either under this Agreement, or by law or otherwise afforded to the Purchaser, shall be cumulative and not alternative.

6.10 Entire Agreement. This Agreement and the Exhibits hereto constitute the full and entire understanding and agreement between the parties with regard to the subjects hereof and no party shall be liable or bound to any other party in any manner by any representations, warranties, covenants and agreements except as specifically set forth herein.

[SIGNATURE PAGES FOLLOW]

IN WITNESS WHEREOF, the parties have executed this NOTE AND WARRANT PURCHASE AGREEMENT as of the date first written above.

COMPANY:

ACELRX PHARMACEUTICALS, INC.

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

Address: 575 Chesapeake Drive
Redwood City, CA 94063

**SIGNATURE PAGE TO ACELRX PHARMACEUTICALS, INC.
NOTE AND WARRANT PURCHASE AGREEMENT**

PURCHASER:

**THREE ARCH PARTNERS III, L.P.
BY THREE ARCH MANAGEMENT III, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan

Mark Wan
Managing Member

**THREE ARCH ASSOCIATES III, L.P.
BY THREE ARCH MANAGEMENT III, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan

Mark Wan
Managing Member

**THREE ARCH PARTNERS IV, L.P.
BY THREE ARCH MANAGEMENT IV, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan

Mark Wan
Managing Member

**THREE ARCH ASSOCIATES IV, L.P.
BY THREE ARCH MANAGEMENT IV, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan

Mark Wan
Managing Member

PURCHASER:

Skyline Venture Partners Qualified Purchaser Fund
IV, L.P.

By: Skyline Venture Management IV, LLC
Its: General Partner

By: /s/ John G. Freund

Name: John G. Freund

Its: Managing Director

**SIGNATURE PAGE TO ACELRX PHARMACEUTICALS, INC.
NOTE AND WARRANT PURCHASE AGREEMENT**

PURCHASER:

ACP IV, L.P.
By: ACMP IV, LLC.
Its: General Partner

By: /s/ Hilary Strain
Chief Financial Officer

**SIGNATURE PAGE TO ACELRX PHARMACEUTICALS, INC.
NOTE AND WARRANT PURCHASE AGREEMENT**

PURCHASER:

Kaiser Foundation Hospitals

By: /s/ Thomas Meier

Name: Thomas Meier

Title: SVP & Treasurer

The Permanente Federation LLC – Series I

By: /s/ Glen Hentges

Name: Glen Hentges

Title: CFO

**SIGNATURE PAGE TO ACELRX PHARMACEUTICALS, INC.
NOTE AND WARRANT PURCHASE AGREEMENT**

EXHIBIT A
SCHEDULE OF PURCHASERS

INITIAL CLOSING – SEPTEMBER 14, 2010

<u>NAME AND ADDRESS</u>	<u>LOAN AMOUNT</u>	<u>WARRANT PURCHASE PRICE</u>	<u>TOTAL AGGREGATE PURCHASE PRICE</u>
THREE ARCH PARTNERS III, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$1,799,869.22	\$179.99	\$1,800,049.21
THREE ARCH ASSOCIATES III, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$96,767.17	\$9.68	\$96,776.85
THREE ARCH PARTNERS IV, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$1,855,663.23	\$185.57	\$1,855,848.80
THREE ARCH ASSOCIATES IV, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$40,973.37	\$4.10	\$40,977.47
SKYLINE VENTURE PARTNERS QUALIFIED PURCHASER FUND IV, L.P. 525 University Avenue Suite 520 Palo Alto, CA 94301 Fax Number: (650) 329-1090 Attention: Stephen J. Sullivan	\$1,977,503.11	\$197.76	\$1,977,700.87
ACP IV, L.P. One Embarcadero Center Suite 3700 San Francisco, CA 94111 Fax Number: (415) 362-6178 Attention: Guy P. Nohra	\$1,742,043.52	\$174.21	\$1,742,217.73

<u>NAME AND ADDRESS</u>	<u>LOAN AMOUNT</u>	<u>WARRANT PURCHASE PRICE</u>	<u>TOTAL AGGREGATE PURCHASE PRICE</u>
KAISER FOUNDATION HOSPITALS One Kaiser Plaza 22 nd Floor Oakland, CA 94612 Fax Number: (510) 891-7943 Attention: Chris M. Grant	\$243,590.07	\$24.36	\$243,614.43
THE PERMANENTE FEDERATION LLC – SERIES I One Kaiser Plaza 22 nd Floor Oakland, CA 94612 Fax Number: (510) 891-7943 Attention: Chris M. Grant	\$243,590.31	\$24.36	\$243,614.67
TOTAL:	<u>\$8,000,000.00</u>	<u>\$800.03</u>	<u>\$8,000,800.03</u>

