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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2013

or

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

For the transition period from to
Commission File Number: 001-35068

ACELRX PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**41-2193603**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

351 Galveston Drive
Redwood City, CA 94063
(650) 216-3500
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.001 par value	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act:
None

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

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

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

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

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

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

Large accelerated filer	☐	Accelerated filer	☑
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐

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

The aggregate market value of the voting stock held by non-affiliates of the registrant on June 28, 2013 (the last business day of the registrant's most recently completed second fiscal quarter), based upon the last sale price reported on the NASDAQ Global Market on that date, was approximately $180,565,000. The calculation excludes 17,958,578 shares of the registrant's common stock held by current executive officers, directors and stockholders that the registrant has concluded are affiliates of the registrant. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of February 25, 2014, the number of outstanding shares of the registrant's common stock was 43,181,363.

DOCUMENTS INCORPORATED BY REFERENCE

None.

ACELRX PHARMACEUTICALS, INC.

2013 ANNUAL REPORT ON FORM 10-K

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

ACELRX and "ACCELERATE.INNOVATE.ALLEVIATE." are registered trademarks of AcelRx Pharmaceuticals, Inc. Other trademarks of AcelRx Pharmaceuticals, Inc., including ZALVISO, appearing in this prospectus are the property of AcelRx Pharmaceuticals, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

Forward-Looking Statements

This Annual Report on Form 10-K, or Form 10-K, contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, which are subject to the "safe harbor" created by that section. The forward-looking statements in this Form 10-K are contained principally under "Item 1. Business," "Item 1A. Risk Factors" and "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations." In some cases, you can identify forward-looking statements by the following words: "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing" or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Form 10-K, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to obtain and maintain regulatory approval of Zalviso and other product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations, including funding necessary for the planned commercialization and manufacturing of Zalviso in the United States and advancement of clinical trials for other product candidates including our planned Phase 3 clinical program for ARX-04;
- the potential achievement of collaboration milestones, including the approval of the Marketing Authorization Application for Zalviso in the European Union and the timing thereof;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates;
- the rate and degree of market acceptance of our product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; and
- our ability to obtain and maintain intellectual property protection for our product candidates.

In addition, you should refer to "Item 1A. Risk Factors" in this Form 10-K for a discussion of these and other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Form 10-K will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. Also, forward-looking statements represent our estimates and assumptions only as of the date of this Form 10-K. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

Item 1. Business

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. Our lead product candidate, Zalviso ™, formerly known as the Sufentanil NanoTab PCA System, or ARX-01, is currently under review by the FDA for marketing approval, and is designed to improve the management of moderate-to-severe acute pain in patients in the hospital setting. The current standard of care for patients with moderate-to-severe pain in the hospital is intravenous patient-controlled analgesia, or IV PCA, which has been shown to cause harm and inconvenience to patients following surgery because of the side effects of commonly used IV PCA opioids, the invasive IV needle route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps.

Zalviso

Zalviso is an investigational pre-programmed, non-invasive, handheld system that allows hospital patients with moderate-to-severe acute pain to self-dose with sublingual sufentanil NanoTabs to manage their pain. Zalviso is designed to address the needs of patients with moderate-to-severe pain in the hospital setting by offering:

- **A high therapeutic index opioid:** Zalviso uses the high therapeutic index, highly lipophilic opioid, sufentanil, enabling delivery via a non-intravenous route, and also supporting fast onset of effect.
- **A non-invasive route of delivery:** The sublingual route of delivery used by Zalviso provides rapid onset of analgesia, therefore eliminating the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV PCA infusion pump through IV tubing, Zalviso allows for ease of patient mobility.
- **A simple, pre-programmed PCA solution:** Zalviso is a pre-programmed PCA system designed to eliminate the risk of programming errors.

Based on the successful results of our Phase 3 clinical program for Zalviso, we submitted a New Drug Application, or NDA, for Zalviso in September 2013 and, in December 2013, we announced that the U.S Food and Drug Administration, or FDA, accepted for filing the Zalviso NDA. In addition, the FDA has established a Prescription Drug User Fee Act, or PDUFA, action date of July 27, 2014 for AcelRx's Zalviso NDA. Assuming successful approval of our NDA on or around the PDUFA action date, we anticipate generating the first commercial sales of Zalviso in the United States in the first quarter of 2015.

The 505(b)(2) NDA submission for Zalviso is based on a development program that includes data from seven Phase 1 studies, three Phase 2 clinical trials, and three Phase 3 clinical trials. The Phase 3 trial program included two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA with morphine. Zalviso successfully achieved the primary efficacy endpoints for each of these trials. A summary of the Phase 3 trials and results is as follows:

- *Active comparator trial (IAP 309)*—in November 2012, we reported top-line data demonstrating that Zalviso met its primary endpoint of non-inferiority in a Phase 3 open-label active comparator trial designed to compare the efficacy and safety of Zalviso (15 mcg/dose, 20 minute lock-out) to IV PCA with morphine (1mg/dose, 6 minute lock-out) for the treatment of moderate-to-severe acute post-operative pain immediately following major abdominal or orthopedic surgery.
- *Double-blind, placebo-controlled, abdominal surgery trial (IAP 310)*—in March 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain

after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 178 adult patients at 13 U.S. sites.

- *Double-blind, placebo-controlled, orthopedic surgery trial (IAP 311)*—in May 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 426 adult patients at 34 U.S. sites. Treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between Zalviso and placebo-treated patients, despite the shorter duration of exposure in the placebo-treated patients caused by early termination due to inadequate analgesia.

As noted above, assuming successful approval of our NDA on or about the PDUFA action date, we anticipate launching the commercial sale of Zalviso in the United States in the first quarter of 2015.

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in the management of moderate-to-severe acute pain within a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Latin America.

Under the terms of the agreement, AcelRx received an upfront cash payment of $30 million. AcelRx is eligible to receive approximately $220 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements obtained by Grünenthal. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

Grünenthal will be responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. AcelRx will be responsible for obtaining and maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

ARX-04

We are also developing a Sufentanil Single-Dose NanoTab, or ARX-04, for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional to a patient in settings of acute pain, such as on the battlefield, in the emergency room or in ambulatory care facilities. In December 2013, we completed an End of Phase 2 Meeting with the FDA to identify a Phase 3 program pathway forward for evaluation of ARX-04. This definition of the Phase 3 program allows us to continue to refine Phase 3 protocols with the FDA in the coming months, with the goal of initiating Phase 3 studies for ARX-04 in the second half of 2014.

In April 2013, we reported top-line data showing that the primary endpoint was achieved in a placebo-controlled, dose-finding, Phase 2 clinical trial of ARX-04 for acute pain. This trial randomized 101 patients following bunionectomy surgery in a 2:2:1 ratio to 30 mcg sufentanil, 20 mcg sufentanil or placebo treatment arms. Ninety-one percent of patients entering the trial completed the 12-hour trial period.

Results demonstrated that patients receiving 30 mcg sufentanil NanoTab doses, administered by a healthcare professional, no more frequently than once per hour, had significantly greater pain reduction as measured by Summed Pain Intensity Difference to baseline during the 12-hour trial period (SPID-12) than placebo-treated patients (p=0.003). The 20 mcg sufentanil-treated patients did not achieve SPID-12 scores that differentiated from placebo.

Adverse events, or AEs, reported in the trial were generally mild-to-moderate in nature, with two serious adverse events, or SAEs, of post-surgical infection reported, both of which were determined by the investigator to be unrelated to trial drug.

Research and development of ARX-04, including the Phase 2 trial and pre-Phase 3 development, was funded by a $5.6 million grant from the U.S. Army Medical Research and Materiel Command, or USAMRMC. As of December 31, 2013, we had recognized the full amount of the grant of $5.6 million.

ARX-02 and ARX-03

In addition to Zalviso and ARX-04, our product candidate pipeline consists of two other sufentanil-based product candidates. The Sufentanil NanoTab Breakthrough Pain, or BTP, Management System, or ARX-02, is a pain management system for the treatment of cancer patients who suffer from BTP. The Sufentanil/Triazolam NanoTab, or ARX-03, is a single, fixed-dose, combination drug product designed to provide mild sedation, anxiety reduction and pain relief for patients undergoing painful procedures in a physician's office. We have successfully completed Phase 2 clinical trials for ARX-02 and ARX-03. Future development of ARX-02 and ARX-03 is contingent on identification of corporate partnership resources.

Sufentanil NanoTabs

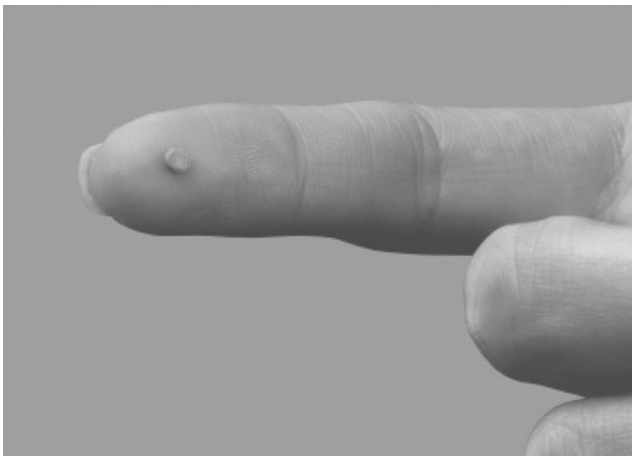
Sufentanil, a high therapeutic index opioid, which has no active metabolites, is 5 to 10 times more potent than fentanyl and is used intravenously as a primary anesthetic to produce balanced general anesthesia for surgery, and for epidural administration during labor and delivery. Sufentanil has many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

Opioid	Therapeutic Index
Meperidine	5
Methadone	12
Morphine	71
Hydromorphone	232
Fentanyl	277
Sufentanil	26,716

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

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

Our portfolio of product candidates leverages the above mentioned advantages of sufentanil delivered via the sublingual route. We believe our non-invasive, proprietary NanoTab sublingual dosage form potentially overcomes many of the limitations of current treatment options available for both acute and breakthrough pain.



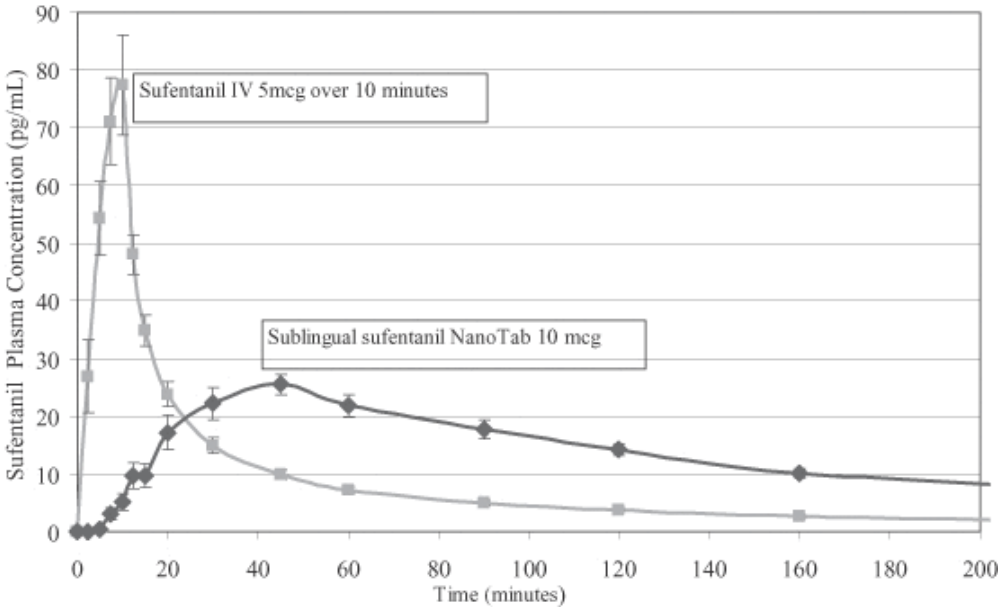
None of our product candidates have been approved by the United States Food and Drug Administration, or FDA. We have not generated any revenue from the sale of any of our product candidates.

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

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

- relatively high bioavailability via the oral mucosa and very low gastrointestinal, or GI, bioavailability;
- prolonged plasma levels relative to IV delivery;
- PK parameters proportional to dose across a wide range of doses (2.5 mcg to 80 mcg);
- lower peak plasma concentration, or C_{max}, than IV delivery;
- time to maximum plasma concentrations, or T_{max}, range from 20 to 120 minutes;
- while clearance increased in younger patients and heavier patients, clearance was not affected by race, sex, renal or hepatic parameters or concomitant CYP3A4 substrates;
- slightly increased C_{max} and prolonged half-life with concomitant administration of the CYP3A4 inhibitor ketoconazole;
- lack of drug accumulation with repeat-dosing and achievement of steady-state plasma concentrations after the 13th dose (with 20 minutes between dosings);
- relatively low patient to patient variability in T_{max} and C_{max}; and
- repeat dosing PK that supports a 20-minute minimum re-dosing interval.

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



In summary, we have demonstrated that sublingual delivery of sufentanil avoids the high peak plasma levels and short duration of action of IV administration, potentially enabling broader use of sufentanil. Our proprietary NanoTab dosage form is a very small disc-shaped tablet with a bioadhesive excipient, or inactive ingredient, that enables the NanoTab to adhere to mucosal tissues. When placed under the tongue, the NanoTab imbibes saliva, adhering it to the sublingual tissues and forming a hydrogel patch. Sufentanil, from the NanoTab, rapidly depots into the fatty tissues under the tongue. The drug then absorbs into the plasma over several hours at roughly the same rate as it is being redistributed and/or cleared from the plasma resulting in a plateau plasma concentration from approximately 20 to 120 minutes. The NanoTab fully disintegrates within 5-10 minutes. The small size of the NanoTab, pictured above, is designed to minimize the saliva response and amount of sufentanil swallowed, resulting in high oral transmucosal uptake, whereby a majority of the drug is absorbed via the oral tissues ultimately into the bloodstream, and thereby provides consistent pharmacokinetics.

Our Product Candidates

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

Product Candidate	Description	Target Indication	Development Status

Zalviso	Sufentanil NanoTab PCA System	Moderate-to-severe acute pain in the hospital setting	• NDA submitted to the FDA in September 2013 and accepted for filing by the FDA in December 2013, with a PDUFA action date set for July 27, 2014.
			• Completion of the Phase 3 clinical development program, which consisted of three trials, each of which achieved their primary endpoint. A summary of the trials is as follows:
			  • In November 2012, we reported results from an open-label active comparator Phase 3 clinical trial (IAP 309) comparing Zalviso to the current standard of care, IV PCA morphine, in patients with acute post-operative pain following open-abdominal surgery or major orthopedic surgery, demonstrating that this trial met its primary endpoint of non-inferiority.
			  • In March 2013, we reported results from a double-blind placebo-controlled efficacy and safety Phase 3 clinical trial (IAP 310) in patients with acute post-operative pain following open-abdominal surgery, demonstrating that this trial met its primary endpoint.
			  • In May 2013, we reported results from a double-blind placebo-controlled efficacy and safety Phase 3 clinical trial (IAP 311) in patients with acute post-operative pain following major orthopedic surgeries, demonstrating that this trial met its primary endpoint.

ARX-04	Sufentanil Single-Dose NanoTab	Moderate-to-severe acute pain	• In April 2013, we reported that a Phase 2 trial of ARX-04 in patients after bunionectomy surgery achieved its primary endpoint, identifying that 30 mcg of sufentanil delivered sublingually no more frequently than once per hour could control pain over a 12 hour period. • End of Phase 2 Meeting completed in December 2013. Phase 3 protocol development is underway, with a view to initiate Phase 3 study in the second half of 2014.

Product Candidate	Description	Target Indication	Development Status
ARX-02	Sufentanil NanoTab BTP Management System	Cancer breakthrough pain	• Phase 2 clinical trial and End of Phase 2 meeting completed. • Future development contingent upon identification of corporate partnership resources.
ARX-03	Sufentanil/Triazolam NanoTab	Mild sedation and pain relief during painful procedures in a physician's office	• Phase 2 clinical trial and End of Phase 2 meeting completed. • Future development contingent upon identification of corporate partnership resources.

Zalviso—Sufentanil NanoTab PCA System

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

The Market Opportunity for Zalviso

According to the 2012 Decision Resources Acute Pain Report, or 2012 DR Report, the acute pain market (represented by treatments for post-operative pain, acute musculoskeletal pain and cancer breakthrough pain) in the United States, Europe and Japan realized 2011 revenues of $14.5 billion, and is expected to reach approximately $17.4 billion by 2021. Opioid analgesic use dominates the management of acute pain, representing 39% of the 2011 market, and is projected to grow to 41% of the 2021 market. Post-operative acute pain treatment in the US is projected to grow significantly in the 2011 to 2021 period, from management of 13.3 million procedures in 2011 to 15.6 million procedures in 2021, a 1.6% CAGR. Despite its size, this market remains underserved. Studies report that up to 75% of patients experience inadequate pain relief after surgery. Inadequate pain relief can lead to decreased mobility, which increases the risks of other medical complications, including deep vein thrombosis and partial lung collapse, and can result in extended hospital stays. The 2012 DR Report supports this finding, identifying that the top attributes for physician selection of a new drug for acute pain in the United States, Europe and Japan are as follows: (1) Superior efficacy in pain (81% of respondents); (2) Superior Safety (39%); (3) Superior tolerability (38%); (4) Improvement in patient quality of life (36%); (5) Superior onset of effect (29%). Additionally, based on an analysis of data published in 2008 from the World Health Organization, we estimate that there are approximately 27 million surgical procedures annually in other moderate-to-high per capita healthcare expenditure nations in which patients experience moderate-to-severe pain.

The 2012 DR Report identifies that surgeons in the United States use on average approximately 1.6 analgesic agents in their acute post-operative pain patients, with approximately 90% of patients receiving an opioid based analgesic agent. In the US, we estimate that approximately one third of all procedures conducted are orthopedic in nature, one third are gastrointestinal, obstetric or gynecologic, and the remaining third are a mix of spinal, cardiothoracic and other procedures. Commissioned market research targeting surgeons and anesthesiologists has identified a consistent positive response to the attributes of Zalviso and indicates an interest in using Zalviso in at least 75% of their eligible patients. Additional market research indicated that physicians expressed interest in using Zalviso for patients who stay in the hospital for less than 24 hours and are not traditionally treated with IV PCA. Regardless of size or affiliation of hospitals, the majority of Pharmacy and Therapeutics, or P&T, committees we surveyed were likely to review and approve Zalviso, subject to demonstration of satisfactory pharmacoeconomic value.

How Zalviso Addresses the Unmet Medical Need in Moderate-To-Severe Acute Pain Management in a Hospital Setting

Hospitalized patients in moderate-to-severe acute pain could significantly benefit from the following items:

- more rapid onset of analgesia;
- fewer medication errors, especially relating to the use of opioids;
- fewer side effects, including infection and bleeding risks due to invasive routes of delivery;
- enhanced ability for patients to ambulate after surgery and avoid falls; and
- patient control over their pain medication which has been shown to increase patient satisfaction.

For example, epidural catheters delivering local anesthetic are invasive and have a significant risk of lower extremity weakness and tethering the patient to a pump attached to an IV pole, creating multiple mobility impediments and fall risks; nerve blocks of the lower extremities (e.g., femoral nerve blocks) are also invasive and create weakness and fall risks; oral multimodal analgesia is not patient-controlled, is nurse-intensive and suffers from slow onset of action. While IV PCA does allow patient control over their pain medication, it suffers from the following:

- side effects associated with the most commonly used opioid, morphine, and its active metabolites;
- infection risk, analgesic gaps and decreased mobility associated with the invasive nature of IV delivery; and
- medication errors, which in some instances may be fatal, due to the complexity of IV PCA pumps, many of which arise from programming errors.

In our clinical studies, Zalviso has demonstrated the following attributes:

- a rapid onset of effect in comparison to intravenous delivery of morphine, and an ability to control pain as a monotherapy after moderate to severely painful surgeries such as knee replacement or colectomies;
- an ability for young and old patients alike to use Zalviso;
- a low rate of severe adverse event experiences;
- a rate of adverse events that is similar to a placebo treated patient population, with the exception of opioid induced itching;
- a high level of Patient Satisfaction as a result of Zalviso usage under patient control to manage pain after surgery over 48 to 72 hours; and
- a high Nurse Ease of Care rating for ease of set-up and use of Zalviso by the health care professional.

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

Zalviso has the potential to address many of the key disadvantages of IV PCA, including:

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

We believe that Zalviso provides a favorable safety, efficacy and tolerability profile, potentially enabling Zalviso to become a new standard of care for moderate to severe acute pain control via patient controlled analgesia.

Zalviso Description

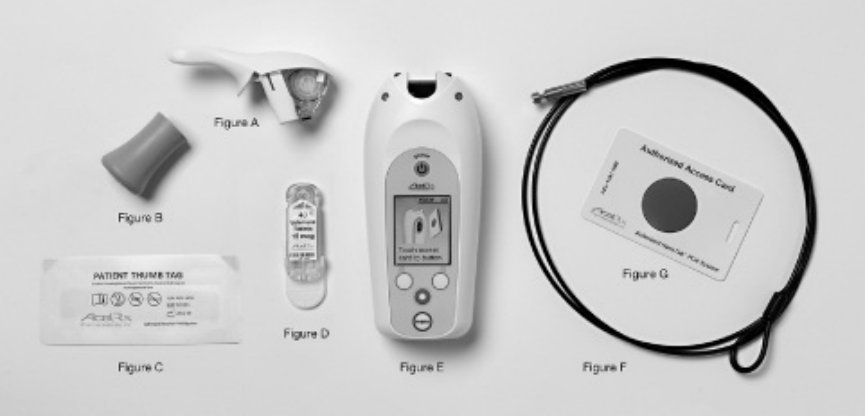
The benefits of Zalviso are the result of combining the following three elements:

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

Zalviso allows patients to self-administer sublingual sufentanil NanoTabs as needed to manage their moderate-to-severe acute pain in the hospital setting, and provides the record-keeping attributes of a conventional IV PCA pump while avoiding some of the key issues, such as programming errors, associated with conventional IV PCA use.

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

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



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

Scheduled drugs, when they are under patient control in a hospital setting, must be secured and have adequate dose access control and tracking mechanisms. Our novel handheld PCA device has the following safety features:

- an authorized access card, which is a wireless system access key for the healthcare professional;
- a wireless, electronic, adhesive thumb tag that acts as a single-patient identification key;
- pre-programmed 20-minute lock-out to avoid overdosing;

- NanoTab singulation, or dispensing, motion that eliminates runaway motor delivery risk;
- a security tether that is designed to prevent theft and misuse; and
- fully automated inventory record of NanoTabs usage.

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

- retrieve the NanoTab cartridge from secure drug storage;
- lock the cartridge and dispenser into the controller; and
- set up the secure patient access system, which is comprised of a security tether and a wireless, electronic, adhesive thumb tag that acts as a single-patient identification key.

To use Zalviso, the patient would:

- confirm that the green indicator light is illuminated, meaning the device is available to dose;
- place dispenser tip under tongue and push the large button on the controller, which dispenses a single NanoTab;
- remove the device from mouth upon hearing a tone confirming delivery of the NanoTab; and
- see the blue indicator light illuminate, indicating no new dose can be dispensed for the next 20 minutes.

Zalviso—Development Status

Based on the successful results of our Phase 3 clinical program for Zalviso, we submitted an NDA for Zalviso in September 2013 and, in December 2013, the U.S Food and Drug Administration, or FDA, accepted for filing the Zalviso NDA. In addition, FDA has established a Prescription Drug User Fee Act, or PDUFA, action date of July 27, 2014 for AcelRx's NDA for Zalviso. Assuming successful approval of our NDA on or around the PDUFA action date, we anticipate the first commercial sale of Zalviso in the United States to be in the first quarter of 2015.

The 505(b)(2) NDA submission for Zalviso is based on a development program that includes data from three Phase 3 clinical trials, including two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA morphine. Zalviso successfully achieved the primary efficacy endpoints for each of these trials.

In December 2013, we announced a commercial collaboration with Grünenthal GmbH, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Latin America and Asia.

Under the terms of the agreement, we received an upfront cash payment of $30.0 million. We are eligible to receive approximately $220 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

Grünenthal will be responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. We will be responsible for obtaining and maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

Zalviso—Clinical Program

Summary

Our Phase 3 program for Zalviso consisted of three Phase 3 clinical trials. We have reported positive top-line results from each of the three clinical trials. Prior to our Phase 3 program, we completed three successful Phase 2 clinical trials of sufentanil NanoTabs in the post-operative setting. These Phase 2 clinical trials demonstrated analgesic efficacy over a 12-hour study period, a low adverse event profile and excellent device functionality. During our End of Phase 2 meeting with the FDA, the FDA stated that the demonstration of efficacy versus placebo in two Phase 3 clinical trials with a total safety database of at least 600 patients exposed to the active drug should suffice to support a new drug application, or NDA. We have designed our Phase 3 clinical trials based on the feedback from the FDA.

