ACELRX PHARMACEUTICALS INC
Form 424B3
July 03, 2012
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Registration No. 333-182245

PROSPECTUS

5,552,440 Shares

ACELRX PHARMACEUTICALS, INC.

Common Stock

This prospectus relates to the sale or other disposition from time to time of up to 5,552,440 shares of our common stock, which includes 2,630,103 shares of our common stock issuable upon the exercise of warrants, which are held by the selling stockholders named in this prospectus. The shares of common stock covered by this prospectus were previously issued by us in a private placement, which is more fully described in the section titled Prospectus Summary The Offering on page 2, or underlie certain common stock purchase warrants that were previously issued by us in that private placement. We are not selling any common stock under this prospectus and will not receive any of the proceeds from the sale or other disposition of shares by the selling stockholders. However, we will receive the proceeds of any cash exercise of the warrants.

The selling stockholders may sell or otherwise dispose of the shares of common stock covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholders may sell or otherwise dispose of their shares of common stock in the section entitled Plan of Distribution on page 19. Discounts, concessions, commissions and similar selling expenses attributable to the sale of shares of common stock covered by this prospectus will be borne by a selling stockholder. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the shares with the Securities and Exchange Commission.

Our common stock is traded on the NASDAQ Global Market under the symbol ACRX. On July 2, 2012, the last reported sales price of our common stock was $3.30 per share.

Investing in our common stock involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors beginning on page 3 of this prospectus, and under similar headings in any amendment or supplements to this prospectus or as updated by any subsequent filing with the Securities and Exchange Commission that is incorporated by reference herein.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 3, 2012.

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ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the selling stockholders have not, authorized anyone to provide you with additional or different information. If anyone provides you with additional, different or inconsistent information, you should not rely on it. You should not assume that the information we have included in this prospectus is accurate as of any date other than the date of this prospectus or that any information we have incorporated by reference is accurate as of any date other than the date of the document incorporated by reference. Our business, financial condition, results of operations and prospects may have changed since that date.

Unless the context requires otherwise, all references to we , us , our , AcelRx or the Company in this prospectus are to AcelRx Pharmaceuticals, Inc. The AcelRx logo, AcelRx, and all product and service names used herein are either registered trademarks or trademarks of AcelRx Pharmaceuticals, Inc. in the United States and/or other countries.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere or incorporated by reference into this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus carefully, including the section entitled Risk Factors and the documents that we incorporate by reference into this prospectus, before making an investment decision.

AcelRx Pharmaceuticals, Inc.

We are a development stage specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. 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. In March 2012, we initiated the first of three Phase 3 clinical trials for our lead product candidate, the Sufentanil NanoTab PCA System, or ARX-01 System, or ARX-01. In April 2012, we initiated the second Phase 3 trial, an open-label active-comparator study. The final planned Phase 3 efficacy and safety study, a double-blind, placebo-controlled trial is expected to begin in the third quarter of 2012. We expect top-line data from all three Phase 3 trials in late 2012 or early 2013.

The ARX-01 System is designed to address the problems associated with IV PCA 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. In May 2011, we announced that the US Army Medical Research and Material Command, or USAMRMC, awarded us a $5.6 million grant to support the development of a new product candidate, ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain. Under the terms of the grant, the USAMRMC will reimburse us for development, manufacturing and clinical expenses necessary to prepare for and complete the planned Phase 2 dose-finding trial in a study of acute moderate-to-severe pain, and to prepare to enter Phase 3 development.

Development of therapeutic products is costly and is subject to a lengthy and uncertain regulatory process by the United States Food and Drug Administration, or FDA. Adverse events in both our own clinical program and other programs may have a negative impact on regulatory approval, the willingness of potential commercial partners to enter into agreements and the perception of the public. We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. To date, none of our product candidates have been commercialized, and if our product candidates are not successfully developed or commercialized, or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail.

Product Development

ARX-01

We continue to make progress in the development of our lead product candidate, ARX-01, including the following activities:

In March 2012, we initiated the first of three Phase 3 clinical trials, a double-blind, placebo-controlled efficacy and safety trial of patients with post-operative pain following open-abdominal surgery. We expect top-line data for this trial in the second half of 2012.

In April 2012, we initiated our second planned Phase 3 clinical trial, an open-label active-comparator study comparing ARX-01 to the current standard of care, IV PCA morphine, in patients with post-operative pain following open-abdominal surgery or major orthopedic surgery. We expect top-line data for this trial in the second half of 2012.

In the third quarter of 2012, we plan to initiate our third planned Phase 3 clinical trial, a double-blind, placebo-controlled efficacy and safety study of patients with post-operative pain following hip and knee replacement surgeries. We expect top-line data for this trial in late 2012 or early 2013.

ARX-04

We continue to make progress towards the initiation of our planned ARX-04 Phase 2 dose-finding clinical trial. In October 2011, we filed an Investigational New Drug application for ARX-04, our product candidate for management of moderate-to-severe acute pain, with the FDA, and we plan to initiate the Phase 2 study contingent on approval of the proposed clinical protocol for the study from the USAMRMC.

We will require additional funding to complete the ARX-01 NDA preparation process and file the NDA with the FDA. Future development of ARX-02 and ARX-03 is contingent upon additional funding or establishing corporate partnerships.

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 351 Galveston 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.

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The Offering

The selling stockholders named in this prospectus may offer and sell up to 5,552,440 shares of our common stock, including 2,630,103 shares of our common stock issuable upon the exercise of warrants. Our common stock is currently listed on The NASDAQ Global Market under the symbol ACRX. Shares of common stock that may be offered in this offering, when issued and paid for, will be fully paid and non-assessable. We will not receive any of the proceeds of sales by the selling stockholders of any of the common stock covered by this prospectus. We will, however, receive the net proceeds of any warrants exercised for cash. Throughout this prospectus, when we refer to the shares of our common stock being registered on behalf of the selling stockholders, we are referring to the shares of common stock that have been issued pursuant to the securities purchase agreement in the private placement described below, or that may be issuable upon exercise of the warrants purchased in the private placement, or the Warrants. Throughout this prospectus, when we refer to the selling stockholders, we are referring to the selling stockholders named herein and, as applicable, any donees, pledgees, transferees or other successors-in-interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, or other non-sale related transfer that may be indentified in a supplement to this prospectus or, if required, a post-effective amendment to the registration statement of which this prospectus is a part.