SECOND CLOSING – _____, 2010

<u>NAME AND ADDRESS</u>	<u>COMMITTED LOAN AMOUNT</u>	<u>COMMITTED WARRANT PURCHASE PRICE</u>	<u>TOTAL COMMITTED AGGREGATE PURCHASE PRICE</u>
THREE ARCH PARTNERS III, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$899,934.60	\$90.00	\$900,024.60
THREE ARCH ASSOCIATES III, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$48,383.58	\$4.84	\$ 48,388.42
THREE ARCH PARTNERS IV, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$927,831.62	\$92.79	\$927,924.41
THREE ARCH ASSOCIATES IV, L.P. 3200 Alpine Road Portola Valley, CA 94208 Fax Number: (650) 529-8039 Attention: Stephen J. Bonelli	\$20,486.69	\$2.05	\$20,488.74
SKYLINE VENTURE PARTNERS QUALIFIED PURCHASER FUND IV, L.P. 525 University Avenue Suite 520 Palo Alto, CA 94301 Fax Number: (650) 329-1090 Attention: Stephen J. Sullivan	\$988,751.55	\$98.88	\$988,850.43
ACP IV, L.P. One Embarcadero Center Suite 3700 San Francisco, CA 94111 Fax Number: (415) 362-6178 Attention: Guy P. Nohra	\$871,021.76	\$87.11	\$871,108.87

<u>NAME AND ADDRESS</u>	<u>COMMITTED LOAN AMOUNT</u>	<u>COMMITTED WARRANT PURCHASE PRICE</u>	<u>TOTAL COMMITTED AGGREGATE PURCHASE PRICE</u>
KAISER FOUNDATION HOSPITALS One Kaiser Plaza 22 nd Floor Oakland, CA 94612 Fax Number: (510) 891-7943 Attention: Chris M. Grant	\$121,795.04	\$12.18	\$121,807.22
THE PERMANENTE FEDERATION LLC – SERIES I One Kaiser Plaza 22 nd Floor Oakland, CA 94612 Fax Number: (510) 891-7943 Attention: Chris M. Grant	\$121,795.16	\$12.18	\$121,807.34
TOTAL:	<u>\$4,000,000.00</u>	<u>\$400.03</u>	<u>\$4,000,400.03</u>
GRAND TOTAL:	<u>\$12,000,000.00</u>	<u>\$1,200.06</u>	<u>\$12,001,200.06</u>

EXHIBIT B

FORM OF CONVERTIBLE PROMISSORY NOTE

THIS CONVERTIBLE PROMISSORY NOTE HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"). NO SALE OR DISPOSITION MAY BE EFFECTED EXCEPT IN COMPLIANCE WITH RULE 144 UNDER THE SECURITIES ACT OR AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL FOR THE HOLDER SATISFACTORY TO THE PAYOR THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OR RECEIPT OF A NO-ACTION LETTER FROM THE SECURITIES AND EXCHANGE COMMISSION.

THIS CONVERTIBLE PROMISSORY NOTE AND THE RIGHTS AND OBLIGATIONS EVIDENCED HEREBY ARE SUBORDINATE IN THE MANNER AND TO THE EXTENT SET FORTH IN SECTION 9 HEREOF, AND EACH HOLDER OF THIS CONVERTIBLE PROMISSORY NOTE, BY ITS ACCEPTANCE HEREOF, SHALL BE BOUND BY THE PROVISIONS THEREOF.

CONVERTIBLE PROMISSORY NOTE

\$ _____

September 14, 2010
Redwood City, California

For value received ACELRX PHARMACEUTICALS, INC., a Delaware corporation ("*Payor*") promises to pay to _____ or its assigns ("*Holder*") the principal sum of _____ with interest on the outstanding principal amount at the rate of four percent (4.0%) per annum, compounded annually. Interest shall commence with the date hereof and shall continue until paid in full or converted. Interest shall be computed on the basis of a year of three hundred sixty days (360) days for the actual number of days elapsed.

1. Purchase Agreement. This convertible promissory note (the "*Note*") is issued as part of a series of similar notes (collectively, the "*Notes*") issued or issuable pursuant to the terms of that certain Note and Warrant Purchase Agreement, dated September 14, 2010, as it may be amended from time to time (the "*Agreement*") to the persons and entities listed on the Schedule of Purchasers thereof (collectively, the "*Holders*"). Any capitalized terms used but not defined herein shall have the meanings ascribed to them in the Agreement.

2. Application of Payments. All payments of interest and principal shall be in lawful money of the United States of America and shall be made pro rata among all Holders. All payments under this Note shall be applied first to accrued interest, and thereafter to principal.

3. Conversion.

(a) Maturity Date; Mandatory Conversion upon a Qualified Financing . In the event that Payor issues and sells shares of its Equity Securities (as defined hereinafter) on or before September 14, 2011 (the "*Maturity Date*"), which shall be subject to extension as provided in Section 4 hereof, in an equity financing with total proceeds to Payor of not less than fifteen million dollars (\$15,000,000) (excluding the conversion of the Notes) (a "*Qualified Financing*"), then the outstanding balance of this Note (including interest accrued hereunder) shall automatically convert in whole without any further action by the Holder into such Equity Securities at a conversion price equal to the price per share paid by the investors purchasing the Equity Securities and on the same terms and conditions as given to the investors in the Qualified Financing. For purposes of this Note, the following terms shall have the meanings as set forth:

(i) “*Equity Securities*” shall mean Payor’s Preferred Stock or any securities conferring the right to purchase Payor’s Preferred Stock or securities convertible into, or exchangeable for (with or without additional consideration), Payor’s Preferred Stock (excluding the Note and the Warrant), issued in the Qualified Financing, following the date hereof, except that such defined term shall not include any security granted, issued and/or sold by Payor to any employee, director or consultant in such capacity.