Phase 3 Clinical Trials for Zalviso

Active comparator trial (IAP 309)

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

Regarding disposition and safety assessments, throughout the course of the trial, 7.3% of patients treated with Zalviso dropped out of the trial prematurely due to lack of efficacy compared to 8.9% of patients treated with IV PCA morphine. Additionally, 7.3% of the patients treated with Zalviso dropped out of the trial due to an adverse event compared to 10.0% of the IV PCA morphine patients. We observed 13 patients who experienced serious adverse events, or SAEs, in the trial, of whom three patients experienced serious adverse events assessed as possibly or probably related to the trial drug, one was related to Zalviso and two were related to IV PCA morphine. Overall the adverse events were similar between the two groups, however, continuous oxygen saturation monitoring demonstrated a lower percentage of patients with desaturations below 95% in the Zalviso group compared to IV PCA morphine ($p = 0.028$).

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

- Zalviso was non-inferior ($p<0.001$) to IV PCA morphine for the primary endpoint of PGA comparison over the 48-hour study period as determined by the combined percentage of patients with PGA ratings of "good" or "excellent" (78.5% vs. 65.6%, respectively). A p-value is a probability with a value ranging from 0 to 1, which indicates the likelihood that a clinical trial is different between treatment and control groups. P-values below 0.05 mean that there is a 95% or greater chance that there is a true difference between the groups, and are typically referred to as statistically significant.
- The assessment of non-inferiority was based on a lower limit of—15% for the 95% confidence interval, or CI, around the difference between these percentages. Because the 95% CI was +3.7% to +22.1% for the 48 hour PGA and therefore did not cross the zero difference line, a secondary comparison of the primary endpoint, specifically a statistical analysis of superiority could be performed. In this trial, Zalviso was statistically superior to IV PCA morphine for the PGA endpoint ($p=0.007$). Statistically superior PGA was also seen at the 24 hour and 72 hour time points.

A number of secondary endpoints were also evaluated, including pain intensity difference, or PID, and pain relief at each evaluation time point, comparison of individual PGA ratings, a Healthcare Professional Global Assessment, or HPGA, of method of pain control, dropouts from the trial due to inadequate analgesia and adverse events, and Patient and Nurse Ease of Care Questionnaires using a validated questionnaire methodology specifically to evaluate PCA systems.

Zalviso had a significantly more rapid onset of action based on both PID and pain relief scores from 1 to 4 hours after initiation of dosing compared to IV PCA morphine (PID: $p \leq 0.001$ for 1 and 2 hours and $p = 0.002$ at 4 hours; pain relief: $p = 0.003$ at 1 hour and $p < 0.001$ at 2 and 4 hours). Zalviso achieved a PGA rating of "excellent" in 42.9% of treated patients, compared to 30.6% for IV PCA with morphine, with a p-value of 0.016.

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

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

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

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

- Patients in the trial reported that they had significantly greater Overall Satisfaction with Zalviso compared to IV PCA morphine (4.15 vs. 3.84, respectively, out of a 0 to 5 scale, with a p-value equal to 0.004).
- Patients in the trial reported that they had greater Overall Ease of Care with Zalviso compared to IV PCA morphine (4.45 vs. 4.07, respectively, out of a 0 to 5 scale, with a p-value less than 0.001).
- Nurses managing patients in the trial reported they had significantly greater Overall Satisfaction with Zalviso compared to IV PCA morphine (3.92 vs. 3.35, respectively, out of a 0 to 5 scale, with a p-value less than 0.001).
- Nurses managing patients in the trial reported they had greater Overall Ease of Care with Zalviso compared to IV PCA morphine (4.27 vs. 3.82, respectively, out of a 0 to 5 scale, with a p-value equal to 0.017).

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

Patient Ease of Care

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

Nurse Ease of Care

Subscale (0-5 scale)	Zalviso	IV PCA morphine	p Value
Time consuming	0.92	1.24	0.076
Bothersome	0.54	1.09	0.006

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

In March 2013, we reported top-line data results demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 178 adult patients at 13 U.S. sites for the treatment of acute post-operative pain immediately following major abdominal surgery. Patients were treated for post-operative pain for a minimum of 48 hours, and up to 72 hours. Patients were randomized 2:1, with 119 patients randomized to sufentanil treatment and 59 to placebo treatment. Both treatments were delivered by the patient, as needed, using Zalviso with a 20-minute lock-out period. Patients in both groups could receive up to 2 mg morphine intravenously per hour as a rescue medication, the primary purpose of this rescue medication being to provide placebo-treated patients access to pain medication to enable them to stay in the trial as long as possible. Pre-rescue pain scores were imputed to minimize the impact of this rescue opioid on efficacy evaluations.

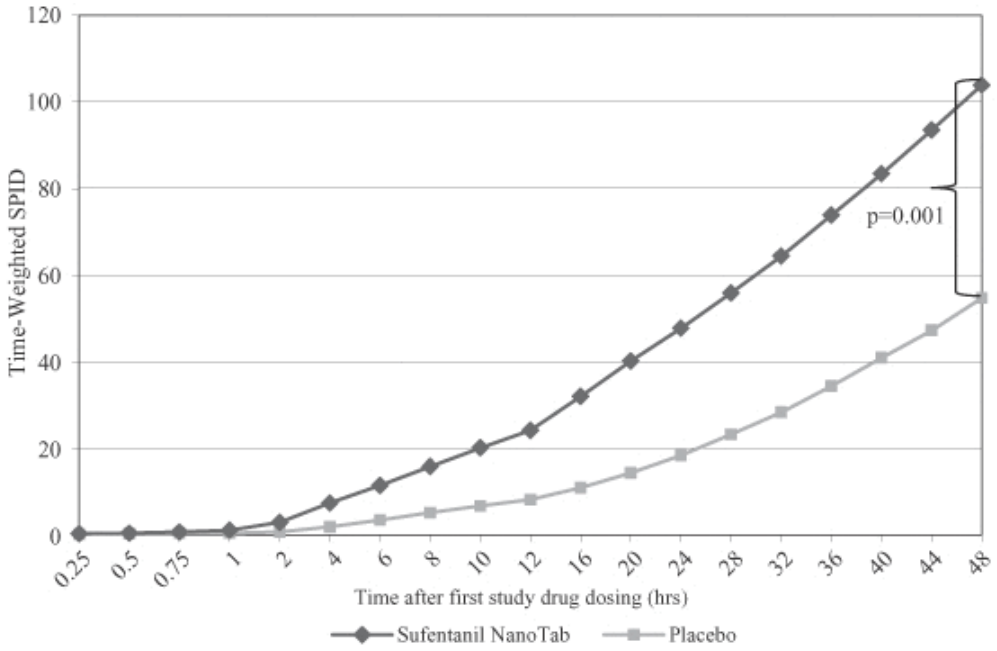
The primary endpoint evaluated pain intensity over the 48-hour study period compared to baseline, or Summed Pain Intensity Difference (SPID-48), in patients following major open abdominal surgery. Patients receiving sufentanil NanoTabs demonstrated a significantly greater SPID-48 compared to placebo-treated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

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

- 24 hours and 72 hours after first dose, SPID was significantly greater in the sufentanil-treated patients than in the placebo-treated patients (p<0.001 and p=0.004, respectively).
- PID and pain relief values separated statistically from placebo as early as 45 minutes (p=0.027 for both).

- A summed pain relief measure over the 48-hour study period, commonly referred to as TOTPAR, was significantly greater for sufentanil-treated patients than placebo-treated patients (p=0.002)
- Eighty, or 70.2%, of the sufentanil NanoTab-treated patients completed the 48-hour study period, compared to 30, or 51.7%, of placebo-treated patients. Reasons for drop-out in the sufentanil-treated and placebo-treated groups were adverse events (5.3% and 6.9%, respectively), lack of efficacy (16.7% and 31.0%, respectively) and other (7.9% and 10.3%, respectively).
- Only one patient, in the sufentanil group, experienced a serious adverse event, which was determined to be unrelated to the study drug by the investigator.
- Patients in the trial who were treated with sufentanil NanoTabs reported an average Overall Ease of Care of 4.39 out of a 0 to 5 scale. In addition, patients in the placebo arm of the trial also reported favorable Overall Ease of Care scores, with an average score of 4.36. These results are comparable to the results from the active comparator trial, which is summarized above.

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



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

In May 2013, we reported top-line data results demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Adverse events reported in the study were generally mild or moderate in nature and were similar in both placebo and treatment groups for the majority of adverse events. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 study enrolled 426 adult patients at 34 U.S. sites for treatment of moderate=to-severe acute pain immediately following major orthopedic surgery. Seven patients did not receive study drug, resulting in 419 patients being included in the intent-to-treat (ITT) population. Patients were treated for a minimum of 48 hours, and up to 72 hours. Patients were randomized 3:1, with 315 patients randomized to sufentanil treatment and 104 to placebo treatment. Both treatments were delivered by the patient, as needed, using the Zalviso NanoTab System with a 20-minute lock-out period. Patients

in both groups could receive up to 2 mg morphine intravenously per hour as a rescue medication, the primary purpose of this rescue medication being to enable placebo-treated patients to stay in the study. Pain scores recorded just prior to the delivery of rescue medication were gathered and imputed forward to minimize the impact of this rescue opioid on efficacy evaluations.

The primary endpoint evaluated pain intensity over the 48-hour study period compared to baseline, or Summed Pain Intensity Difference (SPID-48), in patients following major orthopedic surgery. Patients receiving Zalviso demonstrated a significantly greater SPID-48 compared to placebo-treated patients during the study period (+76.1 and -11.5, respectively; $p < 0.001$). Two hundred fifteen (68.3%) sufentanil-treated patients completed the 48-hour study period, compared to 43 (41.3%) placebo-treated patients. Primary reasons for drop-out in the sufentanil- and placebo-treated groups were adverse events (7.0% and 6.7%, respectively) and lack of efficacy (14.3% and 48.1%, respectively).

Secondary endpoint data included PID and pain relief values for each evaluation time point and demonstrated that PID separated from placebo at 1 hour ($p = 0.03$) and pain relief separated at 45 minutes ($p < 0.01$). SPID at 24 and 72 hours was also assessed and was highly significant as illustrated below.

Group	SPID-24	SPID-48	SPID-72
Sufentanil	33.8	76.1	166.2
Placebo	-8.8	-11.5	-2.6
Statistical Comparison	p<0.001	p<0.001	p<0.001

A secondary endpoint focused on Total Pain Relief measured at 48 hours (TOTPAR-48) was significantly higher in the Zalviso-treated patients than in the placebo-treated patients (p<0.001). In addition, another secondary endpoint, measurement of Patient Global Assessment with Method of Pain Control at 48 hours (PGA-48) was also highly significant in favor of Zalviso-treated patients (p<0.001).

Two patients (one each in the sufentanil group and placebo group) experienced a serious adverse event considered possibly or probably related to the study drug by the investigator.

Combined related adverse events for the two placebo-controlled pivotal studies (IAP 310 and IAP 311) compared to placebo are shown below. Only pruritus (itching) was statistically different for Zalviso compared to placebo ($p = 0.002$).

Adverse Reactions Occurring in ≥ 2% in Either Group

Possibly or Probably Related Adverse Reactions	ZALVISO n=429	Placebo n=162
At least 2% in either group	**Two Placebo-Controlled Phase 3 Studies**	
Nausea	29.4%	22.2%
Vomiting	8.9%	4.9%
Oxygen Saturation Decreased*	6.1%	2.5%
Pruritus	4.7%	0
Dizziness	4.4%	1.2%
Constipation	3.7%	0.6%
Headache	3.3%	3.7%
Insomnia	3.3%	1.9%
Hypotension	3.0%	1.2%
Confusional state	2.1%	0.6%

*3 patients (0.7%) in the Zalviso group had treatment-emergent respiratory events that required naloxone reversal.

ARX-04—Sufentanil Single-Dose NanoTab

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

The Market Opportunity for ARX-04

We believe that ARX-04 could be useful in a variety of medically supervised settings, including for battlefield casualty treatment, by paramedics during patient transport, in the emergency room, or for post-operative patients, following either short-stay or ambulatory surgery, who do not require more long-term patient-controlled analgesia. According to the Centers for Disease Control and Prevention, or CDC, there were more than 136 million emergency room visits in 2009, of which it is estimated that more than 45 million were injury-related emergency room visits, and analgesics were provided or prescribed during more than 94 million of these visits. In 2006, an estimated 53.3 million surgical and nonsurgical procedures were performed during 34.7 million ambulatory surgery visits. Of the 34.7 million visits, 19.9 million occurred in hospitals and 14.9 million occurred in freestanding ambulatory surgery centers. After surgery, patients are in a recovery room typically for 1 to 6 hours, and sometimes kept overnight, dependent on the type of surgery they have had. In the recovery room, they are provided with analgesics to control their post-surgery pain.

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

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

ARX-04 Description

ARX-04 is a non-invasive, fast-onset sufentanil product candidate for treatment of patients with moderate-to-severe acute pain, either on the battlefield or in civilian settings of trauma or injury. ARX-04 features sufentanil, a high therapeutic index opioid, in our proprietary NanoTab technology that enables rapid sublingual absorption when the NanoTab is placed under the tongue. As a result, sufentanil NanoTabs can provide rapid onset of analgesia and display a consistent pharmacokinetic profile due to a high percentage of drug being absorbed sublingually instead of through the gastrointestinal tract. In addition to battlefield casualty treatment, if successfully further developed and approved for commercialization, we anticipate that ARX-04 could be useful

in a variety of medically supervised settings, including by paramedics during patient transport, in the emergency room, for non-surgical patients experiencing pain in the hospital, or for post-operative patients, following either short-stay or ambulatory surgery, who do not require more long-term patient-controlled analgesia.

Sufentanil Single-Dose NanoTab—ARX-04 Clinical Program

Summary

In May 2011, we received a $5.6 million grant from the US Army Medical Research and Materiel Command, or USAMRMC, to conduct a Phase 2 dose-finding trial, and to prepare to enter Phase 3. In November 2012, we initiated the Phase 2 dose-finding trial and in April 2013, we announced that the trial achieved its primary endpoint. Based on our End of Phase 2 Meeting with the FDA in December 2013, we are developing the Phase 3 clinical program for ARX-04.

As of December 31, 2013, we had recognized the $5.6 million grant in full.

Phase 3 Clinical Program for ARX-04

In December 2013 we completed an End of Phase 2 Meeting with the FDA. Key outcomes from the End of Phase 2 Meeting included:

- Agreement on a 500 subject safety database, 100 patients of whom would be studied with multiple doses of ARX-04;
- Agreement that the bunionectomy Phase 2 study was a well-controlled study and could be used as a pivotal study;
- Agreement that a single additional Phase 3 pivotal efficacy and safety study in a model of visceral pain would be sufficient to support an NDA submission; and
- Agreement that the primary endpoint in the remaining Phase 3 study could be the SPID-12, with secondary endpoints following patients out to 48 hours.

Phase 3 protocol development is currently underway, with a goal of initiating the remaining Phase 3 study in the second half of 2014.

Phase 2 Clinical Trial for ARX-04

In April 2013, we announced top-line results demonstrating that a placebo-controlled, dose-finding, Phase 2 trial of our investigational single-dose sublingual sufentanil NanoTab for acute pain, ARX-04, successfully met its primary endpoint. Results demonstrated that patients receiving 30 mcg sufentanil NanoTab doses, administered by a healthcare professional, no more frequently than once per hour, had significantly greater pain reduction as measured by Summed Pain Intensity Difference to baseline during the 12-hour study period (SPID-12) than placebo-treated patients (+6.53 for 30 mcg sufentanil-treated patients and -7.12 for placebo-treated patients; p=0.003). The 20 mcg sufentanil-treated patients did not achieve SPID-12 scores that differentiated from placebo. Adverse events reported in the study were generally mild-to-moderate in nature, with two serious adverse events of post-surgical infection reported, both of which were determined by the investigator to be unrelated to study drug. This dose-ranging study randomized 101 patients following bunionectomy surgery in a 2:2:1 ratio to 30 mcg sufentanil, 20 mcg sufentanil or placebo treatment arms. The intent-to-treat (ITT) population in this study averaged 42.5 years of age and was evenly balanced for males and females (51%:49%). Ninety-one percent of patients entering the study completed the full 12-hour study period.

A number of secondary endpoints were also achieved, as follows:

For the time-weighted sum of pain relief scores over the 12-hour study period, or TOTPAR12, there was a statistically significant difference in favor of the 30 mcg group over placebo (9.73 vs. 4.37 p = 0.002). Patients

treated with the 30 mcg dose of sufentanil showed a rapid onset of action with a statistically significant beneficial difference in pain relief ($p<0.001$) and pain intensity ($p<0.01$) seen at 30 minutes after dosing compared to placebo. Dosing averaged every 2.4 hours over the duration of the 12-hour study. In addition, patient global assessment of the 30 mcg dose at 12 hours was superior to placebo ($p=0.002$) with 43.6% vs. 5.0% of the patients responding good or excellent for overall pain control. The 20 mcg dose was not significantly different from placebo for either endpoint.

Two SAEs, both in the 20 mcg-dose group, occurred one week after the study (surgical infections) and were deemed unrelated to study drug. All but two adverse events reported in the study were mild-to-moderate in nature with 58 patients (58%) reporting a total of 135 adverse events. The most frequently reported adverse events for all patients were nausea (30%), vomiting (17%), dizziness (14%) and somnolence (11%). Two patients discontinued treatment, one unrelated to study drug (anxiety/chest pain) and the other probably related to study drug (somnolence/respiratory depression), however both patients recovered without medical intervention.

ARX-02—Sufentanil NanoTab BTP Management System

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

The Market Opportunity for ARX-02

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

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

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

- elimination half-lives of 6 to 14 hours to treat a cancer breakthrough pain event that typically lasts 15 to 60 minutes;
- inconsistent T_{max} that ranges from 20 to 240 minutes, and can result in erratic onset of action and the potential for dose-stacking;
- local adverse events, such as dental caries and oral mucosal irritation; and
- drug packaging that lacks effective deterrence against abuse and misuse.

We designed ARX-02 to address these problems by:

- providing sufentanil, a shorter duration of action opioid with an elimination half-life ranging from 2 to 4 hours, which more closely matches the duration of a cancer breakthrough pain event;
- utilizing sufentanil, which provides for a consistent T_{max} with a narrow range of 30 to 90 minutes, thereby reducing the risk of dose-stacking;
- avoiding irritation of the oral mucosa, as demonstrated in our clinical trials; and
- packaging technology that enhances patient safety by reducing the possibility of misuse or abuse, while providing healthcare professionals with usage data.

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

ARX-02 Description

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

- protects and dispenses SDAs, one at a time;
- displays a recent dose indicator that is designed to mitigate overdosing;
- has child-resistant, elderly-friendly features; and
- provides electronic date and time stamping of each SDA removal event.

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

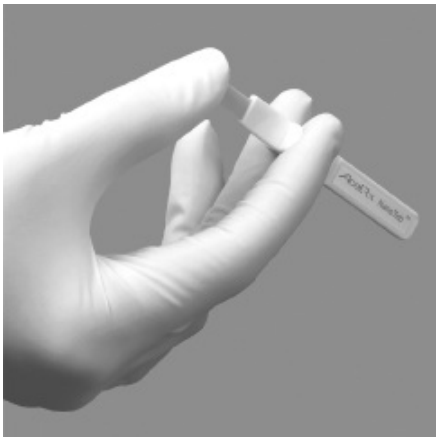
Sufentanil NanoTab BTP Management System—ARX-02 Clinical Program Overview

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

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

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

ARX-03—Sufentanil/Triazolam NanoTab



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

The Market Opportunity for ARX-03

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

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

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

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

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

ARX-03 Description

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

with ARX-03 to be discharged immediately following completion of the procedure. The sublingual route of administration avoids the high plasma concentrations associated with IV delivery, thereby obviating the need for specialized personnel and extensive monitoring.

Sufentanil/Triazolam NanoTab—ARX-03 Clinical Program Overview

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

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

Other Potential Applications for Our NanoTab Technology

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

Our Strategy

Our strategy is to develop and commercialize a portfolio of sufentanil NanoTab-based products and other products in hospital markets in the United States. We have designed and are developing product candidates that meet clearly defined unmet medical needs, have clearly defined clinical development programs, target large commercial market opportunities and require modestly-sized commercial organizations in the United States. We selectively utilize third party contractors in order to maximize the capital efficiency of our development and commercialization efforts. We plan to enter into partnerships to market our product candidates outside the United States. In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States. We continue to seek partnerships to market Zalviso in markets outside of the Grünenthal territory and the United States.

Zalviso

Zalviso is our lead product candidate and we are seeking FDA approval for the use of Zalviso to treat moderate-to-severe acute pain in the hospital setting. Based on the successful results of our Phase 3 clinical program for Zalviso, we submitted a New Drug Application, or NDA, for Zalviso in September 2013 and, in December 2013, the U.S Food and Drug Administration, or FDA, accepted for filing the Zalviso NDA. In addition, The FDA has established a Prescription Drug User Fee Act, or PDUFA, action date of July 27, 2014 for AcelRx's NDA for Zalviso. Assuming successful approval of our NDA on or around the PDUFA action date, we anticipate realization of the first commercial sale of Zalviso in the United States in the first quarter of 2015.

The 505(b)(2) NDA submission for Zalviso is based on a development program that includes data from three Phase 3 clinical trials, including two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA morphine. Zalviso successfully achieved the primary efficacy endpoints for each of these trials.

Our specific strategy with respect to Zalviso is to:

- seek regulatory approval in the United States;
- strengthen our commercial relationships for the manufacturing of the components and assembly of the Zalviso system;
- build a targeted hospital-directed sales force in the United States; and
- collaborate with Grünenthal to seek regulatory approval for Zalviso in their licensed territories.
- seek commercial partnerships for Zalviso in other unlicensed countries outside of the United States.

Development of ARX-04 includes completion of a Phase 3 clinical trial program currently being finalized based on discussions with the FDA. We anticipate initiating this Phase 3 program in late 2014. Further development of ARX-02 and ARX-03 will likely depend on the identification of a partner to support these efforts.

Sales and Marketing

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

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

In parallel with the FDA's review of the NDA for Zalviso, we plan to:

- highlight the clinical and health economic data identifying the limitations of IV PCA in use today;
- increase awareness of the clinical profile of Zalviso through publication of our clinical data;
- create and deploy a focused scientific support team to gather a detailed understanding of individual hospital needs in order to be prepared to present Zalviso effectively at the time of commercial launch;
- establish advisory boards with anesthesiologists, surgeons, nurses and P&T committees to provide us with input on appropriate commercial positioning for Zalviso for each of these key audiences;
- build a marketing organization that can define appropriate segmentation and positioning strategies and tactics for Zalviso; and
- design a post-approval clinical development program.

Assuming FDA approval, we plan to:

- establish Zalviso on hospital formularies through deployment of an experienced team to explain the clinical and economic benefits of Zalviso in comparison to IV PCA;
- create and progressively deploy a high-quality, customer focused and experienced sales organization dedicated to bringing innovative, highly-valued healthcare solutions to patients, payors and healthcare providers, including progressively building a targeted hospital-directed sales force of approximately 60 people in the United States;
- conduct a post-approval clinical program for Zalviso;
- establish Zalviso as the product of choice for traditional post-operative PCA; and
- expand the market through deployment of Zalviso for 24 hour stay patients, and other in-hospital acute pain conditions.

Collaborative Arrangements

Grünenthal Collaboration

In December 2013, we announced a commercial collaboration with Grünenthal for Zalviso covering the countries of the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia, or the Territory, for human use in pain treatment within or dispensed by hospitals hospices, nursing homes and other medically-supervised settings, or the Field. The collaboration included a Collaboration and License Agreement, or License Agreement and a Manufacturing and Supply Agreement, or Supply Agreement.

License Agreement. Under the terms of the License Agreement, Grünenthal has the exclusive right to commercialize the Zalviso in the Field in the Territory. The Company retains control of clinical development, while Grünenthal will be responsible for certain development activities pursuant to a development plan to be agreed between the parties. Grünenthal is exclusively responsible for marketing approval applications and other regulatory filings relating to the sufentanil drug cartridge for Zalviso in the Field in the Territory, while the Company is responsible for the CE Mark and other regulatory filings relating to device portions of Zalviso.

Grünenthal will have a right of first negotiation with respect to proposed exploitation in the Territory of Zalviso outside of the Field or the proposed exploitation in the Territory of another pharmaceutical product delivered with a PCA device for transmucosal application. Either party has the right to remove Australia from the Territory for purposes of the collaboration if Grünenthal's marketing approval or commercialization activities do not meet specified timelines set forth in the GRT License Agreement.

We received an upfront cash payment of $30 million, and are eligible to receive up to $220 million in additional payments contingent upon research, development, regulatory and manufacturing efforts and specified net sales target milestones. Grünenthal will also make tiered royalty and supply and trademark fee payments in the mid-teens up to the mid-twenties percent range on net sales of Zalviso in the Territory.

Unless earlier terminated, the License Agreement continues in effect until the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments, which supply and trademark fee continues for so long as the Company continues to supply Zalviso to Grünenthal. The License Agreement is subject to earlier termination in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party, upon the bankruptcy or insolvency of either party, or by Grünenthal for convenience.