Private Placement

On May 29, 2012, we entered into a securities purchase agreement, or the Purchase Agreement, with certain accredited investors, including entities affiliated with certain members of our board of directors, providing for a private placement, or the Private Placement, of up to $10.0 million of our securities. At the closing of the Private Placement on June 1, 2012, and pursuant to the Purchase Agreement, we sold shares of common stock and warrants to purchase common stock in immediately separable Units, with each Unit consisting of (i) one share of common stock and (ii) a Warrant to purchase 0.9 of a share of common stock. The per share exercise price of the Warrants was $3.40. The offering price per Unit was $3.40 for non-affiliated investors, and $3.5125 for affiliated investors, which equals the sum of (i) $3.40, the closing consolidated bid price of our common stock on May 29, 2012, plus (ii) $0.1125 (which is equal to $0.125 per warrant share, multiplied by 0.9), for an aggregate amount of $10.0 million. The Warrants issued in the Private Placement become exercisable six months after the issuance date, and expire on the five year anniversary of the initial exercisability date. Cowen and Company, LLC served as lead placement agent and JMP Securities served as co-placement agent in the Private Placement.

Pursuant to the Purchase Agreement, we agreed to file the registration statement of which this prospectus is a part with the Securities and Exchange Commission, or the SEC, to register the sale or other disposition of the shares of our common stock we issued and any common stock issued as a result of the exercise of the Warrants, and to use our commercially reasonable best efforts to keep the registrations statement continuously effective until the earlier of (i) such time as all of the such shares registered hereunder have been sold by the selling stockholders or (ii) such time as all of the shares may be sold without restriction pursuant to Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

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RISK FACTORS

An investment in our common stock is highly risky. You should carefully consider the following risks, as well as the other information contained or incorporated by reference in this prospectus, before you decide whether to buy our common stock. We believe the risks and uncertainties described below are the most significant risks we face. If any of the following events actually occurs, our business, business prospects, financial condition, cash flow and results of operations would likely be materially and adversely affected. In these circumstances, the trading price of our common stock would likely decline, and you could lose all or part of your investment.

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. The risks described below are not the only ones we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

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 three additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, the Sufentanil/Triazolam NanoTab, or ARX-03 and Sufentanil Single-Dose Acute Pain NanoTab, or ARX-04. We have incurred significant net losses in each year since our inception in July 2005 and as of March 31, 2012, we had an accumulated deficit of $95.7 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. To date, none of our product candidates have been commercialized, and if our product candidates are not successfully developed or commercialized, or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail. Even if we successfully obtain regulatory approval to market our product candidates in the United States, our revenues are also dependent upon the size of the markets outside of the United States, as well as our ability to obtain market approval and achieve commercial success.

We expect to continue to incur substantial and increased expenses as we expand our research and development activities and advance our clinical programs. We also expect an increase in our expenses associated with preparing for the potential commercialization of ARX-01. As a result of the foregoing, we expect to continue to incur significant and increasing operating losses and negative cash flows for the foreseeable future.

We have never generated any revenue and may never be profitable.

Our ability to generate revenue from commercial sales and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize our product candidates. Other than the revenue received from the US Army Medical Research and Material Command for research and development reimbursement under the terms of the grant for ARX-04, 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 in the U.S. and collaborating with third parties internationally; and

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses, or when, or if, we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we are required by the United States Food and Drug Administration, or FDA, to perform 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, including our Phase 3 ARX-01 studies. As of March 31, 2012, we had working capital of $22.1 million.

We believe that our current cash, cash equivalents and investments will be sufficient to fund our current operations into the second quarter of 2013. We will need to raise substantial additional funds to support our future operations, and such funding may not be available to us on acceptable terms, or at all. Additionally, changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate. For example, we believe our existing cash resources are adequate to complete all three ARX-01 Phase 3 clinical trials; however, our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expected. In any event, we will require substantial additional capital to obtain regulatory approval for, and to commercialize, our product candidates. Raising funds in the current economic environment, when the capital markets have been affected by the global recession, may present additional challenges.

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

- significantly delay, scale back or discontinue the development or commercialization of our product candidates;
- seek corporate partners for ARX-01 at an earlier stage than otherwise would be desirable or on terms that might be less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will not be able to continue our planned level of operations beyond the second quarter of 2013, complete the development activities required to submit a new drug application, or NDA, to the FDA, nor pursue commercialization efforts, all of which would have a material adverse effect on our business, operating results and prospects. If we issue additional common or securities convertible into common stock, our stockholders will experience additional dilution, which may be significant.

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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.

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

In June 2011, we entered into a loan and security agreement with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, under which we may borrow up to $20.0 million in two tranches of $10.0 million each, represented by secured convertible term promissory notes. We drew the first tranche of $10.0 million upon closing of the transaction in June 2011 and the second tranche of $10.0 million in December 2011. We used a portion of the proceeds from the first tranche to repay the remaining obligations under that certain Loan and Security Agreement between us and Pinnacle Ventures, L.L.C., dated September 2008. The interest rate is initially 8.50%, with 12 months of interest only payments. Any notes issued pursuant to the loan and security agreement mature on December 1, 2014. We granted to Hercules a first priority security interest in substantially all of our assets, with the exception of our intellectual property, where the security interest is limited to proceeds of intellectual property.

If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, if we breach the agreement or become insolvent, Hercules could elect to declare all amounts outstanding, together with accrued and unpaid interest and penalty, to be immediately due and payable. 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, Hercules will have a first claim on our assets pledged under the loan agreement. If Hercules should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the loan agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of 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, for the treatment of post-operative pain. We currently have two of our three planned Phase 3 ARX-01 clinical trials ongoing, and we anticipate initiation of our third and final Phase 3 trial in the third quarter of 2012. We expect top-line data from all three Phase 3 trials in late 2012 or early 2013. We believe our existing capital resources will be adequate to support operations into the first quarter of 2013 and will be adequate to complete all three ARX-01 Phase 3 clinical trials. Contingent on our ability to raise additional funding, we intend to use these completed trials as a basis to submit an NDA for ARX-01 later in 2013. There is no guarantee that our Phase 3 clinical trials, or any of the remaining pharmacokinetic studies, or PK studies, or non-clinical studies to be included in the NDA, will be completed, or if completed, will be successful.

Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing ARX-01, generating revenues and achieving profitability. If any of these events occur, we may be forced to abandon our development efforts for ARX-01, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We depend substantially on the successful completion of Phase 3 clinical trials for our product candidates. The positive clinical results obtained for our product candidates in Phase 2 clinical studies may not be repeated in Phase 3.

While we have completed multiple Phase 2 clinical studies for ARX-01, ARX-02 and ARX-03, we have never completed 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. The FDA

could analyze our data using alternative imputation strategies and determine that the trial was negative or inconclusive. 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 conduct three Phase 3 studies in 2012 for ARX-01. We have successfully initiated two of our three planned Phase 3 studies and anticipate initiating the third and final Phase 3 study in the third quarter of 2012. We plan to conduct one Phase 2 study for ARX-04 contingent on approval from the USAMRMC. Our current and planned clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. Our clinical trials for any of our product candidates could be delayed for a variety of reasons, including:

inability to raise funding necessary to initiate or continue a trial;

delays in pharmacokinetic studies required to submit an NDA;

delays in obtaining regulatory approval to commence a trial;

delays in obtaining USAMRMC approval to commence a trial;

delays in reaching agreement with the FDA on final trial design;

delays in completing the required device Human Factors studies and software validation to the satisfaction of the FDA;

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;

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- 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 planned Phase 3 trials or Phase 2 trial are delayed for our product candidates for any of the above reasons, our development costs may increase, our approval process could be delayed and our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

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

Adverse events, or AEs, caused by our product candidates could cause us, other reviewing entities, clinical study sites or regulatory authorities to interrupt, delay or halt clinical studies and could result in the denial of regulatory approval. Phase 2 clinical studies conducted by us with our ARX-01, ARX-02 and ARX-03 product candidates have generated some AEs, but no serious adverse events, or SAEs, related to the study drug. 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 related to the study drug 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 product candidate with both drug and device components submitted in the investigational new drug application. Based on our discussions with the FDA, we believe that ARX-01 is viewed as a combination product by the FDA, and both drug and device components will be required for review as part of an NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as ARX-01. As a result, we have in the past and may in the future experience delays for ARX-01 due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device product approval under an

NDA.

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

We cannot commercialize any of our product candidates, including ARX-01, until the appropriate regulatory authorities, such as the FDA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval for ARX-01. Additional delays may result if ARX-01 is taken before an FDA Advisory Committee which may recommend restrictions on approval or recommend non-approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process.

Even if we obtain regulatory approval for ARX-01 and our other product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the labeling ultimately approved for ARX-01 and our other product candidates will likely include restrictions on use due to the opioid 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, discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;

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

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

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

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and require the adoption of REMS. Our product candidates will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. While we have received information from the FDA regarding certain aspects of the required REMS for 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, ARX-03 and ARX-04, 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 many risks including:

the inability to meet our product specifications and quality requirements consistently;

a delay or inability to procure or expand sufficient manufacturing capacity;

manufacturing and product quality issues related to scale-up of manufacturing;

costs and validation of new equipment and facilities required for scale-up;

a failure to comply with cGMP and similar foreign standards;

the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;

the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms;

the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;

operations of our third party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;

carrier disruptions or increased costs that are beyond our control; and

the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical 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. 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 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, and sufentanil is a highly potent, Schedule II compound. These factors necessitate the use of specialized

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

Manufacturing issues may arise that could 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 our product candidates. In the future we may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our products.

Historically, we have manufactured the majority of our NanoTab supplies at Patheon in Toronto, Canada. During the third quarter of 2011, we transferred our manufacturing capabilities to Patheon s facility in Cincinnati, Ohio where we have built out a suite within their existing buildings that will serve as a manufacturing facility for clinical and commercial supplies of NanoTabs. The new facility has been qualified; however, we have not yet produced clinical or commercial supplies out of this facility and issues may arise in production pertaining to the new facility, or otherwise, which may adversely affect our clinical and commercial plans. In addition, the FDA or other regulatory agencies may require that a bioequivalence study be conducted, which is designed to ensure that the Phase 3 drug lots made at Patheon, Toronto are equivalent to one of the registration drug lots made at Patheon, Cincinnati. There is risk that the study could fail the FDA s bioequivalence requirements which would adversely affect our clinical and commercial plans.

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 are using in Phase 3 clinical trials and plan to use commercially, or the Phase 3 device, has more features than the device used in Phase 2, including additional software. We have conducted multiple Design Validation, Software Verification and Validation, Reprocessing and Human Factors studies, which have informed the design of the Phase 3 device and we plan to conduct one or more summative Human Factors studies in 2012. However, we cannot predict if the Phase 3 device will be fully functional or acceptable throughout the Phase 3 clinical trials or for commercial use. If we need to modify the Phase 3 device either before, during or after the planned 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.

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

We have manufactured ARX-01 devices and supplies on a small scale, including those needed for the first Phase 3 clinical study. We continue to rely on contract manufacturers, component fabricators and secondary service providers to produce the necessary ARX-01 devices for the remaining Phase 3 clinical trials and the commercial marketplace. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the ARX-01 device to third parties and intend to continue to do so. These purchases of Phase 3 devices and components were made and will continue to be made utilizing short term purchase agreements and we may not be able to enter into long-term agreements for commercial supply of ARX-01 with third party manufacturers, or may be unable to do so on acceptable terms. We may encounter unanticipated problems in the scale-up and automation process that will result in delays in the manufacturing of the ARX-01 cartridge, dispenser or controller.

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

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

business priorities.

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

We have selected and executed agreements with our CRO to conduct our first two Phase 3 clinical studies for ARX-01 and for the Phase 2 study for ARX-04. We will rely on this CRO, along with other CROs, as well as clinical trial sites, to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our ongoing clinical programs for 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.

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.

Development of ARX-04 is dependent on funding from our government grant with the US Army Medical Research and Material Command, or USAMRMC.

In May 2011, we entered into an award contract with the USAMRMC, effective June 1, 2011, in which the USAMRMC granted approximately $5.6 million to us in order to support the development of ARX-04, a sufentanil NanoTab for the treatment of moderate-to-severe acute pain. Under the terms of the grant, the USAMRMC will

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reimburse us for development, manufacturing and clinical costs necessary to prepare for and complete the planned Phase 2 dose-finding trial in a study of acute moderate-to-severe pain, and to prepare to enter Phase 3 development. The period of research under the grant ends on August 31, 2012, with a final report due on September 30, 2012. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research.