(b) **Mandatory Conversion Upon a Initial Offering.** If the Payor sells shares in a firm-commitment underwritten initial public offering prior to a Qualified Financing (the “*IPO*”), the outstanding balance of this Note (including interest accrued hereunder) shall automatically convert, effective immediately prior to the closing of the IPO, in whole without any further action by the Holder into the shares of stock issued by the Payor in the IPO at a conversion price equal to eighty percent (80%) of the gross public offering price per share of the stock sold by Payor in the IPO.

(c) **Optional Conversion Upon a Corporate Transaction.** To the extent this Note remains outstanding and has not been earlier converted pursuant to Sections 3(a) or 3(b) above, Payor shall provide the Holder ten (10) days advance written notice of the closing of any proposed Liquidation Transaction (as such term is defined in the Payor’s Amended and Restated Certificate of Incorporation, as amended), and upon the election of the Requisite Holders to convert all of the Notes evidenced by the delivery of a written notice of such election to Payor at least two (2) business days prior to the closing of such proposed Liquidation Transaction, the outstanding balance of this Note (including interest accrued hereunder) shall automatically convert in whole without any further action by the Holder into shares of Payor’s Series C Preferred Stock at the original issue price for such stock, as adjusted for stock splits, stock dividends, reclassification and the like, which as of the date hereof is equal to \$0.9857 per share (the “*Series C Price*”).

(d) **Mandatory Conversion Upon Consent of Requisite Holders .** To the extent this Note remains outstanding after the Maturity Date and has not been earlier converted pursuant to Sections 3(a), 3(b) or 3(c) above, then upon the election of the Requisite Holders to convert all of the Notes evidenced by the delivery of a written notice of such election to Payor at any time after (30) days following the Maturity Date, the outstanding balance of this Note (including interest accrued hereunder) shall automatically convert in whole without any further action by the Holder into shares of Payor’s Series C Preferred Stock at the Series C Price (a “*Maturity Conversion*”).

4. Due On Maturity Date. Unless this Note has been converted in accordance with the terms of Section 3 above, the entire outstanding principal balance and all unpaid accrued interest shall become fully due and payable on the Maturity Date; *provided, however,* the Maturity Date may be extended with the consent of the Requisite Holders.

5. Prepayment. Payor may not prepay this Note prior to the Maturity Date unless the Requisite Holders consent to such prepayment, in which case, this Note may be prepaid by Payor without penalty.

6. Events of Default. If there shall be any Event of Default hereunder, at the option and upon the declaration of the Requisite Holders and upon written notice to the Payor (which election and notice shall not be required in the case of an Event of Default under Section 6(c) or 6(d)), this Note shall accelerate and all principal and unpaid accrued interest shall become due and payable. The occurrence of any one or more of the following shall constitute an Event of Default:

(a) Payor fails to pay timely any of the principal amount due under this Note on the date the same becomes due and payable or any accrued interest or other amounts due under this Note on

the date the same becomes due and payable and such payment shall remain unpaid thirty (30) days following the due date;

(b) Payor shall default in its performance of any covenant under the Agreement and such failure remains unremedied for thirty (30) days following Payor's receipt of notice of such default;

(c) Payor files any petition or action for relief under any bankruptcy, reorganization, insolvency or moratorium law or any other law for the relief of, or relating to, debtors, now or hereafter in effect, or makes any assignment for the benefit of creditors or takes any corporate action in furtherance of any of the foregoing; or

(d) An involuntary petition is filed against Payor (unless such petition is dismissed or discharged within sixty (60) days under any bankruptcy statute now or hereafter in effect, or a custodian, receiver, trustee, assignee for the benefit of creditors (or other similar official) is appointed to take possession, custody or control of any property of Payor.

7. **Waiver of Demand.** Payor hereby waives demand, notice, presentment, protest and notice of dishonor.

8. **Governing Law.** This Note shall be governed by construed and under the laws of the State of California, as applied to agreements among California residents, made and to be performed entirely within the State of California, without giving effect to conflicts of laws principles.