Manufacturing Agreement. Under the terms of the Manufacturing Agreement, we will manufacture and supply Zalviso for use in the Field for the Territory exclusively for Grünenthal. Grünenthal shall purchase from AcelRx, during the first five years after the effective date of the Manufacturing Agreement, 100% and thereafter 80% of Grünenthal's and its sublicensees' and distributors' requirements of Zalviso for use in the Field for the Territory. Zalviso will be supplied at our fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires us to use commercially reasonable efforts to enter stand-by contracts with third parties providing significant supply and manufacturing services and under certain specified conditions permits Grünenthal to use a third party back-up manufacturer to manufacture Zalviso for Grünenthal's commercial sale in the Territory.

Unless earlier terminated, the Manufacturing Agreement continues in effect until the later of the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments or the end of any transition period for manufacturing obligations due to the expiration or termination of the License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the License Agreement, in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party or upon the bankruptcy or insolvency of either party.

Intellectual Property

We seek patent protection in the United States and internationally for our product candidates. Our policy is to pursue, maintain and defend patent rights developed internally and to protect the technology, inventions and

improvements that are commercially important to the development of our business. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents granted to us in the future will be commercially useful in protecting our technology. We also rely on trade secrets to protect our product candidates. Our commercial success also depends in part on our non-infringement of the patents or proprietary rights of third parties. For a more comprehensive discussion of the risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property" appearing elsewhere in this Form 10-K.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for our product candidates;
- defend our patents;
- preserve the confidentiality of our trade secrets; and
- operate our business without infringing the patents and proprietary rights of third parties.

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

As of January 31, 2014, we are the owner of record of 10 issued U.S. patents, which provide coverage over NanoTabs, the device components of Zalviso and of ARX-02, ARX-03 and ARX-04 NanoTab SDA dosing devices. These patents provide coverage through at least 2027. We also hold three issued European patents and a number of other international patents which provide coverage through at least 2027. We are also pursuing a number of U.S. and foreign national patent applications. 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.

We continue to seek and expand our patent protection for both compositions of matter and delivery devices, as well as methods of treatment related to our product candidates. In particular, we are pursuing additional patent protection for our ARX-01, ARX-02, ARX-03 and ARX-04 NanoTabs and formulations, our Zalviso device, the combination of drugs and our Zalviso device, our ARX-02, ARX-03 and ARX-04 SDA, as well as to methods of treatment using such drug and device compositions.

We have filed for additional patent coverage in the United States, Europe as well as many other foreign jurisdictions including, Japan, China, India, Canada and Korea. If issued, and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, we expect that these patents will expire between 2027 and 2030, excluding any additional term for patent term adjustments or patent term extensions in the United States. We note that the patent laws of foreign countries differ from those in United States, and the degree of protection afforded by foreign patents may be different from the protection offered by U.S. patents.

Further, we seek trademark protection in the United States and internationally where available and when appropriate. We have registered our ACELRX mark in Class 5, "Pharmaceutical preparations for treating pain; pharmaceutical preparations for treating anxiety," and Class 10, "Drug delivery systems; medical device, namely, a mechanical and electronic device used to administer medications, perform timed medication delivery, and to provide secure access to and delivery of medications," in the United States.

Our ACELRX mark is also registered in the European Community, Canada, and India. We have also registered our NANOTAB mark in the United States, Hong Kong, and Singapore and our ACCELERATE. INNOVATE. ALLEVIATE. tagline in the United States.

Competition

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

Many of our potential competitors, including many of the organizations named below, have substantially greater financial, technical and human resources than we do and significantly greater experience in the development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining FDA approval for drugs and achieving widespread market acceptance. Our competitors' drugs may be more effective, or may be more effectively marketed and sold, than any drug we may commercialize, which may render our product candidates obsolete or non-competitive before we can recover our losses. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available.

Potential Competition for Zalviso

We are developing Zalviso for the management of moderate-to-severe acute pain in adult patients during hospitalization. We believe that Zalviso would compete with a number of opioid-based and non-opioid based treatment options that are currently available, as well as some products that are in development. These products can be grouped into three classes – PCA-based systems, most commonly using an opioid as the pain control agent; non PCA-based systems that require nurse delivery of oral or parenteral opioids; and other non-opioid based treatment modalities. Due to the difficulty of managing moderate-to-severe pain, healthcare professionals will often use a combination of PCA opioids, parenteral or oral opioids and non-opioid based treatments to manage pain.

The primary competition for Zalviso is the IV PCA pump, which is widely used in the management of moderate-to-severe acute pain in the hospital 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 moderate-to-severe acute pain are morphine, hydromorphone and fentanyl, all of which are available as generics both from generic product manufacturers as well as from compounding pharmacies. In addition, branded manufacturers (e.g., Hospira) sell pre-filled glass syringes of morphine to fit their IV PCA pump systems.

Also available on the market is the Avancen Medication on Demand, or MOD, Oral PCA Device developed by Avancen MOD Corporation. Oral opioids and other agents can be used in this system. In addition, oral and parenteral opioids administered by the nurse are used to manage moderate-to-severe acute pain in the hospital, available both as branded and generic products. These oral opioids, as well as IV PCA opioids, are often used as part of a multi-modal analgesia approach, which might include, in addition to the opioid, NSAIDs, acetaminophen, gabapentanoids and other pain management modalities, as well as local blocks to provide temporary blockage of the pain signal, either as a wound infiltration agent or as a nerve block.

Additional potential competitors for Zalviso 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 now under development by The Medicines Company. Also in development is MoxDuo, an orally administered, fixed ratio combination of morphine and oxycodone being developed by QRx Pharma, an Australian company. This drug is also in development as an IV product. Cara Therapeutics is developing a kappa opioid agonist potentially as an IV agent for the management of post-operative moderate-to-severe pain. Recro Pharma is developing an intranasal form of dexmedetomidine as a potential agent for the management of post-operative pain.

Potential Competition for ARX-04

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

Potential Competition for ARX-02

We are developing ARX-02, the Sufentanil NanoTab BTP Management System, for the treatment of breakthrough pain in opioid tolerant patients, with an initial indication in cancer patients. The market for opioids for treatment of cancer breakthrough pain is large and competitive; however, currently there are no sufentanil products approved by the FDA for this indication. Our potential competitors for ARX-02 include products approved in the United States for cancer breakthrough pain, including: ACTIQ and FENTORA, currently manufactured by Teva Pharmaceuticals; Onsolis, currently manufactured by BioDelivery Sciences International, Inc.; Abstral, currently manufactured by ProStrakan Group plc; Lazanda, currently manufactured by Archimedes Pharma Limited; Subsys, currently manufactured by Insys Therapeutics, Inc., 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.

Potential Competition for ARX-03

We are developing ARX-03, the Sufentanil/Triazolam NanoTab, for use in diagnostic or therapeutic painful procedures of short duration in a physician's office. For these procedures, many practitioners rely primarily on local anesthetics injected to the procedural area to reduce the pain of the procedure, and do not use IV sedatives to manage the anxiety of patients because of the cost of having additional trained staff to monitor the patients. Currently, we are not aware of any products on the market which combine an opioid with a benzodiazepine in a single dosage form to manage the anxiety and pain of procedures in a physician's office. We are not aware of any approved or development stage non-IV sedative/analgesic products that would present competition to ARX-03. In the future, there may be products developed or approved for this market which could directly compete with ARX-03.

Pharmaceutical Manufacturing and Supply

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

In January 2013, we entered into a Manufacturing Services Agreement, or the Services Agreement, with Patheon Pharmaceuticals, Inc, or Patheon, relating to the manufacture of sufentanil NanoTabs for use with Zalviso. Under the terms of the Services Agreement, Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to Zalviso for sale in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. The term of the Services Agreement extends until December 31, 2017, or the Initial Term, and will automatically renew thereafter for periods of two years, unless terminated by either party upon eighteen months' prior written notice; provided, however, that the Services Agreement may not be terminated without cause prior to the end of the Initial Term.

In addition, we entered into a related Capital Expenditure and Equipment Agreement, or the Capital Agreement, related to clinical and commercial production of our product candidates. Under the terms of the Capital Agreement, we have made, and plan to make certain future modifications to Patheon's Cincinnati facility.

Device Manufacturing and Supply

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

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

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

Government Regulation

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

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and regulations. The process of obtaining regulatory approvals and complying with applicable laws and regulations requires the expenditure of substantial time and financial resources. Failure to comply at any time during the product development and approval process, or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. The process required by the FDA before a drug product may be marketed in the United States generally involves the following:

- completion of non-clinical laboratory tests, animal trials and formulation studies according to Good Laboratory Practices regulations;
- submission to the FDA of an investigational new drug, or IND, application which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCP, to establish the clinical safety and efficacy of the proposed drug product for its intended use;

- submission to the FDA of an NDA for a new drug product;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug product and the drug substance(s) are produced to assess compliance with cGMP;
- payment of user and facility fees; and
- FDA review and approval of the NDA.

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

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

- *Phase 1.* The product is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2.* Involves trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted conditions and to determine dosage tolerance and optimal dosage and schedule.
- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical safety and efficacy in an expanded patient population at geographically dispersed clinical trial sites. These trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling.

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

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

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

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

In addition, under the Pediatric Research Equity Act, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric

subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

The approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA issues a Complete Response Letter at the conclusion of its review if the NDA is not yet deemed ready for approval.

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

Post-Approval Requirements

Any drug products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated clinical safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication or when otherwise requested by the FDA in the form of postmarketing requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of NDA approval. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drug products may be promoted only for the approved indications and in accordance with the provisions of the approved label. Further, manufacturers of drug products must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

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

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

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a

product may result in restrictions on the product or even complete withdrawal of the product from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

Foreign Regulation

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

Controlled Substances Regulations

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

The recently enacted federal Drug Supply Chain Security Act, imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

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

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the pharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing,

ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below).

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. Further, civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the PPACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies for which federal healthcare program payment is available to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. FDA and some states require the posting of information relating to clinical studies. In addition, California requires pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. If our operations are found to be in

violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payers. Third-party payers include government health administrative authorities, managed care providers, private health insurers and other organizations. Sales of our products will depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payers. These third-party payers are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. Third-party payers may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Because each third-party payer individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payer separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our products and our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payer-by-payer basis, obtaining acceptable coverage and reimbursement from one payer does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payer. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payers, physicians may limit how much or under what circumstances they will prescribe or administer them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the United States and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to commercialize our products. In particular, there have been and continue to be a number of initiatives

at the United States federal and state level that seek to reduce healthcare costs. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products will likely be lower than the prices we might otherwise obtain from non-governmental payers. Moreover, private payers often follow federal healthcare coverage policy and payment limitations in setting their own payment rates.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental change. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability. In March 2010, PPACA was signed into law. PPACA has the potential to substantially change the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, PPACA established an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payer or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Research and Development

Conducting research and development is central to our business model. We have invested and expect to continue to invest significant time and capital in our research and development operations. Our research and development expenses were $26.3 million, $24.9 million and $13.6 million during the years ended December 31, 2013, 2012 and 2011, respectively. We plan to incur significant expenditures for the foreseeable future as we seek to continue commercial preparations for Zalviso and development of ARX-04, and subsequently advance the development of ARX-02 and ARX-03 contingent upon additional funding or identification of corporate partnership resources.

Employees

As of December 31, 2013, we employed 27 full-time employees, all of whom are located at our headquarters in Redwood City, California. None of our employees are subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were originally incorporated as SuRx, Inc. in Delaware on July 13, 2005. We subsequently changed our name to AcelRx Pharmaceuticals, Inc. on August 13, 2006. We file electronically with the U.S. Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.acelrx.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC.

Item 1A. Risk Factors

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

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception, anticipate that we will continue to incur significant losses in 2014 and may continue to incur losses for the foreseeable future.

Since our inception in 2005, we have focused primarily on developing our lead product candidate, Zalviso ™. We have three additional product candidates, the Sufentanil NanoTab BTP Management System, or ARX-02, the Sufentanil/Triazolam NanoTab, or ARX-03, and Sufentanil Single-Dose Acute Pain NanoTab, or ARX-04. We have incurred significant net losses in each year since our inception in July 2005, and as of December 31, 2013, we had an accumulated deficit of $145.5 million.

We have devoted most of our financial resources to research and development, including our non-clinical development activities and clinical trials. To date, we have financed our operations primarily through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. We expect to continue to incur substantial expenses as we prepare for the potential commercialization of Zalviso and continue our research and development activities for our product candidates. To date, none of our product candidates have been commercialized, and if our product candidates are not successfully developed or commercialized, or if revenues are insufficient following marketing approval, we will not achieve profitability and our business may fail. Our success is also dependent on obtaining regulatory approval to market our product candidates outside of the United States through current and future collaborations which may not materialize or prove to be successful.

We have never generated product 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. We do not anticipate generating revenues from sales of Zalviso in the United States until 2015, if ever. While we have a collaboration with Grünenthal for potential commercialization of Zalviso in Europe and Australia, we may never achieve the development milestones associated with the collaboration, and Grünenthal may never achieve regulatory approval or recognize commercial sales of Zalviso, for which we would receive sales milestone payments and product royalties. In addition, we do not anticipate generating revenues from our other product candidates for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- obtaining and maintaining regulatory approval for Zalviso;
- launching and commercializing Zalviso, including building or contracting out, a hospital-directed sales force in the U.S. and collaborating with third parties internationally, including Grünenthal, which may require additional funding; and
- completing the clinical development of, obtaining regulatory approval for, and launching and commercializing ARX-04, ARX-02 and ARX-03, which may require additional funding or corporate partnership resources.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and regulatory environment, 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 delayed in obtaining approval of, or launching, Zalviso, or are required by the United States Food and Drug Administration, or FDA, to perform trials in addition to those that we have completed.

Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of our products, we may not become profitable and may need to obtain additional funding to continue operations.

We have a limited operating history that may make it difficult to predict our future performance or evaluate our business and prospects.

We were incorporated in 2005. Since inception, our operations have been primarily limited to organizing and staffing our company, developing our technology and undertaking preclinical studies and clinical trials for our product candidates. We have not yet obtained regulatory approval for any of our product candidates. Consequently, any predictions you make about our future success or viability or evaluation of our business and prospects may not be accurate.

We may require additional capital and may be unable to raise capital, which would force us to delay, reduce or eliminate our product development programs and could cause us to cease operations.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect to incur significant expenditures in connection with our ongoing activities, particularly preparation for the potential commercialization of Zalviso and future advancement of our other product candidates.

Future events and circumstances, including those beyond our control may cause us to consume capital more rapidly than we currently anticipate. For example, if we are not able to launch Zalviso for sale in the United States in the first quarter of 2015, due to a delay in approval of Zalviso by the FDA, technical difficulties in our commercialization efforts or otherwise, or revenues or expenses associated with the commercialization of Zalviso are not as estimated, we will likely need to seek additional capital to continue operations. Such capital demands could be substantial. In addition, if we do not receive FDA approval to market Zalviso, we cannot draw the third tranche of $15 million associated with our credit facility with Hercules.

To raise capital, we may seek to sell additional equity or debt securities, obtain a credit facility or enter into product development, license or distribution agreements with third parties or divest one or more of our product candidates. Such arrangements may not be available on favorable terms, if at all. Furthermore, any product development, licensing, distribution or sale agreements that we enter into may require us to relinquish valuable rights. We may not be able to obtain sufficient additional funding or enter into a strategic transaction in a timely manner. If adequate funds are not available, we would be required to reduce our workforce, delay, reduce the scope of or eliminate one or more of our research and development programs in advance of the date on which we exhaust our cash resources to ensure that we have sufficient capital to meet our obligations and continue on a path designed to preserve stockholder value.

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 additional corporate partners for Zalviso 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.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, including under our Sales Agreement with MLV, which would result in dilution to our stockholders or impose restrictive covenants that may adversely impact our business. The sale of additional equity or convertible debt securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected and we may not be able to meet our debt service obligations.

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

In December 2013, we entered into an amended and restated credit facility with Hercules Technology Growth Capital, Inc. that extends our current relationship with Hercules, which was established in June 2011. The new Hercules credit facility provides for up to $40 million of new loans. AcelRx drew the first tranche of $15 million at the closing of the new credit facility. The second tranche of up to $10 million can be drawn, at AcelRx's option, at any time prior to June 30, 2014. The third tranche of up to $15 million is conditioned upon the approval of Zalviso by the FDA, and if approved, can be drawn at AcelRx's option, at any time between December 15, 2014 and March 15, 2015. The scheduled maturity date is October 1, 2017 (which would be extended until January 1, 2018 if the Company obtains FDA approval of Zalviso on or prior to April 1, 2015).

We granted Hercules a first priority security interest in substantially all of our assets, with the exception of our intellectual property, where the security interest is limited to proceeds of intellectual property if it is licensed or sold.

If we do not make the required payments when due, either at maturity, or at applicable installment payment dates, or if we breach the agreement or become insolvent, Hercules could elect to declare all amounts outstanding, together with accrued and unpaid interest and penalty, to be immediately due and payable. Additional capital may not be available on terms acceptable to us, or at all. Even if we were able to repay the full amount in cash, any such repayment could leave us with little or no working capital for our business. If we are unable to repay those amounts, Hercules will have a first claim on our assets pledged under the loan agreement. If Hercules should attempt to foreclose on the collateral, it is unlikely that there would be any assets remaining after repayment in full of such secured indebtedness. Any default under the loan agreement and resulting foreclosure would have a material adverse effect on our financial condition and our ability to continue our operations.

Risks Related to Clinical Development and Regulatory Approval

We depend substantially on the success of Zalviso, which may not receive 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 Zalviso for the management of moderate-to-severe acute pain in patients in the hospital setting. Our Phase 3 program consisted of three Phase 3 clinical trials. We have reported positive top-line data from each of these trials and submitted an NDA for Zalviso to the FDA on September 27, 2013,

which the FDA then filed in December 2013. There is no guarantee that the NDA will be successfully approved by the FDA. For example, the FDA could require us to complete further studies, which could delay or preclude any approval of the NDA and would require us to obtain significant additional funding.

Our proposed tradename of Zalviso has been approved by the FDA, which must approve all drug tradenames to avoid medication errors and misbranding. Any brand recognition or goodwill that we establish with the name Zalviso prior to commercialization may be worthless if the FDA determines there has been significant changes to the Zalviso and the FDA withdraws the approval.

Any delay in approval by the FDA, of the Zalviso NDA may negatively impact our stock price and harm our business operations. Any delay in obtaining, or inability to obtain, regulatory approval would prevent us from commercializing Zalviso in the United States, generating revenues and achieving profitability. If any of these events occur, we may be forced to delay or abandon our development efforts for Zalviso, which would have a material adverse effect on our business and could potentially cause us to cease operations. In addition, Grünenthal may never achieve regulatory approval for Zalviso in their licensed territories, including the European Union and Australia, in which case, we would not receive development or sales milestones or product royalties, which could have a material adverse effect on our business.

Positive clinical results obtained to date for our product candidates may be disputed in FDA review, do not guarantee regulatory approval and may not be obtained from future clinical trials.

We have reported positive top-line data from each of our three Zalviso Phase 3 clinical trials. However, even if we believe that the data from required Phase 3 clinical trials is positive, the FDA could analyze our data using alternative strategies and determine that the data from our trials was negative or inconclusive. Negative or inconclusive results of a Phase 3 clinical trial could cause the FDA to require us to repeat the trial or conduct additional clinical trials prior to obtaining approval for commercialization, and there is no guarantee that additional trials would achieve positive results. Any such determination by the FDA would delay the timing of our commercialization plan for Zalviso and adversely affect our business operations.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

We have experienced and may in the future experience delays in clinical trials of our product candidates. While we have completed our planned trials for Zalviso and the Phase 2 clinical trial for ARX-04, potential future clinical trials, such as the planned ARX-04 Phase 3 clinical trials, may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. Our clinical trials for any of our product candidates could be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required institutional review board approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the device components of our product candidates;

- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment or being delayed in entering data to allow for clinical trial database closure;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If any future clinical trials are delayed for any of the above reasons, our development costs may increase, our approval process could be delayed and our ability to commercialize and commence sales of our product candidates could be materially harmed, which could have a material adverse effect on our business.

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

Adverse events, or AEs, caused by our product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. In our Phase 3 active comparator clinical trial (IAP 309), 7.9% of Zalviso treated patients dropped out of the trial prematurely due to an AE, and we observed one serious adverse event, or SAE, that was assessed as possibly or probably related to Zalviso. In our Phase 3, double-blind, placebo-controlled, abdominal surgery trial (IAP 310), adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. In addition, one patient in the trial, who was in the sufentanil group, experienced an SAE, which was determined to be unrelated to the trial drug. In our Phase 3, double-blind, placebo-controlled, orthopedic surgery trial (IAP 311), treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between sufentanil and placebo treated patients. Two patients (one each in the sufentanil group and placebo group) experienced a serious adverse event considered possibly or probably related to the trial drug by the investigator.

In our Phase 2 ARX-04 trial, two serious adverse events (SAEs), both in the 20 mcg-dose group, occurred one week after the study (surgical infections) and were deemed unrelated to study drug. All but two adverse events reported in the study were mild-to-moderate in nature with 58 patients (58%) reporting a total of 135 adverse events. The most frequently reported adverse events for all patients were nausea (30%), vomiting (17%), dizziness (14%) and somnolence (11%). Two patients discontinued treatment, one unrelated to study drug (anxiety/chest pain) and the other probably related to study drug (somnolence/respiratory depression); however, both patients recovered without medical intervention.

Phase 2 clinical trials conducted by us with our Zalviso, ARX-02, ARX-03 and ARX-04 product candidates have generated some AEs, but no SAEs, related to the trial drug.

Further, if our products cause serious or unexpected side effects after receiving market approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified Risk Evaluation and Mitigation Strategy, or REMS;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

Additional time may be required to obtain regulatory approval for Zalviso because it is a drug/device combination.

Zalviso is a combination product candidate with both drug and device. Zalviso is viewed as a combination product by the FDA, and both drug and device components are required for review as part of our NDA submission. There are very few examples of the FDA approval process for drug/device combination products such as Zalviso. As a result, we have in the past and may in the future experience delays in the development and commercialization of Zalviso due to regulatory uncertainties in the product development and approval process, in particular as it relates to a drug/device combination product approval under an NDA.

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

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

The process for obtaining approval of an NDA is time consuming, subject to unanticipated delays and costs, and requires the commitment of substantial resources.

If the FDA determines that the clinical trials submitted for a product candidate, including Zalviso, in support of an NDA were not conducted in full compliance with the applicable protocols for these trials, as well as with applicable regulations and standards, or if the FDA does not agree with our interpretation of the results of such trials, the FDA may reject the data from such trials. The FDA may audit some of our Zalviso Phase 3 clinical trial sites to determine the integrity of our clinical data. Any rejection of our data would negatively impact our ability to obtain marketing authorization for a product candidate and would have a material adverse effect on our business and financial condition.

In addition, an NDA may not be approved, or approval may be delayed, as a result of changes in FDA policies for drug approval during the review period. For example, although many products have been approved by the FDA in recent years under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, objections have been raised to the FDA's interpretation of Section 505(b)(2). If challenges to the FDA's interpretation of Section 505(b)(2) are successful, the FDA may be required to change its interpretation, which could delay or prevent the approval of such an NDA. Any significant delay in the acceptance, review or approval of an NDA that we have submitted would have a material adverse effect on our business and financial condition.

Regulatory authorities may not approve our product candidates even if they meet safety and efficacy endpoints in clinical trials.

The FDA and other foreign regulatory agencies, such as the EMA, can delay, limit or deny marketing approval for many reasons, including:

- a product candidate may not be considered safe or effective;
- the manufacturing processes or facilities we have selected may not meet the applicable requirements; and
- changes in their approval policies or adoption of new regulations may require additional work on our part.

Part of the regulatory approval process includes compliance inspections of manufacturing facilities to ensure adherence to applicable regulations and guidelines. The regulatory agency may delay, limit or deny marketing approval of our product candidates as a result of such inspections.

Any delay in, or failure to receive or maintain, approval for any of our product candidates could prevent us from generating meaningful revenues or achieving profitability.

Our product candidates may not be approved even if they achieve their endpoints in clinical trials. Regulatory agencies, including the FDA, or their advisors may disagree with our trial design and our interpretations of data from preclinical trials and clinical trials. Regulatory agencies may change requirements for approval even after a clinical trial design has been approved. The FDA exercises significant discretion over the regulation of combination products, including the discretion to require separate marketing applications for the drug and device components in a combination product. To date, our product candidates are being regulated as drug products under the NDA process administered by the FDA. The FDA could in the future require additional regulation of our product candidates under the medical device provisions of the FDCA. Our systems are designed to comply with Quality Systems Regulation, or QSR, which sets forth the FDA's current good manufacturing practice, or GMP, requirements for medical devices, and other applicable government regulations and corresponding foreign standards for drug GMPs. If we fail to comply with these regulations, it could have a material adverse effect on our business and financial condition.

Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing trials. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. For example, we have submitted our NDA seeking approval of Zalviso for the management of moderate-to-severe acute pain in patients in the hospital setting; however, our clinical trial data was generated exclusively from the post-operative segment of this population, and FDA may restrict any approval to post-operative patients only, which would reduce our commercial opportunity.

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

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval trials or post-market surveillance. DEA scheduling of Zalviso, or any of our product candidates, may further delay commercial launch even if FDA approval is received. Additionally, the labeling ultimately approved for Zalviso and our other product candidates will likely include restrictions on use due to the opioid nature of sufentanil. Zalviso 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;
- 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 Zalviso 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, our collaborator, Grünenthal, and we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. In October 2012, we received notice from the EMA that Zalviso was eligible for centralized European review. Outside of Europe, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical trials or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. While Grünenthal does have products approved in international markets, 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. Grünenthal's experience in international markets does not guarantee regulatory approval or compliance with regulatory requirements 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.