Development of ARX-04 is dependent on the continued performance by the USAMRMC of its responsibilities under this agreement, including adequate continued funding of USAMRMC programs as well as the prompt processing of USAMRMC s internal approvals necessary to initiate the Phase 2 clinical study. We have no control over the resources and funding that USAMRMC may devote to this or future agreements, which may be subject to annual renewal and which generally may be terminated by USAMRMC at any time.

USAMRMC may fail to perform their responsibilities under the agreement, which may result in termination of the agreement. In addition, we may fail to perform our responsibilities under the agreement. Our government agreement is subject to audits, which may occur several years after the period to which the audit relates. If an audit identifies significant unallowable costs, we could incur a material charge to our earnings or reduction in our cash position. As a result, we may be unsuccessful in entering, or ineligible to enter, into future government agreements.

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

Risks Related to Commercialization of Our Product Candidates

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

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

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;
- the prevalence and severity of any AEs;
- overcoming the perception of sufentanil as a potentially unsafe drug due to its high potency;
- limitations or warnings contained in the FDA-approved label for ARX-01;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators sales and marketing strategies;

our ability to obtain hospital formulary approval;

our ability to obtain and maintain sufficient third party coverage or reimbursement; and

the willingness of patients to pay out-of-pocket in the absence of third party coverage.

If ARX-01 is approved, but does not achieve an adequate level of acceptance by physicians, patients and health care payors, we may not generate sufficient revenue from ARX-01 and we may not become or remain profitable.

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

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

To date, we have not entered into any strategic partnerships for any of our product candidates. We face significant competition in seeking appropriate strategic partners, and these strategic partnerships can be intricate and time consuming to negotiate and document. We may not be able to negotiate strategic partnerships on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic partnerships because of the numerous risks and uncertainties associated with establishing strategic partnerships. Our strategy for ARX-01 is to develop a hospital-directed sales force and/or collaborate with third parties to promote the product to healthcare professionals and third-party payors in the United States. Our future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our product candidates to healthcare professionals and in geographical 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.

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

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

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

If our product candidates are approved for commercialization, we intend to enter into agreements with third parties to market 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;

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reduced protection for intellectual property rights;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, or political instability in particular foreign economies and markets;

compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

foreign taxes, including withholding of payroll taxes;

foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

workforce uncertainty in countries where labor unrest is more common than in the United States;

production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and

business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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

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

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. Also in development is MoxDuo, an orally administered, fixed ratio combination of morphine and oxycodone being developed by QRx Pharma, an Australian company. This product is also in development as an IV product.

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

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

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

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

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

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generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with the sale of ARX-01 and any other products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

Risks Related to Our Business Operations and Industry

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

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

The DEA limits the availability and production of all Schedule II substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers have applied annually for a quota on our behalf. 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 to meet anticipated increases in demand 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, historically we have purchased sufentanil in the United States and have shipped it to our third party manufacturer, Patheon Inc. in Toronto, Canada, where much of our clinical trial manufacturing has been completed to date. While we transferred manufacturing responsibilities to Patheon s facility in Cincinnati, Ohio in the third quarter of 2011, we may elect or need to use Patheon s facility in Toronto, Canada at some point in the future. Shipping across international borders is a bureaucratic process that takes a minimum of three months and requires permits for both import and export. 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 and imported between Canada and 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 or any of our product candidates, 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. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon s production facility in Cincinnati, Ohio. There can be no assurance that the technology transfer process will be completed in a timely manner which could result in a delay in submission of an NDA.

In addition, we do not yet have a commercial supply contract in place. If we cannot establish a supply contract on commercially reasonable terms, or if equipment manufacture or modifications do not meet expected deadlines, the timing for NDA submission may be delayed.

Switching or adding commercial manufacturing capability can involve substantial cost and require extensive management time and focus, as well as additional regulatory filings. In addition, there is a natural transition period when a new manufacturing facility commences work. As a result, delays may occur, which can materially impact our ability to meet our desired commercial timelines, thereby increasing our costs and reducing our ability to generate revenue.

The facilities of any of our future manufacturers of sufentanil-containing NanoTabs must be approved by the FDA after we submit our 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 do not meet the FDA s strict regulatory requirements, they will not be able to secure FDA approval for their manufacturing facilities. If the FDA does not approve these facilities for the commercial manufacture of sufentanil NanoTabs, we will need to find alternative suppliers, which would result in significant delays in obtaining FDA approval for 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, 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 May 1, 2012, we had 21 full-time employees. As our company matures, we expect to expand our employee base to increase our managerial, scientific and engineering, operational, sales, marketing, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize ARX-01 and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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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 and one issued patent in the United States, and one issued patent in Europe. If our pending patent applications fail to issue, 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.

In addition, there can be no assurance that our pending patent applications will result in issued patents. As of December 31, 2011, we are the owner of record of one issued U.S. patent which expires in 2030, one issued European patent which expires in 2027, and we are pursuing 17 U.S. non-provisional patent applications, two pending international Patent Cooperation Treaty applications and 52 foreign national applications, including six European Regional Phase applications directed to our product candidates. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

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

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

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

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

It is possible that we may in the future receive, particularly as a public company, communications from competitors and other companies alleging that we may be infringing their patents, trade secrets or other intellectual property rights, offering licenses to such intellectual property or threatening litigation. In addition to patent infringement claims, third parties may assert copyright, trademark or other proprietary rights against us. We may need to expend considerable resources to counter such claims and may not be 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. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted

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and may also affect patent litigation. The United States Patent Office is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act will not become effective until one year or 18 months after its enactment. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

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

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

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

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

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

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

We have systems in place, including use of third party vendors, to manage payment of periodic maintenance fees, renewal fees, annuity fees and various other patent and application fees. The United States Patent and Trademark Office, or the USPTO, and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. There 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 registered our NANOTAB mark and have received a notice of allowance for our tagline, ACCELERATE, INNOVATE, ALLEVIATE in Class 5, in the United States. Although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. It is also possible that we have not yet registered all of our trademarks in all of our potential markets, and that there are names or symbols other than ACELRX that may be protectable marks for which we have not sought registration, and failure to secure those registrations could adversely affect our business. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings.