9. **Subordination.** The payment of all amounts owed under this Note and all other obligations, liabilities or indebtedness of every nature of Payor to Holder pursuant to this Note, whether now existing or hereafter arising (collectively, the "**Subordinated Debt**") is hereby subordinated to the payment in full in cash of all Senior Debt (as defined below), and no payments or other distributions whatsoever in respect of any Subordinated Debt shall be made by the Payor and no property or assets of the Payor shall be applied to the purchase, redemption or other acquisition or retirement of any Subordinated Debt, until the Senior Debt shall have been indefeasibly paid in full in cash and discharged and all financing arrangements between the Payor and all of the Senior Lenders (as defined below) under any document or instrument evidencing or securing Senior Debt have been terminated, and all obligations under any letter of credit issued by any Senior Lender for the account of Payor shall have terminated or expired; *provided, however*, nothing in this Section 9 shall prevent or otherwise prohibit Holder from converting the indebtedness evidenced by this Note pursuant to Section 3 of this Note. As used herein, (a) "**Senior Debt**" shall mean any and all obligations, indebtedness and liabilities now or hereafter owing or due from Payor to any Senior Lender howsoever created, arising or evidenced, whether direct or indirect, absolute or contingent, due or to become due, now existing pursuant to that certain Loan and Security Agreement dated September 16, 2008, among Payor, the Lenders and Pinnacle Ventures, L.L.C., as agent to the Lenders (the "**Loan and Security Agreement**"); and (b) "**Senior Lenders**" shall mean the lenders identified on Schedule 1 (the "Lenders") to the Loan and Security Agreement.

10. **Amendment.** Any term of this Note may be amended or waived with the written consent of Payor and the Requisite Holders, provided that all Notes are similarly affected. Upon the effectuation of any amendment or waiver in conformance with this Section 10, Payor shall promptly given written notice thereof to the Holders of the Notes who have not previously consented thereto in writing.

11. Transfer. This Note may be transferred only upon its surrender to Payor for registration of transfer, duly endorsed, or accompanied by a duly executed written instrument of transfer in form satisfactory to Payor. Thereupon, this Note shall be reissued to, and registered in the name of, the transferee, or a new Note for like principal amount and interest shall be issued to, and registered in the name of, the transferee. Interest and principal shall be paid solely to the registered holder of this Note. Such payment shall constitute full discharge of Payor's obligation to pay such interest and principal.

12. Notices. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to Payor at the address listed below and to Holder at the address designated on the records of Payor or at such other address as Payor or Holder may designate by ten (10) days' advance written notice to the other parties hereto.

13. Expenses. Payor hereby agrees, subject only to any limitation imposed by applicable law, to pay all expenses, including reasonable attorneys' fees and legal expenses, incurred by the holder of this Note ("**Costs**") in endeavoring to collect any amounts payable hereunder which are not paid when due, whether by declaration or otherwise. Payor agrees that any delay on the part of Holder in exercising any rights hereunder will not operate as a waiver of such rights. Holder shall not by any act, delay, omission or otherwise be deemed to have waived any of its rights or remedies, and no waiver of any kind shall be valid unless in writing and signed by the party or parties waiving such rights or remedies.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, Payor has executed this Convertible Promissory Note as of the date first written above.

PAYOR:

ACELRX PHARMACEUTICALS, INC.

By: _____

Richard King
Chief Executive Officer

Address: 575 Chesapeake Drive
Redwood City, CA 94063

EXHIBIT C
FORM OF WARRANT

THIS WARRANT AND THE UNDERLYING SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"). THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT AS TO SUCH SECURITIES UNDER THE SECURITIES ACT OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED.

ACELRX PHARMACEUTICALS, INC.

WARRANT TO PURCHASE PREFERRED STOCK

No. PW-_____

September 14, 2010

THIS CERTIFIES THAT, for value received, _____, with its principal office at _____, or its permitted assigns (the "**Holder**"), is entitled to subscribe for and purchase from **ACELRX PHARMACEUTICALS, INC.**, a Delaware corporation, with its principal office at 575 Chesapeake Drive, Redwood City, CA 94063 (the "**Company**") the Exercise Shares at the Exercise Price (each subject to adjustment as provided herein). This Warrant is being issued pursuant to that certain Note and Warrant Purchase Agreement, dated as of September 14, 2010, among Holder and the Company, and the other parties named therein (the "**Purchase Agreement**"). The aggregate number of Exercise Shares that Holder may purchase by exercising this warrant is equal to twenty-five percent (25%) of the Loan Amount advanced to the Company by the Holder at the applicable Closing (as defined in the Purchase Agreement) on the date hereof, in accordance with the Purchase Agreement, divided by the Exercise Price (subject to adjustment pursuant to the terms hereof, including but not limited to adjustments pursuant to Section 5 below).

1. DEFINITIONS. As used herein, the following terms shall have the following respective meanings:

(a) "**Exercise Period**" shall mean the period commencing with the date hereof and ending on September 14, 2017, unless sooner terminated in accordance with Section 7 below.

(b) "**Exercise Price**" shall mean (a) if the Exercise Shares are the type of Preferred Stock issued in the Qualified Financing, an amount equal to the per share selling price of shares of that stock issued in the Qualified Financing and (b) if the Exercise Shares are Series C Preferred Stock, the Series C Price, subject in each case to adjustment pursuant to Section 5 hereof.

(c) "**Exercise Shares**" shall mean (i) if the Qualified Financing is closed on or before the Maturity Date, the Preferred Stock sold in the Qualified Financing and (ii) (x) if the Qualified Financing is not closed on or before the Maturity Date, (y) if an Initial Offering or Liquidation Transaction occurs prior to the closing of the Qualified Financing or (z) in the event of a Maturity Conversion, the Series C Preferred Stock. The number and character of shares of Exercise Shares are subject to adjustment as provided herein and the term "Exercise Shares" shall include stock and other securities and property at any time receivable or issuable upon exercise of this Warrant in accordance with its terms.