Zalviso and our other product candidates will require Risk Evaluation and Mitigation Strategies.

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and require the adoption of REMS. Our product candidates will require REMS. The REMS may include requirements for special labeling or medication guides for patients, special communication plans to health care professionals and restrictions on distribution and use. While we have received information from the FDA regarding certain aspects of the required REMS for Zalviso, we cannot predict the specific REMS to be required as part of any FDA approval of Zalviso. Depending on the extent of the REMS requirements, launch may be delayed and the costs to commercialize Zalviso may increase substantially. ARX-02, ARX-03 and ARX-04, if approved, will also require REMS programs that may significantly increase our costs to commercialize these product candidates. Furthermore, risks of sufentanil that are not adequately addressed through proposed REMS for our product candidates may also prevent or delay their approval for commercialization.

Our relationships with investigators, health care professionals, consultants, hospitals, third-party payors, and customers are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, increased losses or diminished profits.

Healthcare providers, physicians and others play a primary role in the recommendation and prescribing of any products for which we may obtain marketing approval. Our current business operations and future arrangements with investigators, healthcare professionals, consultants, hospitals, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute the products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid;
- the federal civil and criminal false claims laws and civil monetary penalties, including civil whistleblower or qui tam actions, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly or willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, clearinghouses and healthcare providers;
- the federal transparency law, enacted as part of the Patient Protection and Affordable Care Act and Health Care and Education Reconciliation Act of 2010 (collectively, the Health Care Reform Law), and its implementing regulations, requires manufacturers of drugs, devices, biologicals and medical supplies to report to the U.S. Department of Health and Human Services information related to payments and other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state laws and regulations that may apply to our business practices, including but not limited to, state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines; state laws and regulations that require manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our

business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these or any other healthcare regulatory laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses or divert our management's attention from the operation of our business.

Recently enacted and future legislation may increase the difficulty and cost for us to commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, the legislative landscape continues to evolve. There have been a number of legislative and regulatory changes and proposed changes regarding healthcare systems that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

In the United States, the Health Care Reform Law was enacted in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, impose new taxes and fees on the health industry and impose additional health policy reforms. Aspects of the Health Care Reform Law impacting our business include:

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133.0% of the Federal Poverty Level beginning in 2014, thereby potentially increasing manufacturers' Medicaid rebate liability;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs.

The Health Care Reform Law has the potential to substantially change health care financing and delivery by both governmental and private insurers, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and further restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

Risks Related to Our Reliance on Third Parties

We rely on third party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates.

Reliance on third party manufacturers entails many risks including:

- the inability to meet our product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA action, including injunction, recall, seizure, or total or partial suspension of production.

We rely on limited sources of supply for the drug component of our product candidates and any disruption in the chain of supply may cause delay in developing and commercializing our product candidates.

Currently, we use two established suppliers of sufentanil citrate for our NanoTabs. For each product candidate, only one of the two suppliers will be qualified as a vendor with the FDA. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. The alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional trials if a new sufentanil supplier is relied upon for commercial production. In addition, the Drug Enforcement Administration, or the DEA, may reduce, delay or refuse our quota for sufentanil, which would disrupt our supply of sufentanil citrate and cause delay in the development and commercialization of our product candidates.

Manufacture of sufentanil NanoTabs requires specialized equipment and expertise.

Ethanol, which is used in the manufacturing process for our sufentanil NanoTabs, is flammable, and sufentanil is a highly potent, Schedule II compound. These factors necessitate the use of specialized equipment and facilities for manufacture of sufentanil NanoTabs. There are a limited number of facilities that can accommodate our

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

Manufacturing issues may arise that could delay or increase costs related to product and regulatory approval and commercialization.

As we scale up manufacturing of our product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to 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.

Early stage development and manufacture of clinical supplies were conducted at Patheon in Toronto, Canada. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon's production facility in Cincinnati, Ohio, where we initially built out a suite within their existing buildings, and where we have conducted late stage development and manufacture of Zalviso registration stability lots, which were utilized in Phase 3 clinical trials. We expanded the manufacturing facilities at Patheon in Cincinnati, Ohio in late 2013 and this expanded facility will need to be qualified. We have not yet produced commercial supplies out of this expanded facility and we may encounter difficulties in production at the newly expanded facility, which may adversely affect our commercial plans.

We have limited experience manufacturing the Zalviso device on a clinical scale, no experience on a commercial scale and do not own or operate a manufacturing facility.

Related to the Zalviso device, we have conducted multiple Design Validation, Software Verification and Validation, Reprocessing and Human Factors studies, and have manufactured for and completed Phase 3 clinical trials using the intended commercial device. If, due to regulatory request or commercial demand, we need to modify the Phase 3 device, we may incur higher costs and experience delay in regulatory approval and/or commercialization of Zalviso. Furthermore, if the identified changes to the device are substantial, we may need to conduct further clinical trials in order to have the commercial device approved by the FDA.

We have manufactured Zalviso devices and supplies on a small scale, including those needed for our Phase 3 clinical trials. We will continue to rely on contract manufacturers, component fabricators and third party service providers to produce the necessary Zalviso devices for the commercial marketplace. We currently outsource manufacturing and packaging of the controller, dispenser and cartridge components of the Zalviso device to third parties and intend to continue to do so. These purchases 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 Zalviso devices with third party manufacturers, or may be unable to do so on acceptable terms. We may encounter unanticipated problems in the scale-up and automation process that will result in delays in the manufacturing of Zalviso cartridge, dispenser or controller.

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

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

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

We utilized contract research organizations, or CROs, for the conduct of our Phase 3 clinical trials of Zalviso and for the Phase 2 clinical trial of ARX-04 and to assist us in preparing the New Drug Application, or NDA, which we submitted to the FDA in the third quarter of 2013. We rely on CROs, as well as clinical trial sites, to ensure the proper and timely conduct of our clinical trials and document preparation. 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 clinical programs for Zalviso and our other product candidates, as well as the execution of nonclinical trials. We control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We, and our CROs, are required to comply with the FDA's current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The 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. Accordingly, if our CROs or clinical trial sites fail to comply with these regulations, we may be required to repeat the Phase 3 clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may allow our potential competitors to access our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize Zalviso, or our other product candidates. As a result, our financial results and the commercial prospects for Zalviso and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Commercialization of Our Product Candidates

The commercial success of Zalviso and our other product candidates will depend upon the acceptance of these products by the medical community, including physicians, nurses, patients, and pharmacy and therapeutics committees.

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

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and health care payors;
- the prevalence and severity of any AEs or SAEs;

- overcoming the perception of sufentanil as a potentially unsafe drug due to its high potency;
- limitations or warnings contained in the FDA-approved label for Zalviso;
- availability of alternative treatments;
- existing capital investment by hospitals in IV PCA technology;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage or reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third party coverage.

If Zalviso is approved, but does not achieve an adequate level of acceptance by physicians, nurses, patients and pharmacy and therapeutics committees, or P&T Committees, we may not generate sufficient revenue from Zalviso 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 have entered into a collaboration with Grünenthal for the commercialization of Zalviso in Europe and Australia and intend to enter into additional 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. . 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 future 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 Zalviso 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 current or future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to 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.

A key part of our business strategy is to establish collaborative relationships to commercialize and fund development and approval of our product candidates, particularly outside of the United States. We may not succeed in establishing and maintaining collaborative relationships, which may significantly limit our ability to develop and commercialize our products successfully, if at all.

We will need to establish and maintain successful collaborative relationships to obtain international sales, marketing and distribution capabilities for our product candidates. The process of establishing and maintaining collaborative relationships is difficult, time-consuming and involves significant uncertainty, including:

- our partners may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical or regulatory results, manufacturing issues, a change in business strategy, a change of control or other reasons;
- our contracts for collaborative arrangements are terminable at will on written notice and may otherwise expire or terminate and we may not have alternatives available to achieve the potential for our products in those territories or markets;
- our partners may choose to pursue alternative technologies, including those of our competitors;
- we may have disputes with a partner that could lead to litigation or arbitration;
- we have limited control over the decisions of our partners and they may change the priority of our programs in a manner that would result in termination of the agreement or add significant delays to the partnered program;
- our ability to generate future payments and royalties from our partners depends upon the abilities of our partners to establish the safety and efficacy of our drug candidates, obtain regulatory approvals and our ability to successfully manufacture and achieve market acceptance of products developed from our product candidates;
- we or our partners may fail to properly initiate, maintain or defend our intellectual property rights, where applicable, or a party may use our proprietary information in such a way as to invite litigation that could jeopardize or potentially invalidate our proprietary information or expose us to potential liability;
- our partners may not devote sufficient capital or resources towards our product candidates; and
- our partners may not comply with applicable government regulatory requirements necessary to successfully market and sell our products.

If any collaborator fails to fulfill its responsibilities in a timely manner, or at all, any research, clinical development, manufacturing or commercialization efforts pursuant to that collaboration could be delayed or terminated, or it may be necessary for us to assume responsibility for expenses or activities that would otherwise have been the responsibility of our collaborator. If we are unable to establish and maintain collaborative relationships on acceptable terms or to successfully and timely transition terminated collaborative agreements, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of capital.

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 any of our product candidates, including Zalviso, are approved for commercialization, we intend to enter into agreements with third parties to market our product candidates outside the United States, which may require us to supply products to the third party such as our existing collaboration with Grünenthal for marketing Zalviso in European countries and Australia. We may be required to establish international operations in connection with those collaborations and in that regard may be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;

- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

If we, or current and 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 our current and 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.

We believe that Zalviso would compete with a number of opioid-based treatment options that are currently available. The hospital market for opioids for moderate-to-severe acute pain is large and competitive. The primary competition for Zalviso is the IV PCA pump, which is widely used in the moderate-to-severe acute pain in the hospital 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 moderate-to-severe acute pain are morphine, hydromorphone and fentanyl, all of which are available as generics. Also available on the market is the Avancen Medication on Demand, or MOD, Oral PCA Device developed by Avancen MOD Corporation.

Additional potential competitors for Zalviso include products in development, including the fentanyl iontophoretic transdermal system, IONSYS, originally developed by ALZA Corporation and Ortho-McNeil Pharmaceutical, Inc., both Johnson & Johnson subsidiaries, and currently under development by Incline Therapeutics, Inc., which was acquired by The Medicines Company. Also in development is MoxDuo, an orally administered, fixed ratio combination of morphine and oxycodone being developed by QRx Pharma, an Australian company. This drug is also in development as an IV product.

Our potential competitors for ARX-02 include products approved in the United States for cancer breakthrough pain, including: ACTIQ and FENTORA, currently manufactured by Teva Pharmaceuticals; Onsolis, currently manufactured by BioDelivery Sciences International, Inc.; Abstral, currently manufactured by ProStrakan Group plc; Lazanda, currently manufactured by Archimedes Pharma Limited; Subsys, currently manufactured by Insys Therapeutics, Inc., 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.

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 mild-to-moderate acute pain or breakthrough pain could render Zalviso 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 Zalviso 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 Zalviso, or any of our other product candidates, will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, hospitals and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for Zalviso, or any of our other product candidates. Also, reimbursement amounts may reduce the demand for, or the price of, our products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize Zalviso, or any of our other product candidates.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell our products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for our products, following approval. The availability of numerous generic pain medications may also substantially reduce the likelihood of reimbursement for Zalviso or any of our other product candidates. The application of user fees to generic drug products may expedite the approval of additional pain medication generic drugs. We expect to experience pricing pressures in connection with any sale of Zalviso and any of our other product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our products and our business will be harmed.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If we are found to have improperly promoted off-label uses of Zalviso or our other product candidates, if approved, we may become subject to significant liability. Such enforcement has become more common in the industry. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription drug products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we receive marketing approval for our product candidates for our proposed indications, physicians may nevertheless use our products for their patients in a manner that is inconsistent with the approved label, if the physicians personally believe in their professional medical judgment it could be used in such manner. However, if we are found to have promoted our products for any off-label uses, the federal government could levy civil, criminal and/or administrative penalties, and seek fines against us. The FDA or other regulatory authorities could also request that we enter into a consent decree or a corporate integrity agreement, or seek a permanent injunction against us under which specified promotional conduct is monitored, changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, including Zalviso, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

Risks Related to Our Business Operations and Industry

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

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

The DEA limits the availability and production of all Schedule II substances, including sufentanil, through a quota system. The DEA requires substantial evidence and documentation of expected legitimate medical and scientific needs before assigning quotas to manufacturers. Our contract manufacturers have applied annually for a quota on our behalf. In future years, we may need greater amounts of sufentanil to continue development of our product candidates, and we will need significantly greater amounts of sufentanil to implement our commercialization plans for any of our products that may be approved by the FDA, including Zalviso if approved by the FDA. Any delay or refusal by the DEA in establishing the procurement quota or a reduction in our quota for sufentanil or a failure to increase it over time to meet anticipated increases in demand could delay or stop the clinical development or commercial sale of Zalviso or any of our other product candidates. This could have a material adverse effect on our business, results of operations, financial condition and prospects.

We have not yet produced commercial supplies and we may encounter difficulties in production, which may adversely affect our clinical and commercial plans.

Early development and clinical trial manufacturing was conducted at Patheon in Toronto, Canada. Because the DEA requires that sufentanil be manufactured in the United States if our product candidates are marketed in the United States, we transferred our manufacturing capability in the third quarter of 2011 from Patheon in Toronto, Canada to Patheon's production facility in Cincinnati, Ohio, where we have built out a suite within their existing buildings that will serve as a manufacturing facility for clinical and commercial supplies of NanoTabs. Late stage development and manufacture of registration stability lots, which were utilized in clinical trials, were manufactured at Patheon, Cincinnati. However, we have not yet produced commercial supplies at this facility and we may encounter difficulties in production at the new facility, which may adversely affect our clinical and commercial plans.

In January 2013, we entered into a Manufacturing Services Agreement, or the Services Agreement, with Patheon under which Patheon has agreed to manufacture, supply, and provide certain validation and stability services with respect to Zalviso for potential sales in the United States, Canada, Mexico and other countries, subject to agreement by the parties to any additional fees for such other countries. There is no guarantee that Patheon's services will be satisfactory or that they will continue to meet the strict regulatory guidelines of the FDA or other regulatory agencies. In addition, in January 2013, we entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement, with Patheon, relating to the manufacture of sufentanil NanoTabs. Under the terms of the Capital Agreement, we have planned certain future modifications to Patheon's Cincinnati facility.

If Patheon cannot provide us with an adequate supply of NanoTabs, we may be required to pursue alternative sources of manufacturing capacity. 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 before approval of Zalviso and our other product candidates for commercial distribution. We do not fully 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 Zalviso. 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 trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2013, we had 27 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, particularly in preparation for the commercial launch of Zalviso if our NDA submission is approved by the FDA. 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 Zalviso and our other product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

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.

Our employees, independent contractors, principal investigators, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, investigators, consultants, commercial partners and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties

could include intentional, reckless and/or negligent conduct that violates (1) the laws of the FDA and similar foreign regulatory bodies, including those laws requiring the reporting of true, complete and accurate information to such regulatory bodies; (2) healthcare fraud and abuse laws of the United States and similar foreign fraudulent misconduct laws; and (3) laws requiring the reporting of financial information or data accurately. Specifically, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry are subject to extensive laws designed to prevent misconduct, including fraud, kickbacks, self-dealing and other abusive practices. These laws may restrict or prohibit a wide range of pricing, discounting, marketing, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. It is not always possible to identify and deter employee and other third-party misconduct. The precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws. If any such actions are instituted against us, and we are not successful in defending ourselves, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Related to Our Intellectual Property

If we cannot defend our issued patents from third party claims or if our pending patent applications fail to issue, our business could be adversely affected.

To protect our proprietary technology, we rely on patents as well as other intellectual property protections including trade secrets, nondisclosure agreements, and confidentiality provisions. We are the owner of record of over 20 issued patents worldwide. These issued patents cover AcelRx's sufentanil NanoTab, medication delivery devices and platform technology. These issued patents are expected to provide coverage through 2027 – 2031.

In addition, we are pursuing a number of U.S. non-provisional patent applications and foreign national applications directed to our product candidates. The patent applications that we have filed and have not yet been granted may fail to result in issued patents in the United States or in foreign countries. Even if the patents do successfully issue, third parties may challenge the patents.

Our commercial success will depend in part on successfully defending our current sufentanil formulation patents against third party challenges and expanding our existing formulation patent portfolio to provide additional layers of patent protection, as well as extending patent protection to our proprietary delivery devices. There can be no assurance that we will be successful in defending our existing and future patents against third party challenges, or that our pending patent applications will result in issued patents.

The patent positions of pharmaceutical companies, including us, can be highly uncertain and involve complex and evolving legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the United States. Legal developments may preclude or limit the scope of available patent protection.

There is also no assurance that any patents issued to us will not become the subject of adversarial proceedings such as opposition, inter partes review, post-grant review, reissue, re-examination or other post-issuance proceedings, will provide us with competitive advantages, will not be challenged by any third parties, or that the patents of others will not prevent the commercialization of products incorporating our technology. Furthermore, there can be no guarantee that others will not independently develop similar products, duplicate any of our products, or design around our patents.

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

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

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

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

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

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

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

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

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

Leahy-Smith Act, and in particular, the first to file provisions, that became effective March 16, 2013. It is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

Competitors or third parties may infringe our patents. We may be required to file patent infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or that the third party's technology does not in fact infringe upon our patents. An adverse determination of any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our related pending patent applications at risk of not issuing. Litigation may fail and, even if successful, may result in substantial costs and be a distraction to our management. We may not be able to prevent misappropriation of our proprietary rights, particularly in countries outside the United States where patent rights may be more difficult to enforce. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential or sensitive information could be compromised by disclosure in the event of litigation. In addition, during the course of litigation there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

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

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

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

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

We rely on trade secrets to protect our proprietary know-how and technological advances, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could

be necessary to enforce and determine the scope of our proprietary rights. Failure to obtain or maintain trade secret protection could enable competitors to use our proprietary information to develop products that compete with our products or cause additional, material adverse effects upon our competitive business position.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and 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 the United States, Canada, the European Union and India. We have also registered our NANOTAB mark in the United States, Hong Kong and Singapore, and our ACCELERATE. INNOVATE. ALLEVIATE. tagline in the United States. We have additionally applied for registration of our ZALVISO mark in the United States on an intent-to-use basis and that application has been allowed. In early 2014, FDA accepted the ZALVISO mark as part of the NDA review process. Although we are not currently aware of any oppositions to or cancellations of our registered trademarks or pending applications, it is possible that one or more of the applications could be subject to opposition or cancellation after the marks are registered. The registrations will be subject to use and maintenance requirements. It is also possible that we have not yet registered all of our trademarks in all of our potential markets, and that there are names or symbols other than “ACELRX” that may be protectable marks for which we have not sought registration, and failure to secure those registrations could adversely affect our business. Opposition or cancellation proceedings may be filed against our trademarks and our trademarks may not survive such proceedings.

Risks Related to Ownership of Our Common Stock

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

Since our initial public offering, or IPO, in February 2011, the trading price of our common stock has experienced significant volatility and is likely to be volatile in the future. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- any adverse development or perceived adverse development with respect to the FDA's review of the NDA for Zalviso;
- any delay in submitting an NDA for any of our other product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that NDA;
- adverse results or delays in future clinical trials;
- inability to obtain additional funding, including funding necessary for the planned commercialization and manufacturing of Zalviso in the United States and advancement of clinical trials for other product candidates;
- 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, or NASDAQ, in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Until recently our common stock has thinly traded and in the future, may continue to be thinly traded, and our stockholders may be unable to sell at or near asking prices, or at all if they need to sell their shares to raise money or otherwise desire to liquidate such shares.

Until recently, we had a low volume of daily trades in our common stock on NASDAQ. For example, the average daily trading volume in our common stock on NASDAQ during the first quarter of 2013 was approximately

275,000 shares per day. A more active market for our stock has only recently developed and may not be sustained. For example, the average daily trading volume in our common stock on NASDAQ during the fourth quarter of 2013 was approximately 800,000 shares per day. Our stockholders may be unable to sell their common stock at or near their asking prices, which may result in substantial losses to our investors.

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

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 own a significant percentage of our voting stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders are able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, are able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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

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

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

We 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. If we fail to comply with the requirements of Section 404, it may affect the reliability of our internal control over financial reporting and negatively impact the quality of disclosure to our stockholders. If we or our independent registered public accounting firm identify and report a material weakness, it could adversely affect our stock price.

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

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise

capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. As of December 31, 2013, we had 43.1 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.

In addition, certain holders of our securities are entitled to certain rights with respect to the registration of their shares of common stock under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

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

Pursuant to 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. The completion of the July 2013 public equity offering, together with our public equity offering in December 2012, our initial public offering, private placements and other transactions that have occurred, have triggered such an ownership change. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo further ownership changes in the future. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

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

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our loan and security agreement with Hercules. Regardless of the restrictions in our loan and security agreement with Hercules or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

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

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures

Not Applicable.

PART II

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

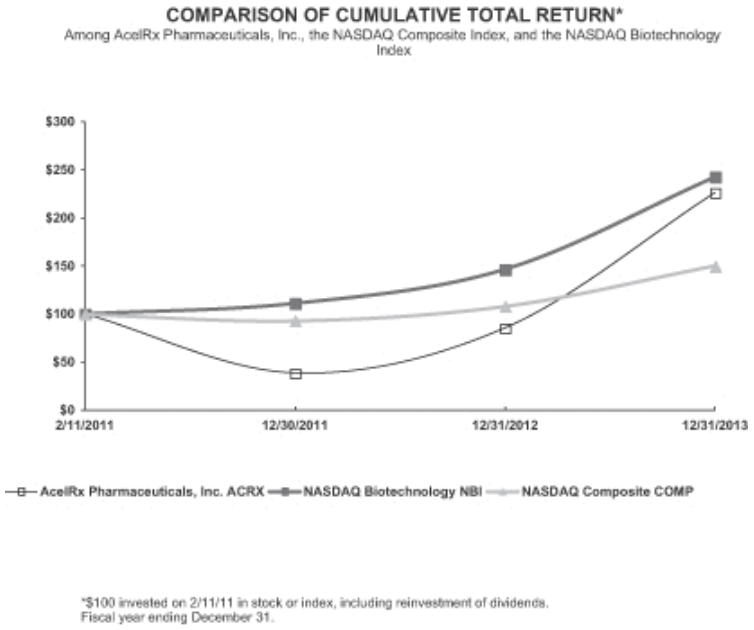
Market Information

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

	Price	
	High	Low
Year ended 2013		
Fourth Quarter	$ 11.35	$ 6.04
Third Quarter	$ 13.50	$ 8.94
Second Quarter	$ 10.59	$ 4.66
First Quarter	$ 5.97	$ 4.12
Year ended 2012		
Fourth Quarter	$ 5.25	$ 2.27
Third Quarter	$ 3.88	$ 2.54
Second Quarter	$ 4.00	$ 2.77
First Quarter	$ 3.76	$ 1.89

Stock Price Performance Graph

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



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

Holders of Record

As of January 31, 2013, there were 18 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock, and we are prohibited from doing so under the terms of our loan and security agreement with Hercules. Regardless of the restrictions in our loan and security agreement with Hercules or the terms of any potential future indebtedness, we anticipate that we will retain all available funds and any future earnings to support our operations and finance the growth and development of our business and, therefore, we do not expect to pay cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Item 6. Selected Financial Data

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

	Year Ended December 31,				
	2013	2012	2011	2010	2009
	(in thousands, except share and per share data)				
Statements of Operations Data:					
Revenue:					
Collaboration agreement	$ 27,370	$ —	$ —	$ —	$ —
Research grant	2,132	2,394	1,072	—	—
Total revenue	29,502	2,394	1,072	—	—
Operating Expenses:					
Research and development	$ 26,292	$ 24,908	$ 13,624	$ 8,193	$ 15,502
General and administrative	9,877	7,199	6,800	3,993	3,529
Total operating expenses	36,169	32,107	20,424	12,186	19,031
Loss from operations	(6,667)	(29,713)	(19,352)	(12,186)	(19,031)
Interest expense	(1,518)	(2,283)	(2,309)	(1,397)	(1,242)
Other income (expense), net	(15,241)	(1,367)	1,560	(761)	154
Net loss	$ (23,426)	$ (33,363)	$ (20,101)	$ (14,344)	$ (20,119)
Net loss per share of common stock, basic and diluted	$ (0.59)	$ (1.51)	$ (1.16)	$ (21.84)	$ (34.93)
Shares used in computing net loss per share of common stock, basic and diluted	39,746,678	22,124,637	17,344,727	656,650	576,021

	As of December 31,				
	2013	2012	2011	2010	2009
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$103,663	$59,763	$35,785	$ 3,682	$ 12,546
Working capital (deficit)	97,692	47,435	30,301	(7,632)	6,931
Total assets	110,031	64,520	40,835	6,830	14,491
Total debt, net, including convertible notes	14,364	15,973	19,079	12,009	9,734
PIPE warrant liability	13,111	7,418	—	—	—
Convertible preferred stock warrant liability	—	—	—	2,529	169
Convertible preferred stock	—	—	—	55,941	55,871
Total stockholders' equity (deficit)	73,159	33,847	17,468	(65,892)	(52,994)

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

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

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. Our lead product candidate, Zalviso ™, formerly known as the Sufentanil NanoTab PCA System, or ARX-01, is currently under review by the FDA for marketing approval, and is designed to improve the management of moderate-to-severe acute pain in patients in the hospital setting. The current standard of care for patients with moderate-to-severe pain in the hospital is intravenous patient-controlled analgesia, or IV PCA, has been shown to cause harm and inconvenience to patients following surgery because of the side effects of commonly used IV PCA opioids, the invasive IV needle route of delivery and the inherent potential for programming and delivery errors associated with the complexity of infusion pumps.