Risks Related to this Offering and Ownership of Our Common Stock

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

Prior to our initial public offering, or IPO, in February 2011, there was no public market for our common stock. An active public trading market may not develop or, if developed, may not be sustained. Moreover, the trading price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in clinical trials;
- inability to obtain additional funding, including funding necessary to complete the ARX-01 NDA preparation process and file the NDA with the FDA;

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

failure to successfully develop and commercialize our product candidates;

changes in laws or regulations applicable to our products;

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

adverse regulatory decisions;

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

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

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

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

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

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

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

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

trading volume of our common stock.

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

Our common stock is thinly traded and in the future, may continue to be thinly traded, and investors may be unable to sell at or near ask prices, their respective purchase prices or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.

To date, we have a low volume of daily trades in our common stock on the NASDAQ Global Market. For example, the average daily trading volume in our common stock on the NASDAQ Global Market during the first quarter of 2012 was approximately 7,500 shares per day. Investors purchasing our common stock in this offering may be unable to sell their common stock at or near ask prices, their respective purchase prices or at all, which may result in substantial losses to investors.

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

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

Our executive officers and directors, together with the stockholders with whom our executive officers and directors are affiliated or associated, beneficially owned approximately 83% of our outstanding voting stock as of March 31, 2012. Therefore, these stockholders have the ability to control us through this ownership position. These stockholders are able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, are able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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

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

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

We plan to continue to assess our internal controls and procedures and intend to take further action as necessary or appropriate to address any other matters we identify. In addition, our independent registered public accounting firm will also be required to deliver an attestation report on the effectiveness of our internal control over financial reporting beginning with the year ending December 31, 2012, unless we qualify for an exemption as a non-accelerated filer under the applicable SEC rules and regulations.

We have been and will continue to be involved in a substantial effort to implement appropriate processes, document the system of internal control over key processes, assess their design, remediate any deficiencies identified and test their operation. We cannot be certain at this time whether our measures to improve internal controls will be successful, that we will be able to successfully complete the procedures, certification and attestation requirements of Section 404 or that we or our independent registered public accounting firm will not identify material weaknesses in our internal control over financial reporting. If we fail to comply with the requirements of Section 404, it may affect the reliability of our internal control over financial reporting and negatively impact the quality of disclosure to our investors. If we or our independent registered public accounting firm identify and report a material weakness, it could adversely affect our stock price.

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

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. As of March 31, 2012, we had 19.7 million shares of common stock outstanding, all of which is eligible for sale in the public market, subject in some cases to the volume limitations and manner of sale requirements of Rule 144 under the Securities Act. Sales of stock by our stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock. On March 29, 2012, we entered into the Purchase Agreement in connection with the Private Placement completed on June 1, 2012. Pursuant to the terms of the Purchase Agreement we have agreed to file this registration statement under the Securities Act registering the resale of 2,922,337 shares of common stock issued in the Private Placement, as well as the 2,630,103 shares of common stock underlying the Warrants issued in the Private Placement, and to maintain the effectiveness of this registration statement until the earlier of (i) the date that all shares registered pursuant to this registration statement have been sold or can be sold publicly without restriction or limitation under Rule 144 (including, without limitation, the requirement to be in compliance with Rule 144(c)(1)), or (ii) June 1, 2014.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

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

We are at risk of securities class action litigation.

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

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

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

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to investors 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 our board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

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INFORMATION REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the information that we incorporate by reference, contains various forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as anticipates, believes, continue estimates, expects, intends, may, plan predicts, should, will, or the negative of these terms or other comparable terminology. These forward-looking statements may also use different phrases. Discussions containing these forward-looking statements may be found, among other places, in Business and Management s Discussion and Analysis of Financial Condition and Results of Operations incorporated by reference from our most recent annual report on Form 10-K and in our most recent quarterly report on Form 10-Q subsequent to the filing of our most recent annual report on Form 10-K with the SEC, as well as any amendments thereto reflected in subsequent filings with the SEC. 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, including the information that we incorporate by reference, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations, including funding necessary to complete the ARX-01 NDA preparation process and file the NDA with the FDA;
- 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, risks and uncertainties that may cause our actual results to differ materially from those expressed or implied by these forward-looking statements. Given these other important factors, risks and uncertainties, you should not place undue reliance on these forward-looking statements. Also, these forward-looking statements represent our estimates and assumptions only as of the date such forward-looking statements are made. You should carefully read this prospectus, together with the information incorporated herein by reference as described under the section entitled Incorporation of Certain Information by Reference, completely and with the understanding that our actual future results may be materially different from what we expect. We can give no assurances that any of the events anticipated by the forward-looking statements will occur or, if any of them do, what impact they will have on our business, results of operations and financial condition.

You should rely only on information contained or incorporated by reference in this prospectus and any prospectus supplement, the registration statement of which this prospectus is a part, including the exhibits that we have filed with the registration statement and, if required, any post-effective amendment to the registration statement of which this prospectus is a part. You should understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Except as required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. You should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to purchase our common stock, you should carefully consider the risk factors discussed and incorporated by reference in this prospectus and any prospectus supplement and, if required, any post-effective amendment to the registration statement of which this prospectus is a part.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale or other disposition of shares of our common stock by the selling stockholders pursuant to this prospectus. A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase our common stock. Upon any exercise of the Warrants for cash, the selling stockholders would pay us the exercise price of the Warrants. The cash exercise price of the warrants is currently $3.40 per share of our common stock. Cash received from exercise of warrants will be used for general corporate purposes. Additionally, under certain conditions set forth in the warrants, the warrants are exercisable on a cashless basis. If any warrants are exercised on a cashless basis, we would not receive any cash payment from the selling stockholders upon any exercise of such warrants.

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SELECTED FINANCIAL DATA

The following table sets forth historical selected financial information. Effective January 1, 2012, we adopted the Financial Accounting Standards Board s (FASB) Accounting Standards Update (ASU) No. 2011-05, Comprehensive Income (Topic 220): Presentation of Comprehensive Income, as amended by ASU 2011-12, Comprehensive Income (Topic 220): Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items Out of Accumulated Other Comprehensive Income in Accounting Standards Update No. 2011-05. These updates revise the manner in which entities present comprehensive income in their financial statements. The following selected financial information revises historical information to illustrate the new presentation required by this pronouncement for the periods presented.