(d) "**Initial Offering**" shall mean the first firm commitment underwritten public offering of its common stock registered under the Securities Act.

(e) "**Investor Rights Agreement**" shall mean the Amended and Restated Investor Rights Agreement, by and among the Company and the persons and entities listed on Exhibit A thereto, dated as of November 23, 2009, as may be amended from time to time.

-
- (f) “*Liquidation Transaction*” shall have the meaning set forth in the Restated Certificate.
 - (g) “*Maturity Conversion*” shall have the meaning set forth in the Notes.
 - (h) “*Maturity Date*” shall have the meaning set forth in the Notes.
 - (i) “*Notes*” shall have the meaning set forth in the Purchase Agreement.
 - (j) “*Loan Amount*” shall have the meaning set forth in the Purchase Agreement.
 - (k) “*Preferred Stock*” shall mean the preferred stock of the Company.
 - (l) “*Qualified Financing*” shall have the meaning set forth in the Notes.
 - (m) “*Requisite Holders*” shall have the meaning set forth in the Purchase Agreement.
 - (n) “*Restated Certificate*” shall mean the Company’s Amended and Restated Certificate of Incorporation, as it may be amended from time to time.
 - (o) “*Securities Act*” shall mean the Securities Act of 1933, as amended.
 - (p) “*Series C Preferred Stock*” shall mean the Series C Preferred Stock of the Company.
 - (q) “*Series C Price*” shall have the meaning set forth in the Notes, which as of the date hereof is equal to \$0.9857.

2. EXERCISE OF WARRANT.

2.1 General. The rights represented by this Warrant may be exercised in whole or in part at any time during the Exercise Period, by delivery of the following to the Company at its address set forth above (or at such other address as it may designate by notice in writing to the Holder):

- (a) An executed Notice of Exercise in the form attached hereto as **EXHIBIT A**;
- (b) Payment of the Exercise Price either (i) in cash or by check, or (ii) by cancellation of indebtedness; and
- (c) This Warrant.

Upon the exercise of the rights represented by this Warrant, a certificate or certificates for the Exercise Shares so purchased, registered in the name of the Holder or persons affiliated with the Holder, if the Holder so designates, shall be issued and delivered to the Holder within a reasonable time after the rights represented by this Warrant shall have been so exercised. In the event that this Warrant is being exercised for less than all of the then-current number of Exercise Shares purchasable hereunder, the Company shall, concurrently with the issuance by the Company of the number of Exercise Shares for which this Warrant is then being exercised, issue a new Warrant exercisable for the remaining number of Exercise Shares purchasable hereunder.

The person in whose name any certificate or certificates for Exercise Shares are to be issued upon exercise of this Warrant shall be deemed to have become the holder of record of such shares on the date on which this Warrant was surrendered and payment of the Exercise Price was made, irrespective of the date of delivery of such certificate or certificates, except that, if the date of such surrender and payment is

a date when the stock transfer books of the Company are closed, such person shall be deemed to have become the holder of such shares at the close of business on the next succeeding date on which the stock transfer books are open.

2.2 Net Exercise. In lieu of exercising this Warrant by payment of cash, the Holder may elect to receive shares equal to the value (as determined below) of this Warrant (or the portion thereof being canceled) by surrender of this Warrant at the principal office of the Company together with the properly endorsed Notice of Exercise in which event the Company shall issue to the Holder a number of Exercise Shares computed using the following formula:

$$X = \frac{Y(A-B)}{A}$$

- Where
- X = the number of Exercise Shares to be issued to the Holder
 - Y = the number of Exercise Shares purchasable under the Warrant or, if only a portion of the Warrant is being exercised, that portion of the Warrant being canceled (at the date of such calculation)
 - A = the fair market value of one Exercise Share (at the date of such calculation)
 - B = Exercise Price (as adjusted to the date of such calculation)

For purposes of the above calculation, the fair market value of one Exercise Share shall be determined by the Company's Board of Directors in good faith; provided, however, that in the event that this Warrant is exercised pursuant to this Section 2.2 in connection with the Initial Offering of the Company's Common Stock, the fair market value per share shall be the product of (i) the per share offering price to the public in the Initial Offering, and (ii) the number of shares of Common Stock into which each Exercise Share is convertible at the time of such exercise.

3. COVENANTS OF THE COMPANY.

3.1 Covenants as to Exercise Shares. The Company covenants and agrees that all Exercise Shares that may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be validly issued and outstanding, fully paid and nonassessable, and free from all taxes, liens and charges with respect to the issuance thereof. The Company further covenants and agrees that the Company will at all times during the Exercise Period, have authorized and reserved, free from preemptive rights, a sufficient number of shares of the series of equity securities comprising the Exercise Shares to provide for the exercise of the rights represented by this Warrant. If at any time during the Exercise Period the number of authorized but unissued shares of such series of the Company's equity securities shall not be sufficient to permit exercise of this Warrant, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of such series of the Company's equity securities to such number of shares as shall be sufficient for such purposes.