Zalviso

Zalviso is an investigational pre-programmed, non-invasive, handheld system that allows hospital patients with moderate-to-severe acute pain to self-dose with sublingual sufentanil NanoTabs to manage their pain. Zalviso is designed to address the needs of patients with moderate-to-severe pain in the hospital setting by offering:

- **A high therapeutic index opioid:** Zalviso uses the high therapeutic index, highly lipophilic opioid, sufentanil, enabling delivery via a non-intravenous route, and also supporting fast onset of effect.
- **A non-invasive route of delivery:** The sublingual route of delivery used by Zalviso provides rapid onset of analgesia, therefore eliminating the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections. In addition, because patients do not require direct connection to an IV PCA infusion pump through IV tubing, Zalviso allows for ease of patient mobility.
- **A simple, pre-programmed PCA solution:** Zalviso is a pre-programmed PCA system designed to eliminate the risk of programming errors.

Based on the successful results of our Phase 3 clinical program for Zalviso, we submitted a New Drug Application, or NDA, for Zalviso in September 2013 and, in December 2013, we announced that the U.S Food and Drug Administration, or FDA, accepted for filing the Zalviso NDA. In addition, the FDA has established a Prescription Drug User Fee Act, or PDUFA, action date of July 27, 2014 for AcelRx's Zalviso NDA. Assuming successful approval of our NDA on or around the PDUFA action date, we anticipate generating the first commercial sales of Zalviso in the United States in the first quarter of 2015.

The 505(b)(2) NDA submission for Zalviso is based on a development program that includes data from seven Phase 1 studies, three Phase 2 clinical trials, and three Phase 3 clinical trials. The Phase 3 trial program included two placebo-controlled efficacy and safety trials and one open-label active comparator trial, in which Zalviso was compared to IV PCA with morphine. Zalviso successfully achieved the primary efficacy endpoints for each of these trials. A summary of the Phase 3 trials and results is as follows:

- *Active comparator trial (IAP 309)*—in November 2012, we reported top-line data demonstrating that Zalviso met its primary endpoint of non-inferiority in a Phase 3 open-label active comparator trial

designed to compare the efficacy and safety of Zalviso (15 mcg/dose, 20 minute lock-out) to IV PCA with morphine (1mg/dose, 6 minute lock-out) for the treatment of moderate-to-severe acute post-operative pain immediately following major abdominal or orthopedic surgery.

- *Double-blind, placebo-controlled, abdominal surgery trial (IAP 310)*—in March 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major open abdominal surgery. Adverse events reported in the trial were generally mild or moderate in nature and similar in both placebo and treatment groups. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 178 adult patients at 13 U.S. sites.
- *Double-blind, placebo-controlled, orthopedic surgery trial (IAP 311)*—in May 2013, we reported top-line data demonstrating that Zalviso met its primary endpoint in a pivotal Phase 3 trial designed to compare the efficacy and safety of Zalviso to placebo in the management of acute post-operative pain after major orthopedic surgery. Utilizing a randomized, double-blind, placebo-controlled design, this pivotal Phase 3 trial enrolled 426 adult patients at 34 U.S. sites. Treatment-emergent adverse events were generally mild to moderate in nature and similar for the majority of adverse events between Zalviso and placebo-treated patients, despite the shorter duration of exposure in the placebo-treated patients caused by early termination due to inadequate analgesia.

As noted above, assuming successful approval of our NDA on or about the PDUFA action date, we anticipate launching the commercial sale of Zalviso in the United States in the first quarter of 2015.

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in the management of moderate-to-severe acute pain within a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Latin America.

Under the terms of the agreement, we received an upfront cash payment of $30.0 million. We are eligible to receive approximately $220 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. The upfront payment along with regulatory and development milestones constitute approximately one third of the total $250M milestone payments, while sales target achievements represent two thirds of the total. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

Grünenthal will be responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. We will be responsible for obtaining and maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

ARX-04

We are also developing a Sufentanil Single-Dose NanoTab, or ARX-04, for the treatment of moderate-to-severe acute pain to be administered by a healthcare professional to a patient in settings of acute pain, such as on the battlefield, in the emergency room or in ambulatory care facilities. In December 2013, we completed an End of Phase 2 Meeting with the FDA to identify a Phase 3 program pathway forward for evaluation of ARX-04. This definition of the Phase 3 program allows AcelRx to continue to refine Phase 3 protocols with the Agency in the coming months, with the goal of initiating Phase 3 studies for ARX-04 in the second half of 2014.

In April 2013, we reported top-line data showing that the primary endpoint was achieved in a placebo-controlled, dose-finding, Phase 2 clinical trial of ARX-04 for acute pain. This trial randomized 101 patients following bunionectomy surgery in a 2:2:1 ratio to 30 mcg sufentanil, 20 mcg sufentanil or placebo treatment arms. Ninety-one percent of patients entering the trial completed the 12-hour trial period.

Research and development of ARX-04, including the Phase 2 trial and pre-Phase 3 development, was funded by a $5.6 million grant from the U.S. Army Medical Research and Materiel Command, or USAMRMC. As of December 31, 2013, we had recognized the full amount of the grant, $5.6 million.

Financial Overview

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

To date, we have funded our operations primarily through the issuance of equity securities, borrowings, payments from our corporate collaboration and our research grants.

Our revenues to date have consisted primarily of revenues from our research grant with the USAMRMC and through our collaboration with Grünenthal. We expect revenues will continue to fluctuate from period to period and there can be no assurance that our existing collaboration will continue beyond the initial term or that we are able to meet the milestones specified in this agreement, or that we will obtain marketing approval for our product candidates and subsequently generate revenue from those products in excess of our operating expenses.

Our net losses were $23.4 million and $33.4 million during the years ended December 31, 2013 and 2012, respectively. As of December 31, 2013, we had an accumulated deficit of $145.5 million. As of December 31, 2013, we had cash, cash equivalents and investments totaling $103.7 million compared to $59.8 million as of December 31, 2012.

In December 2013, we entered into an amended 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 $40.0 million in three tranches, represented by secured convertible promissory notes. The agreement amends and restates the loan and security agreement with Hercules dated as of June 29, 2011. We borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013 and used approximately $8.6 million of the proceeds from the first tranche to repay our obligations under the original loan and security agreement with Hercules. We plan to use the proceeds of the remaining tranches to provide additional funding for the commercialization of Zalviso, as a potential source of funding for clinical trials for other development programs in its pipeline and for general corporate purposes. The second tranche of $10.0 million can be drawn, at the Company's option, anytime prior to June 30, 2014. The third tranche, of $15.0 million, can be drawn at anytime between December 15, 2014 and March 15, 2015, but only if the Company has obtained approval for Zalviso from the FDA (the "Milestone"). The interest rate for each tranche will be calculated at a rate equal to the greater of either (i) 9.10% plus the prime rate as reported from time to time in The Wall Street Journal minus 5.25%, and (ii) 9.10%. Payments under the loan agreement are interest only until April 1, 2015 (which will be extended until January 1, 2016 if we achieve the Milestone on or before April 1, 2015) followed by equal monthly payments of principal and interest through the scheduled maturity date on October 1, 2017 (which would be extended until January 1, 2018 if we achieve the Milestone on or prior to April 1, 2015). In addition, a final payment equal to $1.7 million will be due on the Loan Maturity Date, or such earlier date specified in the Loan Agreement. The Company's obligations under the Loan Agreement are secured by a security interest in substantially all of its assets, other than its intellectual property.

As of December 31, 2013, the outstanding principal owed to Hercules was $15.0 million.

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the U.S. and Asia.

Under the terms of the agreement, we received an upfront cash payment of $30 million. We are eligible to receive approximately $220 million in additional payments, based upon research, development, regulatory and manufacturing efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

Grünenthal will be responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. We will be responsible for obtaining and maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

Since our inception in July 2005, we have not generated any revenue from the sale of our products. We are currently seeking FDA approval for our lead product candidate, Zalviso, and are preparing for the commercial launch of Zalviso in 2015; however, there is no guarantee that we will receive approval from the FDA and there can be no guarantee that we will be able to produce product revenue in the foreseeable future, if ever. As of December 31, 2013, we have recognized in full, as revenue, our $5.6 million grant from the USAMRMC There can be no assurance that we will receive additional funding from USAMRMC or other research-related grant awards or produce other collaborative agreement revenues in the future.

Critical Accounting Estimates

Based on a critical assessment of our accounting policies and the underlying judgments and uncertainties affecting the application of those policies, management believes that our financial statements are fairly stated in accordance with accounting principles generally accepted in the United States, and meaningfully present our financial condition and results of operations.

The accompanying discussion and analysis of our financial condition and results of operations are based upon our financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. Note 1 of Notes to Financial Statements describes the significant accounting policies used in the preparation of the financial statements. Certain of these significant accounting policies are considered to be critical accounting policies, as defined below.

A critical accounting policy is defined as one that is both material to the presentation of our financial statements and requires management to make difficult, subjective or complex judgments that could have a material effect on our financial condition and results of operations. Specifically, critical accounting estimates have the following attributes: (i) we are required to make assumptions about matters that are highly uncertain at the time of the estimate; and (ii) different estimates we could reasonably have used, or changes in the estimate that are reasonably likely to occur, would have a material effect on our financial condition or results of operations.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that

are inherently uncertain. Management has discussed the development, selection and disclosure of the following estimates with the Audit Committee.

Revenue Recognition

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

Revenue generated from collaboration agreements typically includes upfront signing or license fees, cost reimbursements, development and manufacturing services, milestone payments and royalties on future licensee's product sales.

Revenue from non-refundable license, technology access or other payments under license and collaborative agreements where we have a continuing obligation to perform is recognized as revenue over the expected period of the continuing performance obligation. We estimate the performance period at the inception of the arrangement and re-evaluate it each reporting period. This re-evaluation may shorten or lengthen the period over which the remaining revenue is recognized. Changes to these estimates are recorded on a prospective basis.

Multiple Element Arrangements prior to the adoption of ASU No. 2009-13, Revenue Recognition—Multiple Deliverable Revenue Arrangements (ASU 2009-13). For revenue arrangements entered into before January 1, 2011, that include multiple deliverables, the elements of such agreement were divided into separate units of accounting if the deliverables met certain criteria, including whether the fair value of the delivered items could be determined and whether there was evidence of fair value of the undelivered items. In addition, the consideration was allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units of accounting.

Multiple Element Arrangements after the adoption of ASU 2009-13. ASU 2009-13 amended the accounting standards for certain multiple element revenue arrangements to:

- provide updated guidance on whether multiple elements exist, how the elements in an arrangement should be separated, and how the arrangement consideration should be allocated to the separate elements;
- require an entity to allocate arrangement consideration to each element based on a selling price hierarchy, also called the relative selling price method, where the selling price for an element is based on vendor-specific objective evidence ("VSOE"), if available; third-party evidence ("TPE"), if available and VSOE is not available; or the best estimate of selling price ("ESP"), if neither VSOE nor TPE is available; and
- eliminate the use of the residual method and require an entity to allocate arrangement consideration using the selling price hierarchy.

For revenue agreements with multiple element arrangements, such as license and development agreements, the Company will allocate revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using VSOE of selling price or TPE of selling price. If neither exists the Company uses ESP for that deliverable. Revenue allocated is then recognized when the basic four revenue recognition criteria are met for each element. The collaboration and license agreement entered into with Grünenthal in December 2013 was evaluated under these updated accounting standards.

Additionally, the Company recognizes milestone payments, which are subject to substantive contingencies, upon completion of specified milestones, which represents the culmination of an earnings process, according to

contract terms. Royalty revenues are generally recognized when earned and collectability of the related royalty payment is reasonably assured.

The Company recognizes cost reimbursement revenue under agreements, including our grant agreement with the USAMRMC, as the related research and development costs for services are rendered.

Deferred revenue represents the portion of research or license payments received which have not been earned.

Research and Development Expenses

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

Share-Based Compensation

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

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

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

of comparable publicly traded companies in our industry or similar lines of business which were based on key metrics implied by the enterprise values or acquisition values of our comparable publicly traded companies.

Liabilities Associated with Warrants

Warrants to Purchase Common Stock

In connection with the private placement equity financing in June 2012, or PIPE, the Company issued PIPE warrants to purchase up to 2,630,103 shares of common stock. Under the terms of the PIPE warrants, upon certain transactions, including a merger, tender offer, sale of all or substantially all of the assets of the Company or if a person or group shall become the owner of 50% of the Company's issued and outstanding common stock, which is outside of the Company's control, each PIPE warrant holder may elect to receive a cash payment in exchange for the warrant, in an amount determined by application of the Black-Scholes option-pricing model. Accordingly, the PIPE warrants are recorded as a liability at fair value at the end of each reporting period, as determined by the Black-Scholes option-pricing model and changes to the fair value are recorded in other income (expense). The inputs for the Black-Scholes option-pricing model include exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants. These inputs are subjective and generally require significant analysis and judgment to develop. Changes to the inputs could significantly impact the estimated fair value of the PIPE warrants, and since issuance of the PIPE warrants through December 31, 2013, changes in our stock price have had a significant impact to the estimated fair value of the PIPE warrants.

Warrants to Purchase Convertible Preferred Stock

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

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

Bridge Loan

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

Under the terms of the bridge loan agreement, upon the election of the holders of a majority of the aggregate principal amount payable under the 2010 notes, we agreed to issue an additional $4.0 million of the 2010 notes.

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

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

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

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

Income Taxes

Significant management judgment is required in determining our provision or benefit for income taxes, any uncertain tax positions, deferred tax assets and liabilities, and any valuation allowance recorded against our net deferred tax assets. We make these estimates and judgments about our future taxable income that are based on assumptions that are consistent with our future plans. Since inception, and as of December 31, 2013, we have recorded a full valuation allowance on our net deferred tax assets due to uncertainties related to our ability to utilize our deferred tax assets in the foreseeable future. These deferred tax assets primarily consist of certain net operating loss carryforwards and research and development tax credits. Should the actual amounts differ from our estimates, the amount of our valuation allowance could be materially impacted. Since inception, we have incurred operating losses and, accordingly, we have not recorded a provision for income taxes for any of the periods presented.

Results of Operations

Our results of operations have fluctuated from period to period and may continue to fluctuate in the future, based upon the progress of our research and development efforts and variations in the level of expenses related to developmental efforts during any given period. Results of operations for any period may be unrelated to results of operations for any other period. In addition, historical results should not be viewed as indicative of future operating results. We are subject to risks common to companies in our industry and at our stage of development, including risks inherent in our research and development efforts, reliance upon our collaborator, enforcement of our patent and proprietary rights, need for future capital, potential competition and uncertainty of clinical trial results or regulatory approvals or clearances. In order for a product candidate to be commercialized based on our research, we and our collaborators must conduct preclinical tests and clinical trials, demonstrate the efficacy and safety of our product candidates, obtain regulatory approvals or clearances and enter into manufacturing, distribution and marketing arrangements, as well as obtain market acceptance.

Years Ended December 31, 2013, 2012 and 2011

Revenue

To date, we have not generated any commercial product revenue. We do not expect to receive any commercial sales revenue from any product candidates that we develop until we, or our collaborators, obtain regulatory approval and commercialize our products.

Collaboration agreement

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States and Asia.

Under the terms of the agreement, we received an upfront cash payment of $30.0 million. We are eligible to receive approximately $220 million in additional payments, based upon research, development, regulatory and manufacturing efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

Grünenthal will be responsible for all commercial activities for Zalviso, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. We will be responsible for obtaining and maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of Zalviso to Grünenthal for commercial sales.

Research Grant

In May 2011, we received a grant award of $5.6 million from the USAMRMC for the development of ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain. Revenue related to this grant award was recognized as the related research and development expenses were incurred. As of December 31, 2013, $5.6 million grant had been recognized in its entirety.

Revenue for the year ended December 31, 2013 was $29.5 million, $27.4 million of which related to our collaboration with Grünenthal and $2.1 million related to our grant with the USAMRMC. Revenue for the years ended 2012 and 2011 was $2.4 and $1.1 million, respectively, and was generated from our grant from the USAMRMC.

Research and Development Expenses

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

- expenses incurred under agreements with contract research organizations and clinical trial sites;
- employee- and consultant-related expenses, which include salaries, benefits and stock-based compensation;
- payments to third party pharmaceutical and engineering development contractors;
- payments to third party manufacturers; and
- depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities and equipment, and equipment and laboratory and other supply costs.

Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late stage clinical trials. We will incur substantial future expenditures as we seek to continue development of Zalviso, including the requisite activities associated with preparing for the potential commercialization of Zalviso. In addition, we plan to continue to incur significant research and development expenses, including the expenses associated with the continued development of ARX-04. We do not plan to continue development of ARX-02 and ARX-03, unless additional funding or corporate partnership resources are available to support these programs.

We track external development expenses on a program-by-program basis. Our development resources are shared among all of our programs. Compensation and benefits, facilities, depreciation, stock-based compensation, and development support services are not allocated specifically to projects and are considered research and development overhead. Below is a summary of our research and development expenses during the years ended December 31, 2013, 2012 and 2011 (in thousands):

	Years Ended December 31,		
	2013	2012	2011
ARX-01 (Zalviso)	$ 16,009	$ 17,100	$ 7,823
ARX-04	1,957	1,547	523
Overhead	8,326	6,261	5,278
Total research and development expenses	$26,292	$24,908	$13,624

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

Total research and development expenses for years ended December 31, 2013, 2012 and 2011 were as follows (in thousands, except percentages):

	Years Ended December 31,						
	2013	2012	2011	Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
Research and development expenses	$26,292	$24,908	$13,624	$ 1,384	$ 11,284	6%	83%

The $1.4 million increase during the year ended December 31, 2013 was primarily attributable to an increase of $2.1 million in headcount-related expenses, including bonus and stock-based compensation, due to an increase in headcount and a rising stock price, which created higher stock-based compensation expense. In addition, expenses related to ARX-04 increased $0.4 million due primarily to Phase 2 clinical trial expenses, which was completed in February 2013, and ongoing pharmaceutical development work. These increases were partially offset by a $1.1 million decrease in expenses related to our Zalviso development program, as we had completed one of the three Phase 3 trials in 2012 and completed the second and third Phase 3 trials, which were initiated in 2012, by mid-2013.

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

General and Administrative Expenses

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

Total general and administrative expenses for the years ended December 31, 2013, 2012 and 2011 were as follows (in thousands, except percentages):

	Years Ended December 31,						
	2013	2012	2011	Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
General and administrative expenses	$9,877	$7,199	$6,800	$ 2,678	$ 399	37%	6%

The $2.7 million increase during the year ended December 31, 2013 was primarily due to an increase in consulting/outside services of $1.4 million, primarily related to market research activities for Zalviso, an increase of $1.1 million in headcount-related expenses, primarily due to stock-based compensation expense as a result of an increasing stock price, and other corporate-related expenses.

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

Interest Expense

Interest expense consisted primarily of interest accrued or paid on our debt obligation agreements and amortization of debt discounts. Total interest expense for the years ended December 31, 2013, 2012 and 2011 was as follows (in thousands, except percentages):

	Years Ended December 31,						
	2013	2012	2011	Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
Interest expense	$(1,518)	$(2,283)	$(2,309)	$ (765)	$ (26)	(34%)	(1)%

The $0.8 million decrease in interest expense during the year ended December 31, 2013, was due to a lower portion of our monthly payments attributable to interest due to the continued maturity of our original loan agreement with Hercules, which was scheduled to mature on December 1, 2014. The loan agreement was amended with Hercules in December 2013. The overall debt facility was increased to $40.0 million and the maturity was extended to October 1, 2017.

In December 2013, we drew the first tranche of $15.0 million and used a portion of the proceeds to pay down the remaining principal and accrued interest on the original loan agreement with Hercules, which was $8.6 million.

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

Interest and other income (expense), net

Interest income and other income (expense), net, during the years ended December 31, 2013 and 2012 consisted primarily of the change in the fair value of our warrants, or PIPE warrants, issued in connection with our private

placement of our common stock, which was completed in June 2012. During the year ended December 31, 2013, we also recorded a loss of $1.6 million associated with extinguishment of our original loan agreement with Hercules, which we entered into in 2011, and amended in December 2013. During the year ended December 31, 2011 interest income and other income (expense) consisted primarily of the change in the fair value our then-outstanding warrants to purchase convertible preferred stock. The warrants to purchase convertible preferred stock were classified as liabilities and, as such, were remeasured to fair value at each balance sheet date with the corresponding gain or loss from the adjustment recorded as other income (expense), net. Upon the completion of our IPO, all of our warrants to purchase convertible preferred stock were remeasured to fair value and were either exercised or converted into warrants to purchase common stock. At that time, the then-current aggregate fair value of these warrants was reclassified from liabilities to additional paid-in capital and we no longer remeasure the liability associated with these warrants to fair value. Total interest income and other income (expense) for the years ended December 31, 2013, 2012 and 2011 was as follows (in thousands, except percentages):

	Years Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)
	2013	2012	2011	2013 vs. 2012	2012 vs. 2011
Interest and other income (expense), net	$(15,241)	$(1,367)	$1,560	$ 13,874	$ (2,927)

The $13.9 million increase in interest and other income (expense) during the year ended December 31, 2013 was primarily attributable to the increase in the fair value of our PIPE warrants, which was recorded as an expense. The primary determinant of this expense was an increase in share price during 2013 and its resulting impact on the Black-Scholes valuation of these warrants. In addition, we recorded a $1.2 million loss related to entering into an amended and restated loan agreement with Hercules. This transaction, under generally accepted accounting principles, was considered an extinguishment of the original Hercules debt arrangement.

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

Liquidity and Capital Resources

Liquidity

We have incurred losses and generated negative cash flows from operations since inception. We expect to continue to incur significant losses and negative cash flows in 2014 and may incur significant losses and negative cash flows for the foreseeable future. We have funded our operations primarily through the issuance of equity securities and debt financings, and more recently through our collaboration agreement with Grünenthal, which we entered into in December 2013.

As of December 31, 2013, we had cash, cash equivalents and investments totaling $103.7 million compared to $59.8 million as of December 31, 2012. The increase was primarily attributable to proceeds from our equity financing conducted in July 2013 and our collaboration with Grünenthal as described in more detail below. We anticipate that our existing capital resources plus additional cash available under our loan agreement with Hercules, will permit us to meet our capital and operational requirements through at least 2015, excluding any additional proceeds from potential milestones associated with our collaboration with Grünenthal. We base this expectation on our current operating plan, that assumes an NDA approval in the third quarter of 2014, and a Zalviso commercial launch in the first quarter of 2015. These assumptions may change as a result of many factors. For example, the FDA may delay the approval of Zalviso, or may never approve Zalviso. Our existing capital resources may not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations if these delays are substantial.

On July 23, 2013, we completed an underwritten public offering of 4,370,000 shares of common stock, at a price of $11.65 per share to the public. The total gross proceeds of this offering were $50.9 million with net proceeds of $47.9 million after deducting underwriting discounts and commissions and other expenses payable by us.

In December 2013, we announced a commercial collaboration with Grünenthal, covering the territory of the European Union, certain other European countries and Australia for Zalviso for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. We retain all rights in remaining countries, including the United States, Asia and Latin America. Under the terms of the agreement, we received an upfront cash payment of $30.0 million. We are eligible to receive approximately $220 million in additional payments, based upon research, development, regulatory and manufacturing efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of Zalviso in the Grünenthal territory.

In December 2013, we entered into an amended 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 $40.0 million in three tranches, represented by secured convertible promissory notes. The agreement amends and restates the loan and security agreement with Hercules dated as of June 29, 2011. We borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013 and used approximately $8.6 million of the proceeds from the first tranche to repay its obligations under the original loan and security agreement with Hercules. We plan to use the proceeds of the remaining tranches to provide additional funding for the commercialization of Zalviso, as a potential source of funding for clinical trials for other development programs in our pipeline and for general corporate purposes. The second tranche of $10.0 million can be drawn, at our option, anytime prior to June 30, 2014. The third tranche of $15.0 million, can be drawn at anytime between December 15, 2014 and March 15, 2015, but only if the Company has obtained approval for Zalviso from the FDA.