STATEMENTS OF COMPREHENSIVE LOSS

(Unaudited, in thousands)

	December 31, 2009	December 31, 2010	December 31, 2011	Period from July 13, 2005 (Inception) Through December 31, 2011
Net (loss)	$ (20,119)	$ (14,344)	$ (20,101)	$ (88,664)
Unrealized gain (loss) on available-for-sale securities	(41)	2		
Comprehensive (loss)	$ (20,160)	$ (14,342)	$ (20,101)	$ (88,664)

SELLING STOCKHOLDERS

The shares of common stock being offered by the selling stockholders are those issued to the selling stockholders in the Private Placement, including the shares of common stock issuable upon exercise of the Warrants. For additional information regarding the Private Placement, see Prospectus Summary The Offering above. We are registering the shares of common stock in order to permit the selling stockholders to offer the shares for resale from time to time. Certain of the selling stockholders have a position, office or material relationship with us. Each such material relationship is described below.

The table below lists the selling stockholders and other information regarding the beneficial ownership (as determined under Section 13(d) of the Exchange Act and the rules and regulations thereunder) of the shares of common stock held by each of the selling stockholders. The *Shares of Common Stock Beneficially Owned Prior to Offering* column lists the number of shares of common stock beneficially owned by the selling stockholders, based on their respective ownership of shares of common stock as of June 1, 2012. Because the Warrants are not exercisable until six months after June 1, 2012, the shares issuable upon exercise of the Warrants are not included in the *Shares of Common Stock Beneficially Owned Prior to Offering* column.

The *Number of Shares Being Offered* column lists the shares of common stock being offered by this prospectus by the selling stockholders and does not take in account any limitations on exercise of the Warrants set forth therein.

In accordance with the terms of the Purchase Agreement, this prospectus generally covers the resale of the sum of (i) the number of shares of common stock issued in the Private Placement and (ii) the maximum number of common stock issuable upon exercise of the Warrants (without taking into account any limitations on the exercise of the Warrants set forth therein), determined as if the Warrants were exercised in full for cash (without regard to any limitations on exercise contained therein) as of the trading day immediately preceding the date this registration statement was initially filed with the SEC. The *Shares of Common Stock Beneficially Owned After Offering* column assumes the sale of all of the shares offered by the selling stockholders pursuant to this prospectus. The selling stockholders may offer and sell all or part of the common stock covered by this prospectus, but no estimates can be made as to the number of shares of common stock that will be held by the selling stockholders after the completion of this offering.

The selling stockholders may sell all, some or none of their shares in this offering. See Plan of Distribution.

	Number of

Security Holder	Shares of Common Stock Beneficially Owned Prior to Offering (1)		Shares Being Offered	Shares of Common Stock Beneficially Owned After Offering (1)	
	Number	Percent		Number	Percent
Deerfield Special Situations Fund International, Limited(3) 780 Third Avenue, 37th Floor New York, NY 10017	940,121	4.16%	1,303,178	254,238	1.12%
Deerfield Special Situations Fund, L.P.(4) 780 Third Avenue, 37th Floor New York, NY 10017	672,435	2.97%	932,117	181,847	*
Capital Ventures International(2)(5) 101 California Street, Suite 3250 San Francisco, CA 94111	85,294	*	162,059		*
LSP Life Sciences Fund N.V.(6) Johannes Vermeerplein 9 1071 DV Amsterdam	941,176	4.16%	1,788,234		*
RRC Bio Fund, L.P.(7) 217 R. Concord Avenue Cambridge, MA 02138	286,000	1.26%	285,000	136,000	*
Three Arch Partners IV, L.P.(8) 3200 Alpine Road Portola Valley, CA 94028	3,958,829	17.50%	396,931	3,749,918	16.57%
Three Arch Associates IV, L.P.(9) 3200 Alpine Road Portola Valley, CA 94028	87,408	*	8,764	82,795	*
Three Arch Partners III, L.P.(10) 3200 Alpine Road Portola Valley, CA 94028	3,704,712	16.37%	128,332	3,637,169	16.08%
Three Arch Associates III, L.P.(11) 3200 Alpine Road Portola Valley, CA 94028	199,174	*	6,899	195,543	*
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(12) 525 University Avenue Palo Alto, CA 94301	4,171,933	18.44%	540,926	3,887,235	17.18%

* Represents less than 1%.

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(1) Shares beneficially owned include shares of our common stock and shares issuable upon exercise of options or warrants exercisable within sixty days of June 1, 2012, if any, but exclude shares of our common stock issuable pursuant to the Warrants held by the selling stockholders, which Warrants are not exercisable until six months after June 1, 2012. Percentages are based on 22,625,000 shares of common stock outstanding on June 1, 2012. In calculating the percentage for each selling stockholder, shares of common stock issuable pursuant to options and warrants (excluding the Warrants) exercisable within sixty days of June 1, 2012, if any, are treated as shares outstanding for that selling stockholder but are not treated as outstanding for any other selling stockholder. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the selling stockholders named in this table has sole or shared voting and investment power with respect to the shares indicated as beneficially owned.

(2) The selling stockholder has identified itself as an affiliate of a registered broker-dealer. The selling stockholder has represented to us that it purchased the shares in the ordinary course of its business and, at the time of purchase, with no arrangement or understanding, directly or indirectly, with any persons to distribute such shares.

(3) The number of shares offered consists of 685,883 shares of common stock and 617,295 shares of common stock underlying Warrants. James E. Flynn has sole voting and investment power over the shares listed above.

(4) The number of shares offered consists of 490,588 shares of common stock and 441,529 shares of common stock underlying Warrants. James E. Flynn has sole voting and investment power over the shares listed above.

(5) The number of shares offered consists of 85,294 shares of common stock and 76,765 shares of common stock underlying Warrants. Heights Capital Management, Inc., the authorized agent of Capital Ventures International (CVI), has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as an Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the shares held by CVI. Mr. Kobinger disclaims any such beneficial ownership of the shares.

(6) The number of shares offered consists of 941,176 shares of common stock and 847,058 shares of common stock underlying Warrants. M. Wegter and J.P.P. Muijrers, managing directors of LSP Advisory B.V., managing director of LSP Life Sciences Fund N.V., share voting and investment power over the shares listed above.

(7) The number of shares offered consists of 150,000 shares of common stock and 135,000 shares of common stock underlying Warrants. James Silverman has sole voting and investment power over the shares listed above.