3.2 Notices of Record Date. In the event of any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution, the Company shall mail to the Holder, at least ten (10) days prior to the date specified herein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend or distribution.

4. REPRESENTATIONS OF HOLDER.

4.1 Acquisition of Warrant for Personal Account. The Holder represents and warrants that it is acquiring the Warrant and the Exercise Shares solely for its account for investment and not with a view to or for sale or distribution of said Warrant or Exercise Shares or any part thereof. The Holder also represents that the entire legal and beneficial interests of the Warrant and Exercise Shares the Holder is acquiring is being acquired for, and will be held for, its account only.

4.2 Securities Are Not Registered.

(a) The Holder understands that the Warrant and the Exercise Shares have not been registered under the Securities Act on the basis that no distribution or public offering of the stock of the Company is to be effected. The Holder realizes that the basis for the exemption may not be present if, notwithstanding its representations, the Holder has a present intention of acquiring the securities for a fixed or determinable period in the future, selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the securities. The Holder has no such present intention.

(b) The Holder recognizes that the Warrant and the Exercise Shares must be held indefinitely unless they are subsequently registered under the Securities Act or an exemption from such registration is available. The Holder recognizes that the Company has no obligation to register the Warrant or the Exercise Shares of the Company, or to comply with any exemption from such registration.

(c) The Holder is aware that neither the Warrant nor the Exercise Shares may be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met, including, among other things, the existence of a public market for the shares, the availability of certain current public information about the Company, the resale following the required holding period under Rule 144 and the number of shares being sold during any three month period not exceeding specified limitations. Holder is aware that the conditions for resale set forth in Rule 144 have not been satisfied and that the Company presently has no plans to satisfy these conditions in the foreseeable future.

4.3 Disposition of Warrant and Exercise Shares.

(a) The Holder further agrees not to make any disposition of all or any part of the Warrant or Exercise Shares in any event unless and until:

(i) The Company shall have received a letter secured by the Holder from the Securities and Exchange Commission stating that no action will be recommended to the Commission with respect to the proposed disposition;

(ii) There is then in effect a registration statement under the Securities Act covering such proposed disposition and such disposition is made in accordance with said registration statement; or

(iii) The Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and if reasonably requested by the Company, the Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, for the Holder to the effect that such disposition will not require registration of such Warrant or Exercise Shares under the Securities Act or any applicable state securities laws. The Company agrees that it will not require an opinion of counsel with respect to transactions under Rule 144 of the Securities Act, except in unusual circumstances.

(b) The Holder understands and agrees that all certificates evidencing the shares to be issued to the Holder may bear the following legend:

THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE “**SECURITIES ACT**”). THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT AS TO THE SECURITIES UNDER THE SECURITIES ACT OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED.

4.4 Accredited Investor Status. The Holder is an “accredited investor” as defined in Regulation D promulgated under the Securities Act.

5. ADJUSTMENT OF EXERCISE PRICE AND NUMBER OF EXERCISE SHARES.

5.1 Changes in Securities. In the event of changes in the series of equity securities of the Company comprising the Exercise Shares by reason of stock dividends, splits, recapitalizations, reclassifications, combinations or exchanges of shares, separations, reorganizations, liquidations, or the like, the number and class of Exercise Shares available under the Warrant in the aggregate and the Aggregate Exercise Price shall be correspondingly adjusted to give the Holder of the Warrant, on exercise for the same Aggregate Exercise Price, the total number, class, and kind of shares as the Holder would have owned had the Warrant been exercised prior to the event and had the Holder continued to hold such shares until after the event requiring adjustment; provided, however, that such adjustment shall not be made with respect to, and this Warrant shall terminate if not exercised prior to, the events set forth in Section 7 below. For purposes of this Section 5, the “**Aggregate Exercise Price**” shall mean the aggregate Exercise Price payable in connection with the exercise in full of this Warrant. The form of this Warrant need not be changed because of any adjustment in the number of Exercise Shares subject to this Warrant.

5.2 Automatic Conversion. Upon the automatic conversion of all outstanding shares of the series of equity securities comprising the Exercise Shares, this Warrant shall become exercisable for that number of shares of Common Stock of the Company into which the Exercise Shares would then be convertible, so long as such shares, if this Warrant had been exercised prior to such automatic conversion, would have been converted into shares of the Company’s Common Stock pursuant to the Restated Certificate. In such case, all references to “Exercise Shares” shall mean shares of the Company’s Common Stock issuable upon exercise of this Warrant, as appropriate.

6. FRACTIONAL SHARES. No fractional shares shall be issued upon the exercise of this Warrant as a consequence of any adjustment pursuant hereto. All Exercise Shares (including fractions) to be issued upon exercise of this Warrant shall be aggregated for purposes of determining whether the exercise would result in the issuance of any fractional share. If, after aggregation, the exercise would result in the issuance of a fractional share, the Company shall, in lieu of issuance of any fractional share, pay the Holder otherwise entitled to such fraction a sum in cash equal to the product resulting from multiplying the then current fair market value of one Exercise Share by such fraction.