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

Cash Flows

	Years Ended December 31,		
	2013	2012	2011
		(in thousands)	
Net cash used in operating activities	$ (487)	$(24,582)	$ (15,287)
Net cash (used in) provided by investing activities	(6,920)	14,955	(29,579)
Net cash provided by financing activities	47,876	49,765	49,605

Cash Flows from Operating Activities

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

Net cash used in operating activities of $0.5 million during the year ended December 31, 2013 reflected a net loss of $23.4 million, partially offset by aggregate non-cash charges of $20.0 million and a net change of $2.9 million in our net operating assets and liabilities. Non-cash charges primarily included $14.1 million for the revaluation of the PIPE warrant liability and the contingent put option liability, $3.5 million in stock-based compensation and $1.2 million for the loss on extinguishment of debt associated with our original loan agreement with Hercules, which was amended in December 2013. The net change in our operating assets and liabilities was primarily a

result of an increase in deferred revenue of $2.6 million associated with our collaboration agreement with Grünenthal and a decrease in prepaid expenses of $1.1 million due to completion of our Phase 3 clinical trials for Zalviso in 2013.

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

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

Cash Flows from Investing Activities

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

During the year ended December 31, 2013, cash used in investing activities of $6.9 million was primarily a result of $28.0 million in purchases of investments and $3.3 million in purchases of property and equipment, partially offset by $24.4 million in maturities of investments.

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

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

Cash Flows from Financing Activities

Cash flows from financing activities primarily reflect proceeds from the sale of our securities and proceeds from our debt financings, reduced by payments made on such debt financings. As of December 31, 2013, our balance of outstanding principal was $15.0 million associated with our loan and security agreement with Hercules.

During the year ended December 31, 2013, cash provided by financing activities was primarily a result of the receipt of $47.9 million in proceeds from an underwritten public offering in July 2013, net of offering costs and underwriting discounts, and proceeds of $15.0 million from our amended loan agreement with Hercules from December 2013, partially offset by payments of long-term debt of $16.3 million, including payment of the remaining principal of $8.5 million at the time of the amendment, and $7.8 million in principal payments made prior to the amendment.

During the year ended December 31, 2012, cash provided by financing activities was primarily a result of the receipt of $44.1 million in proceeds from an underwritten public offering in December 2012, net of offering costs

and underwriting discounts, and proceeds of $9.1 million from a private placement of our common stock, in June 2012, net of offering costs. During the year ended December 31, 2012, we made payments of $3.7 million associated with our loan and security agreement with Hercules.

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

Operating Capital and Capital Expenditure Requirements

We expect our rate of cash usage to increase in the future, in particular to support our product development activities, including the potential commercialization of Zalviso. We anticipate that our existing capital resources will permit us to meet our capital and operational requirements through at least 2015. We base this expectation on our current operating plan, which may change as a result of many factors. Our current operating plan includes continued preparation for the commercial launch of Zalviso in the first quarter of 2015, which assumes approval of Zalviso by the FDA by the third quarter of 2014. Our operating plan also includes continued development of ARX-04 and initiation of the Phase 3 clinical program. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. Additional capital may not be available in terms acceptable to us, or at all. If adequate funds are not available, or if the terms underlying potential funding sources are unfavorable, our business and our ability to develop our technology and product candidates would be harmed.

Our future capital requirements may vary materially from our expectations based on numerous forward looking factors, including but not limited to the following:

- the outcome, timing and cost of regulatory approvals;
- expenditures related to our commercialization preparation of Zalviso,
- future manufacturing, selling and marketing costs related to Zalviso, if the product is approved for marketing, including our contractual obligations to Grünenthal;
- the initiation, progress, timing and completion of clinical trials for our product candidates, including ARX-04;
- changes in the focus and direction of our business strategy and/or research and development programs;
- milestone and royalty revenue we receive under our collaborative development and commercialization arrangements;
- delays that may be caused by changing regulatory requirements;
- the number of product candidates that we pursue;
- the initiation, progress, timing and completion of clinical trials for our product candidates and potential product candidates;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the timing and terms of future in-licensing and out-licensing transactions;
- the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;
- the cost of procuring clinical and commercial supplies of our product candidates;

- the extent to which we acquire or invest in businesses, products or technologies; and
- the possible costs of litigation.

We will need substantial funds to:

- commercialize any products we market, including Zalviso;
- manufacture and market our product candidates;
- conduct preclinical and clinical testing of our product candidates; and
- conduct research and development programs.

Our existing capital resources may not be sufficient to fund our operations until such time as we may be able to generate sufficient revenues to sustain our operations. To the extent that our capital resources are insufficient to meet our future capital requirements, we will have to raise additional funds through the sale of our equity securities or from development and licensing arrangements to continue our development programs. We may be unable to raise such additional capital on favorable terms, or at all. If we raise additional capital by selling our equity or convertible debt securities, the issuance of such securities could result in dilution of our shareholders' equity positions. If adequate funds are not available we may have to:

- significantly curtail commercialization efforts of our product candidates or other operations;
- obtain funds through entering into collaboration agreements on unattractive terms; and/or
- delay, postpone or terminate planned clinical trials.

Contractual Obligations

The following table and disclosure summarizes our outstanding contractual obligations and commitments as of December 31, 2013 (in thousands):

		Payment by Period			
Contractual Obligations:	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
Operating Lease[1]	$ 938	$ 392	$ 546	$ —	—
Principal Payments on Long-Term Debt [2]	15,000	—	10,106	4,894	—
Interest Payments on Long-Term Debt	3,533	1,327	2,015	191	—
Total	$19,471	$ 1,719	$12,667	$5,085	—

(1) Operating lease includes base rent for facilities we occupy in Redwood City, California.
(2) The loan and security agreement with Hercules also includes a $0.2 million balloon payment due on December 1, 2014 and a $1.7 million balloon payment due on maturity of the loan, October 1, 2017, and are not included in the table above.

Patheon

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

We have also entered into a Capital Agreement, with Patheon. Under the terms of the Capital Agreement, we have the option to make certain future modifications to Patheon's Cincinnati facility, the aggregate cost of which is expected to be less than $4.4 million and which would be the responsibility of the Company. Under the Capital Agreement we made payments in 2012 and 2013 totaling $480,000 to Patheon to partially offset taxes incurred and paid by Patheon in connection with facility modifications already completed by Patheon. We can seek reimbursement from Patheon for these payments if it receives approval from the U.S. Food and Drug Administration for Zalviso. The Capital Agreement further requires that we pay a maximum "overhead fee" of $200,000 annually during the term of the Services Agreement, which amount may be reduced to $0 based on the amount of annual revenues earned by Patheon under the Services Agreement and pre-existing development agreements with Patheon. No fee was due in 2013 based on the amount of revenues earned by Patheon from the Company in 2013.

Expenditures associated with the Services Agreement are primarily driven by the potential commercial requirements and demand for our products, none of which are currently approved for commercial use; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

Grünenthal

On December 16, 2013, AcelRx Grünenthal entered into a Collaboration and License Agreement (the "License Agreement") and related Manufacture and Supply Agreement (the "Manufacturing Agreement" and together with the License Agreement, the "Agreements"). The License Agreement grants Grünenthal rights to commercialize Zalviso, in the countries of the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia (the "Territory"), for human use in pain treatment within or dispensed by hospitals hospices, nursing homes and other medically-supervised settings (the "Field").

Under the terms of the Manufacturing Agreement, we will manufacture and supply the Product for use in the Field for the Territory exclusively for Grünenthal. Grünenthal shall purchase from us, during the first five years after the effective date of the Manufacturing Agreement, 100% and thereafter 80% of Grünenthal's and its sublicensees' and distributors' requirements of Product for use in the Field for the Territory. The Product will be supplied at our fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires us to use commercially reasonable efforts to enter stand-by contracts with third parties providing significant supply and manufacturing services and under certain specified conditions permits Grünenthal to use a third party back-up manufacturer to manufacture the Product for Grünenthal's commercial sale in the Territory.

Unless earlier terminated, the Manufacturing Agreement continues in effect until the later of the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments or the end of any transition period for manufacturing obligations due to the expiration or termination of the License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the License Agreement, in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party or upon the bankruptcy or insolvency of either party.

Under the Supply Agreement, we will exclusively manufacture and supply the Product to Grünenthal for the Field in the Territory.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for our products, and none of our product candidates are currently approved for commercial use; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

Off-Balance Sheet Arrangements

Through December 31, 2013, we have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Not applicable.

Item 8. Financial Statements and Supplementary Data

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

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We have carried out an evaluation, under the supervision, and with the participation, of management including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e)) of the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this Annual Report on Form 10–K. Based on their evaluation, our principal executive officer and principal financial officer concluded that, subject to the limitations described below, our disclosure controls and procedures were effective as of December 31, 2013.

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

Changes in Internal Control over Financial Reporting

There have been no significant changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, internal control over financial reporting during the fiscal quarter ended December 31, 2013.

Management's Report on Internal Control over Financial Reporting

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

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

2. AcelRx Pharmaceuticals management has used the Committee of Sponsoring Organizations of the Treadway Commission, or COSO framework to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of AcelRx Pharmaceuticals' internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.

3. Management has assessed the effectiveness of AcelRx Pharmaceuticals' internal control over financial reporting as of December 31, 2013 and has concluded that such internal control over financial reporting was effective.

Ernst & Young LLP, our independent registered public accounting firm, has attested to and issued a report on the effectiveness of our internal control over financial reporting, which is included herein.

Report of Independent Registered Public Accounting Firm

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

We have audited AcelRx Pharmaceuticals, Inc. internal control over financial reporting as of December 31, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 Framework) (the COSO criteria). AcelRx Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, AcelRx Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2013, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of AcelRx Pharmaceuticals, Inc. as of December 31, 2013 and 2012, and the related statements of comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013 of AcelRx Pharmaceuticals, Inc. and our report dated March 17, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Redwood City, California
March 17, 2014

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Board of Directors

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

The following is a brief biography of each member of our board of directors with each biography including information regarding the experiences, qualifications, attributes or skills of each current board member as of January 31, 2014.

Class I Directors

Adrian Adams, age 63, has served as our Chairman since February 2013. Mr. Adams has been Chief Executive Officer and President of Auxilium Pharmaceuticals Inc. since December, 2011. Prior to joining Auxilium, Mr. Adams served as Chairman and Chief Executive Officer of Neurologix, a company focused on development of multiple innovative gene therapy development programs. Before Neurologix, Mr. Adams served as President and Chief Executive Officer of Inspire Pharmaceuticals, Inc., where he oversaw the commercialization and development of prescription pharmaceutical products and led the company through a strategic acquisition by global pharmaceutical leader Merck & Co., Inc. in May 2011. Prior to Inspire, Mr. Adams served as President and Chief Executive Officer of Sepracor Inc. from December 2006 until February 2010. Under his leadership, Sepracor conducted multiple strategic corporate development activities, including the in-licensing of seven products and out-licensing deals with two major pharmaceutical companies, prior to its acquisition by Dainippon Sumitomo Pharma Co. Prior to joining Sepracor, Mr. Adams was President and Chief Executive Officer of Kos Pharmaceuticals, Inc. from 2002 until the acquisition of the company by Abbott Laboratories in December 2006. During his tenure he led the transformation of Kos into a fully integrated and profitable pharmaceutical company with annual revenues approaching $1 billion. Mr. Adams graduated from the Royal Institute of Chemistry at Salford University in the U.K. Mr. Adams has extensive national and international experience and has been instrumental in launching major global brands in addition to driving successful corporate development activities encapsulating financing, product and company acquisitions, in-licensing and company M&A activities, all of which provide him with the qualifications and skills to serve as a director.

Richard Afable, M.D., age 60, has served as our director since December 2013. Since 2013, Dr. Afable has been the Chief Executive Officer of Covenant Health Network, based in Irvine, California, a non-profit healthcare delivery system formed through the affiliation of Hoag Memorial Hospital Presbyterian and St. Joseph Health System. Prior to Covenant Health Network, Dr. Afable served as the President and Chief Executive of Hoag Memorial Hospital Presbyterian from 2005 to 2013. Prior to Hoag Memorial Hospital Presbyterian, Dr. Afable served as the Chief Medical Officer of Catholic Health East from 1999 to 2005. He earned a B.S. in biology, an M.D. degree from Loyola University of Chicago, and a masters in public health from the University of Illinois at Chicago. Dr. Afable's scientific, financial and business expertise, including his experience as an executive officer in the health care industry, provides him with the qualifications and skills to serve as a director.

Mark G. Edwards, age 56, has served as our director since September 2011. Mr. Edwards is Managing Director of Bioscience Advisors Inc., a biopharmaceutical consulting firm he founded in 2011. From July 2008 until December 2010, he was Managing Director and a Principal of Deloitte Recap LLC, a wholly-owned subsidiary of Deloitte Touche Tohmatsu, an audit and financial consulting services firm. Mr. Edwards was previously the Managing Director and founder of Recombinant Capital, Inc. (Recap), a consulting and database firm based in Walnut Creek, California, from 1988 until the sale of Recap to Deloitte in 2008. Prior to founding Recap in 1988, Mr. Edwards was Manager of Business Development at Chiron Corporation, a biotechnology company. He received his B.A. and M.B.A. degrees from Stanford University. Mr. Edwards' financial and business expertise, including his background as a business advisor to pharmaceutical and biotechnology companies, provides him with the qualifications and skills to serve as a director.

Class II Directors

Stephen J. Hoffman, Ph.D., M.D., age 59, has served as our director since February 2010. Dr. Hoffman has been a Senior Advisor to PDL BioPharma, Inc. since February 2014. Prior to that he served as a managing director at Skyline Ventures, a venture capital firm, from May 2007 until February 2014. From January 2003 to March 2007, Dr. Hoffman was a general partner at TVM Capital, a venture capital firm. Prior to that, he served as President, Chief Executive Officer and a director of Allos Therapeutics, a biopharmaceutical company, from 1994 to 2002. From 1990 to 1994, Dr. Hoffman completed a fellowship in clinical oncology and a residency/fellowship in dermatology, both at the University of Colorado. Dr. Hoffman was the scientific founder of Somatogen Inc., a biotechnology company that was acquired by Baxter International, Inc., a global medical products and services company, in 1998, where he held the position of Vice President of Science and Technology from 1987 until 1990. He serves on the board of directors of several biopharmaceutical companies: Allos Therapeutics, Inc., Concert Pharmaceuticals, Inc., Collegium Pharmaceuticals, Inc., Dicerna Pharmaceuticals, Inc., Genocea Biosciences, Inc., and Proteon Therapeutics, Inc. Previously, Dr. Hoffman served on the board of directors of Sirtris Pharmaceuticals, Inc., a pharmaceutical company that was acquired by GlaxoSmithKline, a global pharmaceutical company, in 2008. Dr. Hoffman holds a Ph.D. in bio-organic chemistry from Northwestern University and an M.D. from the University of Colorado School of Medicine. Dr. Hoffman's scientific, financial and business expertise, including his diversified background as an executive officer and investor in public pharmaceutical companies, provides him with the qualifications and skills to serve as a director.

Richard A. King, age 49, has served as our director and President and Chief Executive Officer since May 2010. From April 2009 until May 2010, Mr. King acted as an independent consultant to a number of private and public biotechnology and venture capital companies. From October 2008 to April 2009, Mr. King served as President and General Manager of Tercica, Inc., a biotechnology company that was acquired by Ipsen, SA in 2008, and from February 2008 to October 2008, Mr. King served as President and Chief Operating Officer of Tercica, Inc., and from February 2007 until February 2008, he served as Chief Operating Officer of Tercica, Inc. From January 2002 to October 2006, Mr. King served as Executive Vice President of Commercial Operations of Kos Pharmaceuticals, Inc., a pharmaceutical company that was acquired by Abbott Laboratories, a global, broad-based health care company, in 2006. From January 2000 to January 2002, Mr. King served as Senior Vice President of Commercial Operations at Solvay Pharmaceuticals, a pharmaceutical company that was acquired by Abbott Laboratories in 2009. From April 1992 to January 2000, Mr. King held various marketing positions at SmithKline Beecham Pharmaceuticals, now known as GlaxoSmithKline, a global pharmaceutical company. Mr. King holds a B.Sc. in Chemical Engineering from University of Surrey and an M.B.A. from Manchester Business School. Mr. King's extensive experience as an executive officer of public pharmaceutical companies and his knowledge of the day-to-day operations of our company provide him with the qualifications and skills to serve as a director.

Pamela P. Palmer, M.D., Ph.D., age 51, has served as our director and Chief Medical Officer since she co-founded the company in July 2005. Dr. Palmer has been on faculty at the University of California, San Francisco since 1996 and is currently a Clinical Professor of Anesthesia and Perioperative Care. Dr. Palmer was Director of UCSF PainCARE-Center for Advanced Research and Education from 2005 to 2009, and was Medical Director of the UCSF Pain Management Center from 1999 to 2005. Dr. Palmer has been a consultant of Omeros Corporation, a biopharmaceutical company, since she co-founded that company in 1994. Dr. Palmer holds an M.D. from Stanford University and a Ph.D. from the Stanford Department of Neuroscience. Dr. Palmer's extensive clinical and scientific experience in the treatment of acute and chronic pain as well as historical knowledge of our company provide her with the qualifications and skills to serve as a director.

Class III Directors

Howard B. Rosen, age 55, has served as our director since 2008. Since 2008, Mr. Rosen has served as a consultant to several companies in the biotechnology industry. He has also served as a lecturer at Stanford University in Chemical Engineering since 2008 and in Management since 2011. Mr. Rosen served as interim

President and Chief Executive Officer of Pearl Therapeutics, Inc., a company focused on developing combination therapies for the treatment of highly prevalent chronic respiratory diseases, from June 2010 to March 2011. From 2004 to 2008, Mr. Rosen was Vice President of Commercial Strategy at Gilead Sciences, Inc., a biopharmaceutical company. Mr. Rosen was President of ALZA Corporation, a pharmaceutical and medical systems company that merged with Johnson & Johnson, a global healthcare company, in 2001, from 2003 until 2004. Prior to that, from 1994 until 2003, Mr. Rosen held various positions at ALZA Corporation. Mr. Rosen is a member of the board of directors of Alcobra, Ltd., a public pharmaceutical company. Mr. Rosen is also a member of the board of directors of a number of private biotechnology companies as follows: PaxVax, Inc., Entrega, Inc., Kala Pharmaceuticals, Inc. and ALDEA Pharmaceuticals. Mr. Rosen holds a B.S. in Chemical Engineering from Stanford University, an M.S. in Chemical Engineering from the Massachusetts Institute of Technology and an M.B.A. from the Stanford Graduate School of Business. Mr. Rosen's experience in the biopharmaceutical industry, including his specific experience with commercialization of pharmaceutical products, provides him with the qualifications and skills to serve as a director.

Mark Wan, age 48, has served as our director since August 2006. Mr. Wan is a founding general partner of Three Arch Partners, a venture capital firm. Prior to co-founding Three Arch Partners in 1993, Mr. Wan was a general partner at Brentwood Associates, a private equity firm from 1987 until 1993. Since 1999, Mr. Wan has served on the board of directors of Epocrates, Inc., a company focused on providing mobile drug reference tools. Mr. Wan also serves on the board of directors of numerous private companies. Mr. Wan holds a B.S. in Engineering from Yale University and an M.B.A. from the Stanford Graduate School of Business. Mr. Wan's financial experience and extensive knowledge of our company provides him with the qualifications and skills to serve as a director.

Executive Officers of the Registrant

The following table sets forth certain information concerning our executive officers as of January 31, 2014:

Name	Age	Position
Richard A. King	49	Director, President and Chief Executive Officer
James H. Welch	56	Chief Financial Officer
Pamela P. Palmer, M.D., Ph.D.	51	Director, Chief Medical Officer and Co-Founder
David H. Chung	47	Chief Commercial Officer
Lawrence G. Hamel	62	Chief Development Officer
Badri Dasu	50	Chief Engineering Officer

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

James H. Welch has served as our Chief Financial Officer since October 1, 2010. From June 2006 until September 2010, Mr. Welch served as Chief Financial Officer and Corporate Secretary for Cerimon Pharmaceuticals, a biopharmaceutical company. Mr. Welch served as Vice President, Chief Financial Officer and Corporate Secretary for Rigel Pharmaceuticals, Inc., a drug development company from October 2000 until May 2006, and as Vice President, Finance and Administration for Rigel Pharmaceuticals, Inc. from May 1999 until October 2000. From June 1998 until May 1999, Mr. Welch served as an independent consultant at various companies. Mr. Welch served as Chief Financial Officer of Biocircuits Corporation, a company focused on developing immunodiagnostic testing systems from February 1997 until June 1998, and from June 1992 until February 1997, he served as Corporate Controller of Biocircuits Corporation. Mr. Welch holds a B.A. in Business Administration from Whitworth College and an M.B.A. from Washington State University.

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

David H. Chung has served as our Chief Commercial Officer since September 2013. From August 2012 until June 2013, Mr. Chung has served as chief commercial officer at Conceptus, Inc., a women's, device-based, permanent birth control solution company. From January 2011 until July 2012, Mr. Chung served as president and chief executive officer of Mitralis, an early stage, transcatheter mitral valve repair company. Prior to Mitralis, Mr. Chung held the position of global vice president, commercial operations, heart valve therapy at Edwards Lifesciences/Baxter Healthcare, the culmination of 15 years at the company in various commercial roles of increasing responsibility. Prior to Baxter, Mr. Chung began his career at Pfizer in a sales capacity in both the medical device and pharmaceutical sales arenas. Mr. Chung holds a B.S. in general engineering from the United States Military Academy, West Point, N.Y.

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

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

Section 16(a) Beneficial Ownership Reporting Compliance

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

To our knowledge, based solely on a review of the copies of such reports furnished to us and written representations that no other reports were required, during the fiscal year ended December 31, 2013, our officers, directors and greater than ten percent beneficial owners complied with all applicable Section 16(a) filing requirements.

Certain Corporate Governance Matters

Code of Business Conduct and Ethics

The AcelRx Pharmaceuticals, Inc. Code of Business Conduct and Ethics applies to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is available on our website at *www.acelrx.com*. Stockholders may request a free copy of the Code of Business Conduct and Ethics

by submitting a written request to: AcelRx Pharmaceuticals, Inc., Attention: Investor Relations, 351 Galveston Drive, Redwood City, CA 94063. If we make any substantive amendments to the Code of Business Conduct and Ethics or grant any waiver from a provision of the Code of Business Conduct and Ethics to any executive officer or director, we will promptly disclose the nature of the amendment or waiver on our website.

Director Nominations

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

Audit Committee

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

Item 11. Executive Compensation

Summary Compensation Table

The following table sets forth certain summary information for the years indicated with respect to the compensation earned by our Chief Executive Officer, our Chief Financial Officer and each of our three other most highly compensated executive officers as of December 31, 2013. We refer to these individuals as our "named executive officers" elsewhere in this Form 10-K.

Summary Compensation Table

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($)[1]	Option Awards ($)[2]	Non-Equity Incentive Plan Compensation ($)[3]	Total ($)
Richard A. King	2013	475,000	—	—	1,871,040	277,875	2,623,915
President and Chief Executive Officer	2012	426,006	—	—	616,203	170,400	1,212,609
	2011	411,600	—	425,927	279,955	100,842	1,218,324
James H. Welch	2013	307,500	—	—	523,150	124,845	955,495
Chief Financial Officer	2012	299,000	—	—	170,561	95,232	564,793
	2011	290,000	—	—	60,750	67,425	418,175
Pamela P. Palmer, M.D., Ph.D.	2013	409,000	—	—	1,432,226	174,643	2,015,869
Chief Medical Officer	2012	396,550	—	—	544,991	134,034	1,075,575
	2011	385,000	—	233,199	243,000	89,513	950,712
David H. Chung[4]	2013	110,000	16,500	—	1,111,500	45,430	1,283,430
Chief Commercial Officer							
Badri Dasu	2013	301,000	—	—	484,556	128,527	914,083
Chief Engineering Officer	2012	278,000	—	—	120,600	93,964	492,564
	2011	270,500	—	51,305	127,575	59,645	509,025

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

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

(3) The dollar amounts reflect the cash awards made to the named executive officers under the Company's 2013, 2012 and 2011 Cash Bonus Plans.

(4) Mr. Chung's employment with the Company began in September 2013. Compensation reported is for a partial year of employment. Mr. Chung received a one-time sign-on bonus in the amount of $16,500. A partial living cost reimbursement of $5,000 has not been included in the table above, as the amounts below $10,000 are not required to be disclosed per the SEC regulations.

Employment Agreements and Arrangements

Executive Employment Agreements and Termination Benefits

Offer Letter Agreements

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

initial stock option grant. We amended and restated these offer letter agreements in December 2010, excluding the offer letter for David Chung, as he did not begin employment until September 2013, to clarify certain terms for compliance with tax laws, to specify the terms of the option to be granted to Mr. King upon achievement of certain milestones and to provide additional change of control severance benefits to Mr. Welch and Dr. Palmer.

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

In August 2013, we entered in an offer letter agreement with Mr. Chung, which provides for his initial annual salary of $330,000, eligibility for an annual target bonus of up to 35% of his annual salary, based upon achievement of a series of personal and company objectives, as determined by the Compensation Committee of the Board of Directors on an annual basis. The offer letter also provides for a one-time sign on bonus of $16,500, and a partial living cost reimbursement of $1,250 per month for a maximum of two years, and an initial stock option grant of 150,000 shares of our common stock, vesting with respect to 25% of the shares subject to this grant on September 2, 2014, with the remaining shares vesting on an equal monthly basis over the following 36 months, subject to his continued employment.