(8) The number of shares offered consists of 208,911 shares of common stock and 188,020 shares of common stock underlying Warrants. Mark A. Wan and Wilfred E. Jaeger, Managing Members of Three Arch Management IV, LLC, General Partner of Three Arch Partners IV, L.P., share voting and investment power over the shares listed above. Mr. Wan is a member of our board of directors.

(9) The number of shares offered consists of 4,613 shares of common stock and 4,151 shares of common stock underlying Warrants. Mark A. Wan and Wilfred E. Jaeger, Managing Members of Three Arch Management IV, LLC, General Partner of Three Arch Associates IV, L.P., share voting and investment power over the shares listed above. Mr. Wan is a member of our board of directors.

(10) The number of shares offered consists of 67,543 shares of common stock and 60,789 shares of common stock underlying Warrants. Mark A. Wan and Wilfred E. Jaeger, Managing Members of Three Arch Management III, LLC, General Partner of Three Arch Partners III, L.P., share voting and investment power over the shares listed above. Mr. Wan is a member of our board of directors.

(11) The number of shares offered consists of 3,631 shares of common stock and 3,268 shares of common stock underlying Warrants. Mark A. Wan and Wilfred E. Jaeger, Managing Members of Three Arch Management III, LLC, General Partner of Three Arch Associates III, L.P., share voting and investment power over the shares listed above. Mr. Wan is a member of our board of directors.

(12) The number of shares offered consists of 284,698 shares of common stock and 256,228 shares of common stock underlying Warrants. The shares are held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. John G. Freund and Yasunori Kaneko are the Managing Members of Skyline Venture Management IV, LLC, which is the sole 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 held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. Stephen Hoffman, a member of our board of 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 held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Each of Drs. Freund, Kaneko and Hoffman disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

Information about any other selling stockholders will be included in prospectus supplements or post-effective amendments, if required. Information about the selling stockholders may change from time to time. Any changed information with respect to which we are given notice will be included in prospectus supplements or, if required, in a post-effective amendment to the registration statement of which this prospectus is a part.

Material Relationships with Certain Selling Stockholders

The following is a summary of transactions since June 1, 2009 to which we have been a party and in which entities affiliated with Three Arch Partners and Skyline Venture Partners, each of which is a selling stockholder, had or will have a direct or indirect material interest.

Private Placement Financings

Preferred Stock Financing

The following table summarizes purchases of our Series C convertible preferred stock by entities affiliated with Three Arch Partners and Skyline Venture Partners.

Name	Series C Preferred Stock	Aggregate Purchase Price of Series C Preferred Stock
Funds affiliated with Three Arch Partners(1)	1,752,337	$ 6,909,117
Funds affiliated with Skyline Venture Partners(2)	915,798	3,610,810
Approximate price per share	$ 3.94	
Date of purchase	11/23/09	

(1) Includes 44,702 shares of Series C convertible preferred stock purchased by Three Arch Associates III, L.P., 18,928 shares of Series C convertible preferred stock purchased by Three Arch Associates IV, L.P., 831,466 shares of Series C convertible preferred stock purchased by Three Arch Partners III, L.P. and 857,241 shares of Series C convertible preferred stock purchased by Three Arch Partners IV, L.P. Mark A. Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners.

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

2010 Bridge Loan Financing

On September 14, 2010, we sold to entities affiliated with Three Arch Partners and Skyline Venture Partners convertible notes, or the 2010 notes, and warrants, or

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the 2010 warrants, which 2010 warrants were potentially exercisable into (1) shares of preferred stock sold in the next equity financing with proceeds in excess of $15.0 million with an exercise price equal to the price of the preferred stock sold in such equity financing or (2) shares of our Series C convertible preferred stock at a price $3.94 per share. The aggregate number of shares exercisable under the 2010 warrants was to equal 25% of the principal amount of the corresponding 2010 notes divided by (1) the per share price of the equity securities sold in the next qualified equity financing or (2) the price of the Series C convertible preferred stock of $3.94 per share. Upon the election of the holders of a majority of the aggregate principal amount payable under all of the 2010 notes outstanding, we were to sell an additional $4.0 million of 2010 notes and corresponding 2010 warrants, a portion of which would have been sold to entities affiliated with Three Arch Partners and Skyline Venture Partners. However, this call option expired upon the closing of our initial public offering, or IPO.

The 2010 notes bore interest at a rate of 4.0% per annum. No payment of principal or interest was paid on the 2010 notes and the aggregate amount of principal outstanding on 2010 notes held by entities affiliated with Three Arch Partners and Skyline Venture Partners was approximately $5.8 million as of February 16, 2011, the closing of our IPO. In connection with our IPO, the outstanding principal and accrued interest under the 2010 notes automatically converted into common stock at a conversion price equal to $4.00.

The 2010 warrants held by entities affiliated with Three Arch Partners and Skyline Venture Partners became exercisable by their terms for an aggregate of 77,365 shares of Series C preferred stock at an exercise price of approximately $3.94 immediately prior to the closing of our IPO. Each 2010 warrant contained a customary net issuance feature, which allowed 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. The entities affiliated with Three Arch Partners and Skyline Venture Partners elected to exercise the 2010 warrants on a net issuance basis contingent upon and effective immediately prior to the completion of our IPO.

2010 Bridge Loan Financing Participation

The following table summarizes the participation in the 2010 bridge financing by entities affiliated with Three Arch Partners and Skyline Venture Partners:

Name	Aggregate Loan Amount	Aggregate Shares of Series C Preferred Stock Issued Upon Exercise of 2010 Warrants(1)
Funds affiliated with Three Arch Partners(2)	$ 3,793,273	50,854
Funds affiliated with Skyline Venture Partners(3)	1,977,503	26,511

(1) The above table and footnotes give effect to the exercise, on a net issuance basis, of the 2010 warrants, which were exercised upon and effective immediately prior to the completion of our IPO. The shares of Series C preferred stock issued upon the exercise of the 2010 warrants were automatically converted into common stock in connection with our IPO.