7. EARLY TERMINATION. In the event of, at any time during the Exercise Period, an Initial Offering or a Liquidation Transaction, the Company shall provide to the Holder ten (10) days’ advance written notice of such Initial Offering or Liquidation Transaction, and this Warrant shall terminate unless exercised immediately prior to the date such Initial Offering is closed or the closing of such Liquidation Transaction.

8. REGISTRATION RIGHTS. To the extent the Holder is a party to the Investor Rights Agreement, the Exercise Shares issuable upon exercise of this Warrant shall be deemed “Registrable Securities” for all purposes under the Investor Rights Agreement and shall be subject to the rights and covenants therein.

9. MARKET STAND-OFF AGREEMENT. The Holder acknowledges and agrees that any and all shares of common stock of the Company acquired by Holder pursuant to the exercise of this Warrant shall be irrevocably and unconditionally subject to the “Market Stand-Off” provision set forth in Section 5 of the Purchase Agreement.

10. NO STOCKHOLDER RIGHTS. This Warrant in and of itself shall not entitle the Holder to any voting rights or other rights as a stockholder of the Company.

11. TRANSFER OF WARRANT. Subject to applicable laws and the restriction on transfer set forth on the first page of this Warrant, this Warrant and all rights hereunder are transferable in full only, by the Holder in person or by duly authorized attorney, upon delivery of this Warrant and the form of assignment attached hereto as **EXHIBIT B** to any transferee designated by Holder. The transferee shall sign an investment letter in form and substance satisfactory to the Company.

12. LOST, STOLEN, MUTILATED OR DESTROYED WARRANT. If this Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as the Warrant so lost, stolen, mutilated or destroyed. Any such new Warrant shall constitute an original contractual obligation of the Company, whether or not the allegedly lost, stolen, mutilated or destroyed Warrant shall be at any time enforceable by anyone.

13. AMENDMENT. Any term of this Warrant may be amended or waived with the written consent of the Company and the Requisite Holders, provided that all Warrants are similarly affected. Upon the effectuation of any such amendment or waiver in conformance with this Section 13, the Company shall promptly give written notice thereof to the record holders of the Warrants who have not previously consented thereto in writing.

14. NOTICES. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the Company at the address listed above and to Holder at the address listed above or at such other address as the Company or Holder may designate by ten (10) days’ advance written notice to the other parties hereto.

15. ACCEPTANCE. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

16. GOVERNING LAW. This Warrant and all rights, obligations and liabilities hereunder shall be governed by and construed under the laws of the State of California as applied to agreements among California residents, made and to be performed entirely within the State of California without giving effect to conflicts of laws principles.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its duly authorized officer as of the date first written above.

ACELRX PHARMACEUTICALS, INC.

By: _____
Richard King
Chief Executive Officer

EXHIBIT A

NOTICE OF EXERCISE

TO: ACELRX PHARMACEUTICALS, INC.

(1) The undersigned hereby elects to purchase _____ shares of Preferred Stock (as such term is defined in the foregoing Warrant) (the “*Exercise Shares*”) of **ACELRX PHARMACEUTICALS, INC.** (the “*Company*”) pursuant to the terms of the attached Warrant, and tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any; or

The undersigned hereby elects to purchase _____ shares of Preferred Stock (as such term is defined in the foregoing Warrant) (the “*Exercise Shares*”) of **ACELRX PHARMACEUTICALS, INC.** (the “*Company*”) pursuant to the terms of the net exercise provisions set forth in Section 2.1 of the attached Warrant, and shall tender payment of all applicable transfer taxes, if any.

(2) Please issue a certificate or certificates representing said Exercise Shares in the name of the undersigned or in such other name as is specified below:

(Name)

(Address)

(3) The undersigned represents that (i) the aforesaid Exercise Shares are being acquired for the account of the undersigned for investment and not with a view to, or for resale in connection with, the distribution thereof and that the undersigned has no present intention of distributing or reselling such shares; (ii) the undersigned is aware of the Company’s business affairs and financial condition and has acquired sufficient information about the Company to reach an informed and knowledgeable decision regarding its investment in the Company; (iii) the undersigned is experienced in making investments of this type and has such knowledge and background in financial and business matters that the undersigned is capable of evaluating the merits and risks of this investment and protecting the undersigned’s own interests; (iv) the undersigned understands that Exercise Shares issuable upon exercise of this Warrant have not been registered under the Securities Act of 1933, as amended (the “*Securities Act*”), by reason of a specific exemption from the registration provisions of the Securities Act, which exemption depends upon, among other things, the bona fide nature of the investment intent as expressed herein, and, because such securities have not been registered under the Securities Act, they must be held indefinitely unless subsequently registered under the Securities Act or an exemption from such registration is available; (v) the undersigned is aware that the aforesaid Exercise Shares may not be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met and until the undersigned has held the shares for the time period prescribed by Rule 144, that among the conditions for use of the Rule is the availability of current information to the public about the Company and the Company has not made such information available and has no present plans to do so; and (vi) the undersigned agrees not to make any disposition of all or any part of the aforesaid shares of Exercise Shares unless and until there is then in effect a registration statement under the Securities Act covering such proposed disposition and such disposition is made in accordance with said registration statement, or, if reasonably requested by the Company, the undersigned has provided the Company with an opinion of counsel satisfactory to the Company, stating that such registration is not required.