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

Long-Term Equity Incentive Award Vesting Acceleration

Under Mr. King's, Mr. Dasu's, Mr. Welch's and Dr. Palmer's respective offer letter agreements, they are entitled to full "double-trigger" stock option and RSU vesting acceleration benefits (for all currently outstanding stock options and RSUs and any stock options and RSUs that may be granted in the future) in the event their service with us is terminated by us without cause or, in the case of acceleration of stock options only for Messrs. Welch, Dasu and Dr. Palmer, in a manner that constitutes an involuntary termination, or, in the case of acceleration of RSUs only for Messrs. Welch, and Dasu and Dr. Palmer and for acceleration of stock options and RSUs for Mr. King, such executive resigns for good reason, in each case within 18 months following a change in control, subject to signing an effective release of claims, and in the case of acceleration of stock options for Mr. King and Dr. Palmer, resignation from our board of directors if so requested by the board of directors. Under Mr. Chung's offer letter, he is entitled to full "double-trigger" stock option vesting acceleration benefits with respect to his currently outstanding stock option in the event his service with us is terminated by us without cause or in a manner that constitutes an involuntary termination, in each case within 12 months following a change in control.

Cash Bonus Plan

Our annual Cash Bonus Plan is designed to reward executive officers and other employees for attaining our corporate performance objectives, as well as to reward them for their individual contributions to the achievement of those objectives. Target bonus levels under the annual Bonus Plan are assigned based on various categories of employees. The actual bonus awarded in any year, if any, may be more or less than the target, depending primarily on the achievement of our corporate objectives, and an individual employee's achievement of his or her

objectives. Whether or not a bonus is paid for any year is within the discretion of our Compensation Committee, and our Compensation Committee has the discretion to award bonuses even if the applicable performance criteria set forth under the annual Bonus Plan have not been met or to award a bonus based on other criteria.

2013 Cash Bonus Plan

Target bonuses for our named executive officers under the 2013 Cash Bonus Plan, or the 2013 Bonus Plan, ranged from 35% to 45% of such executive's 2013 base salary based on market data established for each executive position. The amount of cash bonus, if any, for each named executive officer was based on both the named executive officer achieving his or her individual performance goals and on our attainment of the 2013 corporate objectives approved by our board of directors. Our 2013 corporate objectives were primarily related to product development, business development, clinical trial milestones and financial objectives. The target bonuses for our named executive officers for 2013 were as follows:

Named Executive Officer	Target Bonus (as a percentage of FY 2013 Base Salary)
Richard A. King	45%
James H. Welch	35%
Pamela P. Palmer, M.D., Ph.D.	35%
David H. Chung	35%
Badri Dasu	35%

Mr. King's cash bonus under the 2013 Bonus Plan was based 100% on the achievement of the 2013 corporate objectives. The cash bonus for all other named executive officers was based 40% on the achievement of his or her individual performance goals, as determined by our board of directors, and 60% on the achievement of the 2013 corporate objectives. The named executive officers' actual bonuses could have exceeded 100% of target in the event performance exceeded the predetermined target goals.

In February 2014, the Compensation Committee determined, and the Board of Directors confirmed, that the Company had achieved a 130% attainment level of the 2013 corporate objectives. In addition to achieving the target goals, the Company achieved certain other predetermined goals related to positive clinical data for Zalviso and ARX-04, commercial development plans for Zalviso, equity financing and the collaboration agreement with Grünenthal, resulting in 130% attainment of the 2013 corporate objectives. At that same time, the Board of Directors also confirmed the attainment levels of each named executive officers' individual performance goals for 2013. Pursuant to the 2013 Bonus Plan, the Board of Directors awarded cash bonuses to our executives based on the confirmed attainment level of the 2013 corporate objectives and the confirmed attainment level of their respective individual performance goals for 2013. All bonus amounts were paid on February 15, 2014.

The table below sets forth the target and actual non-equity incentive plan awards for our named executive officers for fiscal 2013 performance:

Name	Target Award	Actual Award
Richard A. King	$ 213,750	$277,875
James H. Welch	$107,625	$ 124,845
Pamela P. Palmer, M.D., Ph.D.	$ 143,150	$ 174,643
David H. Chung[1]	$ 38,500	$ 45,430
Badri Dasu	$ 105,350	$128,527

(1) Target Award prorated for David Chung's employment start date of September 2013.

2012 Cash Bonus Plan

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

Named Executive Officer	Target Bonus (as a percentage of FY 2012 Base Salary)
Richard A. King	40%
James H. Welch	32.5%
Pamela P. Palmer, M.D., Ph.D.	32.5%
Badri Dasu	32.5%

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

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

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

Name	Target Award	Actual Award
Richard A. King	$ 170,400	$170,400
James H. Welch	$ 97,175	$95,232
Pamela P. Palmer, M.D., Ph.D.	$128,879	$134,034
Badri Dasu	$ 90,350	$93,964

2011 Cash Bonus Plan

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

Named Executive Officer	Target Bonus (as a percentage of FY 2011 Base Salary)
Richard A. King	35%
James H. Welch	30%
Pamela P. Palmer, M.D., Ph.D.	30%
Badri Dasu	30%

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

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

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

Name	Target Award	Actual Award
Richard A. King	$ 144,060	$100,842
James H. Welch	$ 87,000	$ 67,425
Pamela P. Palmer, M.D., Ph.D.	$115,500	$ 89,513
Badri Dasu	$ 81,150	$59,645

Outstanding Equity Awards at December 31, 2013

The following table presents information regarding outstanding equity awards held by our named executive officers as of December 31, 2013.

Outstanding Equity Awards at December 31, 2013

	Option Awards				Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)[1]	Market Value of Shares or Units of Stock That Have Not Vested ($)[2]
Richard A. King	—	507,057[3]	5.31	02/05/2023		
	120,181	142,033[4]	3.39	02/13/2022		
	79,205	36,003[6]	3.45	03/02/2021		
	28,538[7]	—	2.56[8]	06/15/2020		
	392,399	35,672[9]	2.56[8]	06/15/2020		
					30,865	349,083
James H. Welch	—	141,775[3]	5.31	02/05/2023		
	33,265	39,314[5]	3.39	02/07/2022		
	17,187	7,813[6]	3.45	03/02/2021		
	101,562	23,438[10]	5.32	11/04/2020		
					—	—
Pamela P. Palmer, M.D., Ph.D.	—	388,137[3]	5.31	02/05/2023		
	106,292	125,619[5]	3.39	02/07/2022		
	68,749	31,251[6]	3.45	03/02/2021		
	250,000	—	2.56[8]	06/15/2020		
	37,500	—	5.52	03/25/2019		
	37,500	—	4.00	08/14/2018		
	25,000	—	1.32	04/03/2017		
					16,899	191,128
David H. Chung	—	150,000[11]	10.55	09/02/2023		
Badri Dasu	—	131,316[3]	5.31	02/05/2023		
	23,521	27,798[5]	3.39	02/07/2022		
	36,093	16,407[6]	3.45	03/02/2021		
	30,000	—	2.56[8]	06/15/2020		
	25,000	—	2.56[8]	06/15/2020		
	6,250	—	5.52	03/25/2019		
	37,500	—	1.20	10/25/2017		
					3,718	42,051

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

(2) The dollar amounts in this column represent the aggregate grant date fair value of all restricted stock unit awards granted that have not vested. The estimated fair value of restricted stock unit awards is calculated based on the market price of our common stock as of December 31, 2013, which is $11.31.

(3) The shares subject to this stock option vested as to 1/4 of the shares on February 5, 2014, with the remaining shares vesting on an equal monthly basis over the following 36 months.

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

(5) The shares subject to this stock option vested as to 1/4 of the shares on February 7, 2013, with the remaining shares vesting on an equal monthly basis over the following 36 months.

(6) The shares subject to this stock option vested as to 1/4 of the shares on March 2, 2012, with the remaining shares vesting on an equal monthly basis over the following 36 months.

(7) The shares subject to this stock option were fully vested as of the June 15, 2010 grant date.
(8) The dollar amounts reflect the increase in the exercise price of the options, effective December 27, 2010, we granted to our named executive officers on June 15, 2010 from an original estimated fair value of $1.20 to a revised estimate of fair value of $2.56 in consideration of IRC Section 409a.
(9) The shares subject to this stock option vested as to 28,538 shares on June 15, 2010, and another 85,614 shares vested on March 3, 2011, with the remaining shares vesting on an equal monthly basis over the following 36 months.
(10) The shares subject to this stock option will vest as to 1/4 of the shares on September 30, 2011, with the remaining shares vesting on an equal monthly basis over the following 36 months.
(11) The shares subject to this stock option vested as to 1/4 of the shares on September 2, 2014, with the remaining shares vesting on an equal monthly basis over the following 36 months.

Employee Benefits and Stock Plans

2011 Equity Incentive Plan

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

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

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

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

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

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

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

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

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

2011 Employee Stock Purchase Plan

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

2006 Stock Plan

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

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

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

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

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

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

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

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

401(k) Plan

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

Pension Benefits

We do not maintain any pension or retirement plans.

Nonqualified Deferred Compensation

We do not maintain any nonqualified deferred compensation plans.

Director Compensation

Non-Employee Director Compensation

Cash Compensation Arrangements

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

- the board chair receives an additional annual retainer of $20,000;
- the audit committee chair receives an additional annual retainer of $15,000;
- the compensation committee chair receives an additional annual retainer of $7,500;
- the nominating and corporate governance committee chair receives an additional annual retainer of $6,000;
- an audit committee member receives an additional annual retainer of $7,500;
- a compensation committee member receives an additional annual retainer of $3,750; and
- a nominating and corporate governance committee member receives an additional retainer of $3,000

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

Equity Compensation Arrangements

Our non-employee director compensation policy provides for automatic grants of stock options to our non-employee directors under our 2011 Incentive Plan. Upon election or appointment to our board, each non-employee director will receive an initial grant of a stock option to purchase 15,000 shares of our common stock, which will vest as to 1/36th of the shares subject to the option on an equal monthly basis over a three-year period. Additionally, on the date of each annual meeting of stockholders, each non-employee director who is then serving as a director or who is elected to our board of directors on the date of such annual meeting was eligible to receive a grant of a stock option to purchase 12,500 shares of our common stock, prior to our amended director compensation policy, effective January 1, 2013, which vest as to 1/24th of the shares subject to the option on an equal monthly basis over a two-year period. Beginning with our 2013 annual meeting, each non-employee director who is then serving as a director or who is elected to our board of directors on the date of such annual meeting was eligible to receive a grant of a stock option to purchase 15,000 shares of our common stock, which will vest as to 1/24 th of the shares subject to the option on an equal monthly basis over a two-year period. All these options will be granted with an exercise price equal to the fair market value of our common stock on the date of the grant, and shall be entitled to full vesting acceleration as of immediately prior to the effective date of certain change in control transactions involving us, such as our liquidation or a dissolution of or an event that results in a material change in the ownership of our company. For a description of the terms of the 2011 Incentive Plan, see "—Employment Agreements and Arrangements—Employee Benefits and Stock Plans—2011 Equity Incentive Plan."

Director Compensation Table

The following table sets forth certain summary information for the year ended December 31, 2013 with respect to the compensation of our non-employee directors. Neither Mr. King nor Dr. Palmer, each of whom are executive officers, received or receives any additional compensation for serving on our board of directors or its committees.

2013 Director Compensation Table

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)[1][2]	Total ($)
Adrian Adams	59,148	158,972	218,120
Howard B. Rosen	49,778	104,007	153,785
Stephen J. Hoffman Ph.D., M.D.	50,500	104,007	154,507
Richard Afable, M.D.	2,494	83,247	85,741
Mark Wan	50,688	104,007	154,695
Mark G. Edwards	55,000	104,007	159,007
Guy P. Nohra	44,069	104,007	148,076
Thomas A. Schreck	4,556	—	4,556

(1) The dollar amount in this column represents the grant date fair value of the stock option award granted to each of the directors on July 24, 2012, the date of our Annual Meeting of Shareholders. This amount has been calculated in accordance with ASC 718 using the Black-Scholes option-pricing model and excluding the effect of estimated forfeitures. For a discussion of valuation assumptions, see Note 1 to our financial statements and the discussion under "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Estimates—Share-Based Compensation" included elsewhere in this Form 10-K. These amounts do not necessarily correspond to the actual value that may be recognized from the option award.

(2) As of December 31, 2013, the following directors held options to purchase the following number of shares of the Company's common stock: Adrian Adams, 30,000, Mr. Rosen, 66,250; Dr. Hoffman, 27,500; Dr. Afable, 15,000; Mr. Nohra, 9,583; Mr. Wan, 27,500; Mr. Edwards, 42,500.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Equity Compensation Plan Information

The following table provides certain information with respect to our equity compensation plans in effect as of December 31, 2013.

Plan Category	Column A: Number of securities to be issued upon exercise of outstanding options, warrants and rights (2)	Column B: Weighted-average exercise price of outstanding options, warrants and rights (3)	Column C: Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column A) (4)(5)
Equity compensation plans approved by security holders[1]	4,975,170	$ 4.29	743,479
Equity compensation plans not approved by security holders	—	$ —	—
Total	4,975,170		743,479

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

(2) Includes 65,765 shares subject to outstanding restricted stock units that will entitle the holder to one share of common stock for each unit that vests over the holder's period of continued service with us.

(3) The calculation does not take into account the 65,765 shares of common stock subject to outstanding restricted stock units. Such shares will be issued at the time the restricted stock units vest, without any cash consideration payable for those shares.

(4) Consists of shares available for future issuance under the 2011 Incentive Plan, including shares that were previously available for future issuance under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for our IPO, and the ESPP. As of December 31, 2013, 273,290 shares of common stock were available for issuance under the 2011 Incentive Plan and 470,189 shares of common stock were available for issuance under the ESPP.

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

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information regarding the ownership of our common stock as of January 31, 2014 by: (i) each director; (ii) each named executive officer; (iii) all of our executive officers and directors as a group; and (iv) all those known by us to be beneficial owners of more than five percent of our common stock.

	Beneficial Ownership[1]	
Name of Beneficial Owner	**Number of Shares**	**% of Total**
5% Stockholders:		
Funds affiliated with Three Arch Entities[2]	10,623,269	24.5%
Fund affiliated with Skyline Venture Partners[3]	4,428,161	10.2%
Fund affiliated with Alta Partners[4]	2,507,974	5.8%
Fund affiliated with Perceptive Advisors LLC[5]	6,574,060	15.2%
Named Executive Officers and Directors:		
Richard A. King[6]	949,159	2.2%
James H. Welch[7]	228,438	0.5%
Pamela P. Palmer, M.D., Ph.D.[8]	988,505	2.3%
Badri Dasu[9]	220,327	0.5%
David H. Chung	—	— %
Adrian Adams[10]	84,166	0.2%
Mark Wan[11]	10,637,435	24.5%
Stephen J. Hoffman, Ph.D., M.D.[12]	4,442,327	10.2%
Richard Afable, M.D.[13]	1,250	0%
Howard B. Rosen[14]	57,310	0.1%
Mark G. Edwards[15]	86,666	0.2%
All executive officers and directors as a group (12 persons)[16]	17,932,757	39.1%

(1) This table is based upon information supplied by officers, directors and principal stockholders. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned. Applicable percentages are based on 43,152,190 shares outstanding on January 31, 2013, adjusted as required by rules promulgated by the SEC. The number of shares beneficially owned includes shares of common stock issuable pursuant to the exercise of stock options and warrants that are exercisable within 60 days of January 31, 2014, and RSUs which have or are scheduled to vest within 60 days of January 31, 2014. Shares issuable pursuant to the exercise of stock options and warrants that are exercisable within 60 days of January 31, 2014 and RSUs which have or are scheduled to vest within 60 days of January 31, 2014 are deemed to be outstanding and beneficially owned by the person to whom such shares are issuable for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

(2) Includes 199,174 shares held by Three Arch Associates III, L.P., 139,621 shares held by Three Arch Associates IV, L.P., 3,704,712 shares held by Three Arch Partners III, L.P. and 6,323,534 shares held by Three Arch Partners IV, L.P. The number also includes

256,228 shares of common stock issuable pursuant to the exercise of stock warrants that are exercisable within 60 days of January 31, 2014. The voting and dispositive decisions with respect to the shares held by Three Arch Associates III, L.P. and Three Arch Partners III, L.P., are made by the following Managing Members of their general partner, Three Arch Management III, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The voting and dispositive decisions with respect to the shares held by Three Arch Partners IV, L.P. and Three Arch Associates IV, L.P. are made by the following Managing Members of their general partner, Three Arch Management IV, L.L.C.: Mark Wan and Wilfred Jaeger, each of whom disclaims beneficial ownership of such shares. The address for the funds affiliated with Three Arch Partners is 3200 Alpine Road, Portola Valley, CA 94028.

(3) Includes 4,171,933 shares held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. and 256,228 shares of common stock issuable pursuant to the exercise of stock warrants that are exercisable within 60 days of January 31, 2014. John G. Freund and Yasunori Kaneko are the Managing Members of Skyline Venture Management IV, LLC, which is the general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P., and as such Drs. Freund and Kaneko may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. In addition, Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Each of Drs. Freund, Kaneko and Hoffman disclaims beneficial ownership of such shares. The address for the funds affiliated with Skyline Venture Partners is 525 University Avenue, Ste. 610, Palo Alto, CA 94301.

(4) The 2,507,974 shares are held by ACP IV, L.P., or ACPIV. ACMP IV, LLC, or ACMPIV, is the general partner of ACPIV. Dan Janney, David Mack and Guy Nohra are directors of ACMPIV and they exercise shared voting and investment power with respect to the securities held by ACPIV. Each of Messrs. Janney, Mack and Nohra disclaims beneficial ownership of such securities, except to the extent of their pecuniary interest therein. The address for funds affiliated with Alta Partners is One Embarcadero Center, Suite 3700, San Francisco, CA 94111.

(5) The indicated ownership is based on a Schedule 13G/A filed with the SEC by the reporting persons on February 14, 2014, reporting beneficial ownership as of December 31, 2013. According to the Schedule 13G, the reporting persons beneficially own a total of 6,574,060 shares of Common Stock held by a private investment fund to which Perceptive Advisors LLC serves as the investment manager. Mr. Edelman is the managing member of Perceptive Advisors LLC. The Schedule 13G filed by the reporting persons provides information only as of December 31, 2013, and, consequently, the beneficial ownership of the above-mentioned reporting persons may have changed between December 31, 2013 and January 31, 2014.

(6) Includes 807,993 shares issuable pursuant to stock options exercisable, and 123,457 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2014.

(7) Includes 204,323 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014.

(8) Includes 650,906 shares issuable pursuant to stock options exercisable, and 67,593 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2014.

(9) Includes 200,417 shares issuable pursuant to stock options exercisable, and 10,643 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2014.

(10) Includes 9,166 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014.

(11) Includes 14,166 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014. Mr. Wan, one of our directors, is a managing partner of Three Arch Management III, L.L.C. and Three Arch Management IV, L.L.C., and in such capacities he may be deemed to beneficially own the shares owned by the funds affiliated with Three Arch Partners. Mr. Wan disclaims beneficial ownership of these shares. The address of Mr. Wan is c/o Three Arch Partners, 3200 Alpine Road, Portola Valley, CA 94028.

(12) Includes 14,166 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014. Dr. Hoffman, one of our directors, is a Managing Director of Skyline Ventures and as such may be deemed to share voting and dispositive power with respect to all shares of common stock held by Skyline Venture Partners Qualified Purchasers Fund IV, L.P. Dr. Hoffman disclaims beneficial ownership of such shares. The address for Dr. Hoffman is c/o Skyline Ventures, 525 University Avenue, Suite 610, Palo Alto, CA 94301.

(13) Includes 1,250 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014.

(14) Represents 52,916 shares issuable pursuant to stock options exercisable, and 4,394 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2014.

(15) Includes 26,666 shares issuable pursuant to stock options exercisable within 60 days of January 31, 2014.

(17) Includes 2,147,810 shares issuable pursuant to stock options exercisable, 512,456 shares issuable pursuant to warrants exercisable and 218,357 RSUs which have vested or are scheduled to vest, within 60 days of January 31, 2014.

Item 13. Certain Relationships and Related Transactions and Director Independence

Policy and Procedures for Review of Related Party Transactions

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

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

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

Certain Transactions With or Involving Related Persons

The following is a summary of transactions since January 1, 2012 to which we have been a party in which the amount involved exceeded the lesser of $120,000 or one percent of the average of our total assets at fiscal years ended 2012 and 2013 and in which any of our executive officers, directors or holders of more than 5% of our capital stock, or any member of the immediate family of any of the foregoing persons, had or will have a direct or indirect material interest, other than compensation arrangements which are described under "Item 11. Executive Compensation" appearing elsewhere in this Form 10-K.

2012 Private Placement

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

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

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

2012 Public Offering

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

Name	Common Stock Purchased in Public Offering	Aggregate Purchase Price
Funds affiliated with Three Arch Partners (1)	2,416,918	$ 8,000,000
Price per share	$ 3.31	

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

Investors' Rights Agreements

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

Indemnification Agreements

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

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

Other Transactions

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

Director Independence

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

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

Item 14. Principal Accounting Fees and Services

Independent Registered Public Accounting Firm Fees and Services

In connection with the audit of our 2013 financial statements, we entered into an engagement agreement with Ernst & Young LLP which sets forth the terms by which Ernst & Young LLP will perform audit and interim services for us. That agreement is subject to alternative dispute resolution procedures and an exclusion of punitive damages.

The following table represents aggregate fees for the fiscal years ended December 31, 2013 and 2012 for professional services rendered by Ernst & Young LLP, our independent registered public accounting firm:

	Fiscal Year Ended	
	2013	2012
Audit Fees	$843,875	$616,375
Audit-Related Fees	—	—
Tax Fees	—	—
All Other Fees	—	—
Total Fees	$843,875	$616,375

Audit Fees: Consists of fees for professional services rendered for the audit of our financial statements and internal controls over financial reporting, review of interim financial statements and fees for assistance with registration statements filed with the SEC, comfort letters and services that are normally provided by Ernst & Young LLP in connection with statutory and regulatory filings or engagements. Fees for the 2013 audit and 2013 quarterly reviews of financial statements were $795,000. Fees for the 2012 audit and the 2012 quarterly reviews of financial statements were $435,000.

Pre-Approval Policies and Procedures

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

PART IV

Item 15. Exhibits, Financial Statement Schedules

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

1. Financial Statements:

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

2. Financial Statement Schedules:

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

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

SIGNATURES

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

Date: March 17, 2014

AcelRx Pharmaceuticals, Inc.
(Registrant)

/s/ Richard A. King
Richard A. King
Chief Executive Officer and Director
(Principal Executive Officer)

/s/ James H. Welch
James H. Welch
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ Richard A. King **Richard A. King**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 17, 2014
/s/ James H. Welch **James H. Welch**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 17, 2014
/s/ Adrian Adams **Adrian Adams**	Chairman	March 17, 2014
/s/ Pamela P. Palmer, M.D., Ph.D. **Pamela P. Palmer, M.D., Ph.D.**	Chief Medical Officer and Director	March 17, 2014
/s/ Mark G. Edwards **Mark G. Edwards**	Director	March 17, 2014
/s/ Stephen J. Hoffman, Ph.D., M.D. **Stephen J. Hoffman, Ph.D., M.D.**	Director	March 17, 2014

Signature	Title	Date
/s/ Richard Afable, M.D. **Richard Afable, M.D.**	Director	March 17, 2014
/s/ Howard B. Rosen **Howard B. Rosen**	Director	March 17, 2014
/s/ Mark Wan **Mark Wan**	Director	March 17, 2014

ACELRX PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
AcelRx Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of AcelRx Pharmaceuticals, Inc. as of December 31, 2013 and 2012, and the related statements of comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of AcelRx Pharmaceuticals, Inc. at December 31, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013 in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of AcelRx Pharmaceuticals, Inc. internal control over financial reporting as of December 31, 2013, based on the criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 Framework) and our report dated March 17, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Redwood City, California
March 17, 2014

AcelRx Pharmaceuticals, Inc.

Balance Sheets
(in thousands, except share data)

	December 31, 2013	December 31, 2012
Assets		
Current Assets:		
Cash and cash equivalents	$ 88,401	$ 47,932
Short-term investments	15,262	11,831
Prepaid expenses and other current assets	897	2,003
Total current assets	104,560	61,766
Property and equipment, net	5,179	2,485
Restricted cash	250	205
Other assets	42	64
Total Assets	$ 110,031	$ 64,520
Liabilities and Stockholders' Equity		
Current Liabilities:		
Accounts payable	$ 2,341	$ 2,235
Accrued liabilities	3,904	4,653
Deferred revenue, current portion	623	—
Long-term debt, current portion	—	7,443
Total current liabilities	6,868	14,331
Deferred rent	188	312
Long-term debt, net of current portion	14,364	8,530
Deferred revenue	2,007	—
Contingent put option liability	334	82
Warrant liability	13,111	7,418
Total liabilities	36,872	30,673
Stockholders' Equity:		
Common stock, $0.001 par value—100,000,000 shares authorized as of December 31, 2013 and 2012; 43,050,580 and 37,055,027 shares issued and outstanding as of December 31, 2013 and 2012	43	37
Additional paid-in capital	218,568	155,836
Accumulated deficit	(145,453)	(122,027)
Accumulated other comprehensive income	1	1
Total stockholders' equity	73,159	33,847
Total Liabilities and Stockholders' Equity	$ 110,031	$ 64,520

See notes to financial statements.