(2) Includes a note purchased by Three Arch Associates III, L.P. with a principal amount of $96,767, a note purchased by Three Arch Associates IV, L.P. with a principal amount of $40,973, a note purchased by Three Arch Partners III, L.P. with a principal amount of $1,799,869 and a note purchased by Three Arch Partners IV, L.P. with a principal amount of $1,855,663. Includes a warrant purchased by Three Arch Associates III, L.P., exercised, on a net issuance basis, for 1,297 shares of Series C preferred stock, a warrant purchased by Three Arch Associates IV, L.P., exercised, on a net issuance basis, for 549 shares of Series C preferred stock, a warrant purchased by Three Arch Partners III, L.P., exercised, on a net issuance basis, for 24,130 shares of Series C preferred stock and a warrant purchased by Three Arch Partners IV, L.P., exercised, on a net issuance basis, for 24,878 shares of Series C preferred stock. Mark A. 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.

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

Bridge Note and Warrant Transfer

In February 2011, one of our affiliated investors agreed to transfer a 37% interest in the 2010 note and the associated portion of the 2010 warrant then held by such affiliated investor for nominal consideration to certain other of our affiliated investors, including funds affiliated with Three Arch Partners and Skyline Venture Partners, pro rata among them based on each entity s affiliated funds current beneficial ownership of our

outstanding capital stock, with such transfer effective immediately prior to the closing of our IPO. As a result of the foregoing transfer, effective immediately prior to the closing of our IPO:

- funds affiliated with Three Arch Partners acquired 2010 warrants which were subsequently exercised, on a net issuance basis, for an aggregate of 5,236 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and 2010 notes in an aggregate principal amount of $390,704; and

- funds affiliated with Skyline Venture Partners acquired a 2010 warrant which was subsequently exercised, on a net issuance basis, for 2,730 shares of Series C preferred stock (which shares were converted into the same number of shares of common stock in connection with our IPO) and a 2010 note in a principal amount of $203,676.

Investors Rights Agreement

We entered into an investors rights agreement with certain holders of our previously outstanding preferred stock and previously outstanding warrants to purchase our preferred stock, including entities affiliated with Three Arch Partners and Skyline Venture Partners. Pursuant to the investors rights agreement, these holders will have the right to demand that we file a registration statement or request that the common stock issued upon conversion of our previously outstanding preferred stock and the common stock issuable upon the exercise of outstanding warrants to purchase common stock (which, in connection with our IPO, were converted from previously outstanding warrants to purchase our preferred stock), collectively, the registrable securities, be covered by a registration statement that we are otherwise filing. In the event that we propose to register any of our securities under the Securities Act, either for our own account or for the account of other security holders, these holders, including the entities affiliated with Three Arch Partners and Skyline Venture Partners, are entitled to notice of our registration and are entitled to certain piggyback registration rights allowing them 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, including the entities affiliated with Three Arch Partners and Skyline Venture Partners, 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 that such holders may include.

Voting Agreement

We entered into a voting agreement under which holders of our previously outstanding preferred stock, including entities affiliated with Three Arch Partners and Skyline Venture Partners, 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 previously outstanding preferred stock agreed to vote such that one director be a designee of Three Arch Partners IV, L.P. or its affiliates, who is currently Mark A.

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Wan; 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 our IPO, the voting agreement terminated in its entirety and none of our stockholders have any special rights regarding the election or designation of members of our board of directors.

Participation in Our Initial Public Offering

Entities affiliated with Three Arch Partners and Skyline Venture Partners, each of which is a selling stockholder, purchased an aggregate of 3,815,522 shares of our common stock in our IPO, as follows:

Name	Common Stock Purchased in Initial Public Offering	Aggregate Purchase Price
Funds affiliated with Three Arch Partners(1)	2,579,579	$ 12,897,895
Funds affiliated with Skyline Venture Partners(2)	1,235,943	6,179,715
Price per share	$ 5.00	
Date of purchase	2/11/11	

(1) Includes 65,806 shares of common stock purchased by Three Arch Associates III, L.P., 27,863 shares of common stock purchased by Three Arch Associates IV, L.P., 1,223,983 shares of common stock purchased by Three Arch Partners III, L.P. and 1,261,927 shares of common stock purchased by Three Arch Partners IV, L.P. Mark A. Wan, one of our directors, is managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares.

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

Indemnification Agreements

We have entered into indemnification agreements with each of our current directors and officers, including Mark A. Wan, managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and Stephen Hoffman, Managing Director of Skyline Ventures. 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 and officers. Furthermore, we have obtained director and officer liability insurance to cover liabilities our directors and officers may incur in connection with their services to us and have increased the level upon the completion of the our IPO.

Private Placement

We have entered into a Private Placement with the selling stockholders as further described in the section entitled The Offering Private Placement. Entities affiliated with Three Arch Partners and Skyline Venture Partners purchased an aggregate of 569,396 shares of our common stock and 512,456 Warrants in the Private Placement, as follows:

Name	Common Stock Purchased in Private Placement	Warrants Purchased in Private Placement	Aggregate Purchase Price
Funds affiliated with Three Arch Partners(1)	284,698	256,228	$ 1,000,001.73
Funds affiliated with Skyline Venture Partners(2)	284,698	256,228	$ 1,000,001.73

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

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

PLAN OF DISTRIBUTION

The selling stockholders may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

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The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(7) or other applicable provision of the Securities Act supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(7) or other applicable provision of the Securities Act or, if required, a post-effective amendment to the registration statement of which this prospectus is a part, supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act.

We are required to pay all fees and expenses incident to the registration of the shares of common stock. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any selling stockholder. If we are notified by any selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

The anti-manipulation rules of Regulation M under the Securities Exchange Act of 1934 may apply to sales of our common stock and activities of the selling stockholders.

LEGAL MATTERS

The validity of the common stock being offered hereby was passed upon by Cooley LLP, Palo Alto, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2011, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. You may also read and copy any document we file 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. We maintain a website at *www.acelrx.com*. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-35068):

- our annual report on Form 10-K for the year ended December 31, 2011 filed with the SEC on March 23, 2012;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2012, filed with the SEC on May 9, 2012;
- our current reports on Form 8-K filed with the SEC on January 25, 2012, February 13, 2012, April 12, 2012, May 30, 2012 and June 4, 2012; and
- the description of our common stock, which is registered under Section 12 of the Exchange Act, in our registration statement on Form 8-A, filed with the SEC on February 1, 2011, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange

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Act, including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of such registration statement, until we file a post-effective amendment that indicates the termination of the offering of the common stock covered by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents to James H. Welch, Chief Financial Officer, AcelRx Pharmaceuticals, Inc., 351 Galveston Drive, Redwood City, CA 94063; telephone: (650) 216-3500.