(Date)

(Signature)

(Print name)

EXHIBIT B

ASSIGNMENT FORM

(To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.)

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned to

Name: _____

(Please Print)

Address: _____

(Please Print)

Dated: _____, 20__

Holder's

Signature: _____

Holder's

Address: _____

NOTE: The signature to this Assignment Form must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

AMENDMENT TO NOTE AND WARRANT PURCHASE AGREEMENT

This Amendment to Note and Warrant Purchase Agreement (the “*Amendment*”) is made as of the 28th day of January, 2011 by and among AcelRx Pharmaceuticals, Inc., a Delaware corporation (the “*Company*”), and the undersigned Purchasers.

RECITALS

The Company entered into that certain Note and Warrant Purchase Agreement dated as of September 14, 2010 (the “*Purchase Agreement*”), pursuant to which certain convertible promissory notes (the “*Notes*”) and warrants to purchase preferred stock of the Company (collectively, the “*Warrants*”) were issued to the Purchasers named therein. Pursuant to Section 6.6 of the Purchase Agreement, any provision of the Purchase Agreement may be amended with the written consent of the Company and Purchasers who hold a majority in interest of the Notes outstanding. Capitalized terms used but not defined herein have the meanings ascribed to them in the Purchase Agreement.

AGREEMENT

NOW, THEREFORE, the parties agree as follows:

1. **Amendment to Purchase Agreement.** The first sentence of Section 2.2 of the Purchase Agreement is hereby amended and restated in its entirety to read as follows:

“**2.2. Second Closing.** At any time on or before the earlier of (i) one hundred eighty (180) days following the Initial Closing or at such later time as the Requisite Holders (as hereinafter defined) may mutually agree or (ii) the closing of the Company’s first firm commitment underwritten public offering of its common stock registered under the Securities Act, and upon receipt of the written election of the Requisite Holders, the Company shall issue up to the balance of the authorized Notes and Warrants not sold at the Initial Closing pursuant to this Agreement to Purchasers in their respective amounts as indicated in the Schedule of Purchasers under the heading “Second Closing” (the “*Second Closing*,” together with the Initial Closing, the “*Closings*” and each a “*Closing*”).”

2. **No Other Amendment.** Except as modified by this Amendment, the Purchase Agreement, the Notes and the Warrants shall remain in full force and effect in all respects without any further modification.

3. **Counterparts.** This Amendment may be executed in counterparts, each of which shall constitute an original and all of which, when taken together, shall constitute one agreement.

4. **Entire Agreement.** This Amendment, along with the Purchase Agreement and the exhibits thereto, constitute the full and entire understanding and agreement between the parties with regard to the subjects hereof and no party shall be liable or bound to any other party in any manner by any representations, warranties, covenants and agreements except as specifically set forth herein.

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

COMPANY:

ACELRX PHARMACEUTICALS, INC.

By: /s/ Richard King

Name: Richard King

Title: President & Chief Executive Officer

**SIGNATURE PAGE TO AMENDMENT TO
NOTE AND WARRANT PURCHASE AGREEMENT**

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

PURCHASERS:

**THREE ARCH PARTNERS III, L.P.
BY THREE ARCH MANAGEMENT III, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan
Mark Wan
Managing Member

**THREE ARCH ASSOCIATES III, L.P.
BY THREE ARCH MANAGEMENT III, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan
Mark Wan
Managing Member

**THREE ARCH PARTNERS IV, L.P.
BY THREE ARCH MANAGEMENT IV, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan
Mark Wan
Managing Member

**THREE ARCH ASSOCIATES IV, L.P.
BY THREE ARCH MANAGEMENT IV, L.L.C.,
ITS GENERAL PARTNER**

By: /s/ Mark Wan
Mark Wan
Managing Member

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

PURCHASER:

Skyline Venture Partners Qualified Purchaser Fund
IV, L.P.

By: Skyline Venture Management IV, LLC
Its: General Partner

By: /s/ John G. Freund
Name: John G. Freund
Its: Managing Director

**SIGNATURE PAGE TO AMENDMENT TO
NOTE AND WARRANT PURCHASE AGREEMENT**

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first written above.

PURCHASER:

ACP IV, L.P.

By: ACMP IV, LLC.

Its: General Partner

By: /s/ Guy Nohra

Director

**SIGNATURE PAGE TO AMENDMENT TO
NOTE AND WARRANT PURCHASE AGREEMENT**

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated June 30, 2010, except for the last paragraph of Note 1, as to which the date is January 28, 2011, in the Registration Statement (Amendment No. 3 to Form S-1) and related Prospectus of AcelRx Pharmaceuticals, Inc. for the registration of shares of its common stock.

/s/ Ernst & Young LLP

San Francisco, California

January 31, 2011