AcelRx Pharmaceuticals, Inc.

Statements of Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2013	2012	2011
Revenue:			
Collaboration agreement	$ 27,370	$ —	$ —
Research grant	2,132	2,394	1,072
Total revenue	29,502	2,394	1,072
Operating expenses:			
Research and development	26,292	24,908	13,624
General and administrative	9,877	7,199	6,800
Total operating expenses	36,169	32,107	20,424
Loss from operations	(6,667)	(29,713)	(19,352)
Interest expense	(1,518)	(2,283)	(2,309)
Interest income and other income (expense), net	(15,241)	(1,367)	1,560
Net loss	(23,426)	(33,363)	(20,101)
Other comprehensive loss:			
Unrealized gains on available for sale securities	—	1	—
Comprehensive loss	$ (23,426)	$ (33,362)	$ (20,101)
Net loss per share of common stock, basic and diluted	$ (0.59)	$ (1.51)	$ (1.16)
Shares used in computing net loss per share of common stock, basic and diluted	39,746,678	22,124,637	17,344,727

See notes to financial statements.

AcelRx Pharmaceuticals, Inc.

Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Other Comprehensive Income (loss)	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2010	7,151,802	55,941	674,353	3	2,668	(68,563)	—	(65,892)
Conversion of convertible preferred stock to common stock	(7,151,802)	(55,941)	8,555,713	8	55,933	—	—	55,941
Conversion of Bridge Note and warrants to common stock	—	—	2,141,684	2	9,579	—	—	9,824
Issuance of Warrants	—	—	—	—	967	—	—	967
Stock-based compensation	—	—	—	—	1,833	—	—	1,833
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	—	—	147,792	1	60	—	—	61
Issuance of common stock upon ESPP purchase	—	—	48,236	—	139	—	—	139
Issuance of common stock upon IPO, net of offering-related costs of $5.1 million	—	—	8,000,000	8	34,931	—	—	34,939
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	(20,101)	—	(20,101)
Balance as of December 31, 2011	—	—	19,567,778	22	106,110	(88,664)	—	17,468
Issuance of Warrants	—	—	—	—		—	—	
Stock-based compensation	—	—	—	—	2,150	—	—	2,150
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	—	—	122,108	—	80	—	—	80
Issuance of common stock upon ESPP purchase	—	—	67,804	—	169	—	—	169
Issuance of common stock upon private placement offering, net of offering-related costs of $0.9 million	—	—	2,922,337	1	3,245	—	—	3,246
Issuance of common stock upon underwritten public offering, net of offering-related costs of $3.5 million	—	—	14,375,000	14	44,082	—	—	44,096
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	1	1
Net loss	—	—	—	—	—	(33,363)	—	(33,363)
Balance as of December 31, 2012	—	—	37,055,027	$ 37	$155,836	$(122,027)	1	$ 33,847

AcelRx Pharmaceuticals, Inc.

Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Convertible Preferred Stock		Common Stock					
	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Deficit	Other Comprehensive Income (loss)	Total Stockholders' Equity (Deficit)
Balance as of December 31, 2012	—	—	37,055,027	$ 37	$155,836	$(122,027)	1	$ 33,847
Issuance of Warrants	—	—	—	—	1,130	—	—	1,130
Stock-based compensation	—	—	—	—	3,479	—	—	3,479
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	—	—	520,365	1	1,276	—	—	1,277
Issuance of common stock upon exercise of stock warrants	—	—	1,050,062	1	8,689	—	—	8,690
Issuance of common stock upon ESPP purchase	—	—	55,126	—	219	—	—	219
Issuance of common stock upon underwritten public offering, net of offering-related costs of $3.0 million	—	—	4,370,000	4	47,939	—	—	47,943
Change in unrealized gains and losses on investments, net of taxes	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	(23,426)	—	(23,426)
Balance as of December 31, 2013	—	—	43,050,580	$ 43	$218,568	$(145,453)	1	$ 73,159

See notes to financial statements.

AcelRx Pharmaceuticals, Inc.

Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2013	2012	2011
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (23,426)	$ (33,363)	$ (20,101)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	593	605	513
Amortization of premium/discount on investments, net	202	380	195
Interest expense related to debt financing	442	647	1,619
Stock-based compensation	3,479	2,150	1,833
Revaluation of convertible preferred stock warrant, call option, put option and PIPE warrant liabilities	14,071	1,439	(1,512)
Loss on extinguishment of debt	1,202	—	—
Other	—	43	—
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	1,132	429	(434)
Restricted cash	(45)	—	—
Accounts payable	106	705	987
Accrued liabilities	(760)	2,029	1,788
Deferred revenue	2,630	—	—
Deferred rent	(113)	354	(175)
Net cash used in operating activities	(487)	(24,582)	(15,287)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property and equipment	(3,287)	(826)	(2,019)
Purchase of investments	(28,009)	(27,167)	(39,367)
Proceeds from sales of investments	—	—	2,082
Proceeds from maturities of investments	24,376	42,948	9,725
Net cash provided by (used in) investing activities	(6,920)	14,955	(29,579)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock in equity offerings, net of offering costs	47,943	53,174	34,939
Proceeds from the issuance of long-term debt	14,958	—	19,762
Payment of long-term debt	(16,345)	(3,655)	(5,297)
Extinguishment of debt	(437)	—	—
Net proceeds from issuance of common stock through equity plans and exercise of warrants	1,757	246	201
Net cash provided by financing activities	47,876	49,765	49,605
NET INCREASE IN CASH AND CASH EQUIVALENTS	40,469	40,138	4,739
CASH AND CASH EQUIVALENTS—Beginning of period	47,932	7,794	3,055
CASH AND CASH EQUIVALENTS—End of period	$ 88,401	$ 47,932	$ 7,794
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for interest	$ 1,105	$ 1,632	$ 1,162
NONCASH INVESTING AND FINANCING ACTIVITIES:			
Conversion of convertible promissory notes into common stock	$ —	$ —	$ 8,137
Issuance of common stock upon cashless exercise of warrants	$ 8,428	$ —	$ 536
Reclassification of warrant liability and call option liability to equity	$ —	$ —	$ 906
Issuance of warrants for common stock	$ 1,130	$ 5,828	$ 967
Contingent put option liability	$ 334	$ —	$ 232
Purchases of property and equipment in Accrued Liabilities	$ 725	$ —	$ —

See notes to financial statements.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

1. Organization and Summary of Significant Accounting Policies

The Company

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

AcelRx is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. AcelRx intends to commercialize its product candidates in the United States and license the development and commercialization rights to its product candidates for sale outside of the United States through strategic partnerships and collaborations. The Company's lead product candidate, Zalviso ™, formerly known as the Sufentanil NanoTab PCA System, or ARX-01, is currently under review by the FDA for marketing approval, and is designed to improve the management of moderate-to-severe acute pain in patients in the hospital setting. In addition, in December 2013, the Company entered into a collaboration agreement with Grünenthal for the commercialization of Zalviso in Europe and Australia.

The Company has incurred recurring operating losses and negative cash flows from operating activities since inception and expects to continue to incur negative cash flows until its product candidates are approved for marketing in the United States and other countries, in which it has and intends to license its products, which may never occur. In previous years, prior to the completion of the clinical development program for Zalviso and the commercial collaboration of Zalviso, AcelRx was considered a development stage company.

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

Basis of Presentation

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

Concentration of Risk

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

Cash, Cash Equivalents and Marketable Securities

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

All marketable securities are classified as available-for-sale and consist of U.S. Treasury and U.S. government sponsored enterprise debt securities. These securities are carried at estimated fair value, which is based on quoted

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

Property and Equipment

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

Impairment of Long-Lived Assets

The Company periodically assesses the impairment of long-lived assets and, if indicators of asset impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through an analysis of the undiscounted future expected operating cash flows. If impairment is indicated, the Company records the amount of such impairment for the excess of the carrying value of the asset over its estimated fair value. For example, purchased equipment and manufacturing-related facility improvements the Company has made at Patheon's facility in Ohio, are utilized for continued research and development, and potential commercial manufacturing of our product candidates. If the Company does not receive regulatory approval for our product candidates, the Company may determine that it is no longer probable that the Company will realize the future economic benefit associated with the costs of these assets through future manufacturing activities, and if so, the Company would record an impairment charge associated with these assets. As of December 31, 2013, the Company has not written down any of its long-lived assets as a result of impairment.

Restricted Cash

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

Revenue Recognition

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

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Collaboration Revenue

Collaboration revenue, which is earned under license agreements with third parties, may include nonrefundable license fees, cost reimbursements, research and development services, commercial manufacturing services, contingent development and commercial milestones and royalties.

In October 2009, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2009-13 *Revenue Arrangements with Multiple Deliverables,* or ASU 2009-13, which amended the accounting standards for certain multiple element revenue arrangements to:

- provide updated guidance on whether multiple elements exist, how the elements in an arrangement should be separated, and how the arrangement consideration should be allocated to the separate elements;
- require an entity to allocate arrangement consideration to each element based on a selling price hierarchy, also called the relative selling price method, where the selling price for an element is based on vendor-specific objective evidence ("VSOE"), if available; third-party evidence ("TPE"), if available and VSOE is not available; or the best estimate of selling price ("ESP"), if neither VSOE nor TPE is available; and
- eliminate the use of the residual method and require an entity to allocate arrangement consideration using the selling price hierarchy.

The revenue allocated to each element is then recognized when the basic revenue recognition criteria are met for that element.

VSOE is based on the price charged when the element is sold separately and is the price actually charged for that deliverable. Establishing VSOE may not be possible for the elements of a license arrangement because each arrangement is unique, an arrangement typically consists of multiple elements and AcelRx has limited history of entering into license arrangements.

When VSOE cannot be established, AcelRx attempts to establish the selling price of the elements of a license arrangement based on TPE. TPE is determined based on a competitor's price for similar deliverables when sold separately. AcelRx may not be able to determine TPE for license arrangements, as they contain a significant level of differentiation such that the comparable pricing of a competitor's license arrangement with similar functionality cannot be obtained, and AcelRx is therefore unable to reliably determine what a similar competitor's license arrangement's selling price would be on a standalone basis.

When AcelRx is unable to establish the selling price of an element using VSOE or TPE, ESP is utilized in the allocation of the elements of the arrangement. The objective of the ESP is to determine the price at which AcelRx would transact a sale if the element of the license arrangement were sold on a standalone basis.

The process for determining ESPs involves management's judgment. Our process considers multiple factors such as discounted cash flows, estimated direct expenses and other costs and available data, which may vary over time, depending upon the circumstances, and relate to each deliverable. If the estimated obligation period of one or more deliverables should change, the future amortization of the revenue would also change.

AcelRx recognizes a contingent milestone payment as revenue in its entirety upon our achievement of the milestone. A milestone is substantive if the consideration earned from the achievement of the milestone (i) is

consistent with performance required to achieve the milestone or the increase in value to the delivered item, (ii) relates solely to past performance and (iii) is reasonable relative to all of the other deliverables and payments within the arrangement.

Research Grant Revenue

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

Research and Development Expenses

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

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive income (loss) and is disclosed in the Statement of Comprehensive Loss. For the Company, other comprehensive income (loss) consists of changes in unrealized gains and losses on the Company's investments.

Fair Value of Financial Instruments

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

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

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

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

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

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Income Taxes

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

Stock-Based Compensation

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

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

Net Loss per Share of Common Stock

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

Segment Information

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

Recently Issued Accounting Pronouncements

In February 2013, Accounting Standards Codification Topic 220, Comprehensive Income was amended to require companies to report, in one place, information about reclassifications out of accumulated other comprehensive income. Accordingly, a company can present this information on the face of the financial statements, if certain requirements are met, or the information must be presented in the notes to the financial

statements. The Company adopted this guidance as of January 1, 2013, on a retrospective basis, and the items reclassified out of accumulated other comprehensive income are not material for all periods presented.

2. Investments and Fair Value Measurement

Investments

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

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

	As of December 31, 2013			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 88,390	$ —	$ —	$ 88,390
Money market funds	11	—	—	11
Total cash and cash equivalents	88,401	—	—	88,401
Marketable securities:				
U.S. government agency securities	15,261	1	—	15,262
Total marketable securities	15,261	1	—	15,262
Total cash, cash equivalents and investments	103,662	1	—	103,663

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

None of the available-for-sale securities held by the Company had material unrealized losses and there were no realized losses for the years ended December 31, 2013 and 2012. There were no other-than-temporary impairments for these securities as of December 31, 2013 or 2012.

As of December 31, 2013 and 2012, the contractual maturity of all investments held was less than one year.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Fair Value Measurement

The Company's financial instruments consist of Level I and Level II assets and Level III liabilities. Level I securities include highly liquid money market funds and are valued based on quoted market prices. For Level II instruments, the Company estimates fair value by utilizing third party pricing services in developing fair value measurements where fair value is based on valuation methodologies such as models using observable market inputs, including benchmark yields, reported trades, broker/dealer quotes, bids, offers and other reference data. Such Level II instruments typically include U.S. treasury and U.S. government agency obligations. As of December 31, 2013 and December 31, 2012, the Company held, in addition to Level I and Level II assets, a contingent put option liability associated with the Company's loan and security agreement with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., collectively referred to as Hercules, which was classified as a Level III liability. The Company's estimate of fair value of the contingent put option liability was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in consideration of an estimated probability of default and expected recovery rate in default, and discounting such cash flows back to the reporting date using a risk-free rate. As of December 31, 2013 and 2012, the Company also held a Level III liability associated with warrants, or PIPE warrants, issued in connection with the Company's private placement equity offering, completed in June 2012. For a detailed description, see Note 10 "Stockholders' Equity." The PIPE warrants are considered a liability and are valued using the Black-Scholes option-pricing model, the inputs for which include exercise price of the PIPE warrants, market price of the underlying common shares, expected term, volatility based on a group of the Company's peers and the risk-free rate corresponding to the expected term of the PIPE warrants. Changes to any of the inputs can have a significant impact to the estimated fair value of the PIPE warrants.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

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

	As of December 31, 2013			
	Fair Value	Level I	Level II	Level III
Assets				
Money market funds	$ 11	$ 11	$ —	$ —
U.S. government agency obligations	15,262	—	15,262	—
Total assets measured at fair value	$ 15,273	$ 11	$15,262	$ —
Liabilities				
PIPE warrant	$ 13,111	$ —	$ —	$13,111
Contingent put option	334	—	—	334
Total liabilities measured at fair value	$ 13,445	$ —	$ —	$ 13,445

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

The following table sets forth the assumptions used in the Black-Scholes option-pricing model to estimate the fair value of the PIPE warrants as of December 31, 2013 and 2012:

	As of December 31, 2013	As of December 31, 2012
Market Price	$ 11.31	$ 4.26
Exercise Price	$ 3.40	$ 3.40
Risk-free interest rate	1.27%	0.72%
Expected volatility	69.0%	78.0%
Expected life (in years)	3.92	4.9
Expected dividend yield	0.0%	0.0%

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

The following table sets forth a summary of the changes in the fair value of the Company's Level III financial liabilities for the years ended December 31, 2013 and 2012 (in thousands):

	Year Ended December 31, 2013
Fair value—beginning of period	$ 7,500
Change in fair value of PIPE warrants	5,693
Change in fair value of contingent put option associated with 2011 loan and security agreement with Hercules	(82)
Addition of contingent put option associated with 2013 loan and security agreement with Hercules	334
Fair value—end of period	$ 13,445

	Year Ended December 31, 2012
Fair value—beginning of period	$ 232
Addition of PIPE warrants in June 2012	5,828
Change in fair value of PIPE warrants	1,590
Change in fair value of contingent put option	(150)
Fair value—end of period	$ 7,500

3. Property and Equipment

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

	As of December 31,	
	2013	2012
Research equipment	$ 2,014	$ 2,014
Leasehold improvements	1,425	1,418
Computer equipment and software	189	167
Construction in process	3,277	—
Tooling	318	337
Furniture and fixtures	59	59
Total property, plant and equipment	7,282	3,995
Less accumulated depreciation and amortization	(2,103)	(1,510)
	$5,179	$ 2,485

Depreciation and amortization expense was $0.6 million, $0.6 million and $0.5 million during the years ended December 31, 2013, 2012 and 2011. Construction in process includes $2.5 million related to certain modifications the Company is making at Patheon's Cincinnati facility under the terms of a capital and equipment agreement related to the manufacture of the Company's product candidates.

4. Research Grant

In May 2011, AcelRx received a grant from the US Army Medical Research and Materiel Command, or USAMRMC, in which the USAMRMC granted $5.6 million to the Company in order to support the development

of a new product candidate, ARX-04, a Sufentanil NanoTab for the treatment of moderate-to-severe acute pain. Under the terms of the grant, the USAMRMC will reimburse the Company for development, manufacturing and clinical costs necessary to prepare for and complete the planned Phase 2 dose-finding trial in a study of acute moderate-to-severe pain, and to prepare to enter Phase 3 development. The grant gives the USAMRMC the option to extend the term of the grant and provide additional funding for the research. As of December 31, 2013, the full amount of the grant, $5.6 million, had been recognized as revenue.

Revenue is recognized based on expenses incurred by AcelRx in conducting research and development activities set forth in the agreement. Revenue attributable to the research and development performed under the USAMRMC grant was $2.1 million, $2.4 million and $1.1 million for the years ended December 31, 2013, 2012, 2011, respectively.

5. Collaboration

On December 16, 2013, AcelRx and Grünenthal GmbH, or Grünenthal, entered into a Collaboration and License Agreement (the "License Agreement") and related Manufacture and Supply Agreement (the "Manufacturing Agreement" and together with the License Agreement, the "Agreements"). The License Agreement grants Grünenthal rights to commercialize Zalviso the Company's novel sublingual patient-controlled analgesia (PCA) system (the "Product"), in the countries of the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia (the "Territory"), for human use in pain treatment within or dispensed by hospitals hospices, nursing homes and other medically-supervised settings (the "Field"). The Company retains rights with respect to the Product in countries outside the Territory, including the U.S., Asia and Latin America. Under the Supply Agreement, the Company will exclusively manufacture and supply the Product to Grünenthal for the Field in the Territory.

License Agreement

Under the terms of the License Agreement, Grünenthal has the exclusive right to commercialize the Product in the Field in the Territory. The Company retains control of clinical development, while Grünenthal and the Company will be responsible for certain development activities pursuant to a development plan as agreed between the parties. The Company will not receive separate payment for such development activities. Grünenthal is exclusively responsible for marketing approval applications and other regulatory filings relating to the sufentanil drug cartridge for the Product in the Field in the Territory, while the Company is responsible for the CE Mark and other regulatory filings relating to device portions of the Product.

The Company received an upfront non-refundable cash payment of $30.0 million, and is eligible to receive up to $220.0 million in additional payments contingent upon research, development, regulatory and manufacturing efforts and specified net sales target milestones. Grünenthal will also make tiered royalty and supply and trademark fee payments in the mid-teens up to the mid-twenties percent range on net sales of Product in the Territory.

Unless earlier terminated, the License Agreement continues in effect until the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments, which supply and trademark fee continues for so long as the Company continues to supply the Product to Grünenthal. The License Agreement is subject to earlier termination in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party, upon the bankruptcy or insolvency of either party, or by Grünenthal for convenience.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Manufacturing Agreement

Under the terms of the Manufacturing Agreement, the Company will manufacture and supply the Product for use in the Field for the Territory exclusively for Grünenthal. Grünenthal shall purchase from AcelRx, during the first five years after the effective date of the Manufacturing Agreement, 100% and thereafter 80% of Grünenthal's and its sublicensees' and distributors' requirements of Product for use in the Field for the Territory. The Product will be supplied at the Company's fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires the Company to use commercially reasonable efforts to enter stand-by contracts with third parties providing significant supply and manufacturing services and under certain specified conditions permits Grünenthal to use a third party back-up manufacturer to manufacture the Product for Grünenthal's commercial sale in the Territory.

Unless earlier terminated, the Manufacturing Agreement continues in effect until the later of the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments or the end of any transition period for manufacturing obligations due to the expiration or termination of the License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the License Agreement, in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party or upon the bankruptcy or insolvency of either party.

The Company identified the following four significant non-contingent performance deliverables under the agreements: 1) intellectual property (license), 2) the obligation to provide research and development services, 3) the significant and incremental discount on the manufacturing of Zalviso for commercial purposes, and 4) the obligation to participate on the joint steering committee.

The Company considered the provisions of the multiple-element arrangement guidance in determining whether the deliverables outlined above have standalone value and thus should be treated as separate units of accounting. Company's management determined that the license has standalone value and represents a separate unit of accounting because the rights conveyed permit Grünenthal to perform all efforts necessary to commercialize and begin selling the product upon regulatory approval. In addition, Grünenthal has the appropriate development, regulatory and commercial expertise with products similar to the product licensed under the agreement and has the ability to engage third parties to manufacture the product allowing Grünenthal to realize the value of the license without receiving any of the remaining deliverables. Grünenthal can also sublicense its license rights to third parties. Also, the Company's management determined that the research services, committee participation and implied discount associated with the manufacturing services each represent individual units of accounting as Grünenthal could perform such services and/or could acquire these on a separate basis.

The Company developed best estimates of selling prices for each deliverable in order to allocate the noncontingent arrangement consideration to the four units of accounting.

The Company's management determined the best estimate of selling price for the license based on Grünenthal's estimated future cash flows arising from the arrangement. Embedded in the estimate were significant assumptions regarding regulatory expenses, revenue, including potential customer market for the product and product price, costs to manufacture the product and the discount rate. The Company's management determined the best estimate of selling price of the research and development services and committee participation based on the nature and timing of the services to be performed and in consideration of personnel and other costs incurred in the delivery of the services. For the discount on manufacturing services, Company's management estimated the selling price based on the market level of contract manufacturing margin it could have received if it were engaged to supply products to a customer in a separate transaction.

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The Agreements entitle the Company to receive additional payments upon the achievement of certain development and sales milestones. Based on ASC Topic 605-28, *Revenue Recognition — Milestone Method*, the Company evaluates contingent milestones at inception of the agreement, and recognizes consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is considered substantive in its entirety. Milestones are events which have the following characteristics: (i) they can be achieved based in whole or in part on either the Company's performance or on the occurrence of a specific outcome resulting from the Company's performance, (ii) there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and, (iii) they would result in additional payments due to the Company. A milestone is considered substantive if the following criteria are met: (i) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item (s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, , (ii) the consideration relates solely to past performance and, (iii) the consideration is reasonable relative to all of the other deliverables and payment terms, including other potential milestone consideration, within the arrangement.

The substantive milestone payments will be recognized as revenue in their entirety upon the achievement of each substantive milestone. Based on the criteria noted above, the identified substantive milestones in the agreement pertain to post approval product enhancements, expanded market opportunities and manufacturing efficiencies for Zalviso. Each of these potential achievements is based primarily on the Company's performance and involves substantive uncertainty as achievement of these milestones require future research, development and regulatory activities, which are inherently uncertain in nature. The Company determined that the consideration for each milestone was commensurate with the Company's performance to achieve the milestone, including future research, development, manufacturing and regulatory activities and that the consideration is reasonable relative to all of the other deliverables and payments within the arrangement. Aggregate potential payments for these milestones total $28.5 million.

In addition to substantive milestones, two milestones associated with the Agreements were deemed not to be substantive. These milestones pertain to regulatory developments for Zalviso in Europe, which Company's management deemed to be not substantive due to the level of performance associated with future achievement of these milestones. Aggregate potential payments for these milestones total $20.0 million. When achieved, the value of these milestones will be allocated to the four separate units of accounting based on estimated selling prices and recognized as revenue in the period of achievement to the extent the services underlying the separate units of accounting have been performed. The Company anticipates receiving the first milestone payment of $5.0 million in 2014, for the submission of the Marketing Authorization Application for Zalviso to the European Medicines Agency.

The Agreement also include milestone payments related to specified net sales targets, totaling $171.5 million. The sales-based milestones do not meet the definition of a milestone under ASU 2010-17 because the achievement of these milestones is solely dependent on counter-party performance and not on any performance obligations of the Company.

The Company allocated the $30.0 million upfront fee across the four deliverables based on estimated selling prices.

Based on the relative estimated selling price method, the amount of consideration allocated to the license was $27.4 million, which was recognized as revenue for the year ended December 31, 2013, as the license had been delivered. The remaining upfront consideration, of $2.6 million, was allocated to the remaining deliverables and recorded as deferred revenue as of December 31, 2013.

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6. Long-Term Debt

Hercules Loan and Security Agreements

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

The Company borrowed the first tranche of $10.0 million upon the closing of the transaction on June 29, 2011 and borrowed the second tranche of $10.0 million in December 2011. The Company used a portion of the proceeds from the first tranche to repay the remaining obligations under that certain loan and security agreement between the Company and Pinnacle Ventures, L.L.C., or Pinnacle Ventures, dated September 16, 2008. The agreement with Pinnacle Ventures is described further below. The interest rate for each tranche was 8.50%. In connection with the loan, the Company issued Hercules seven-year warrants to purchase an aggregate of 274,508 shares of common stock at a price of $3.06 per share. See Note 8 "Warrants," for further description.

On December 16, 2013, AcelRx entered into an Amended and Restated Loan and Security Agreement (the "Loan Agreement") with Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc. (together, the "Lenders") under which the Company may borrow up to $40.0 million in three tranches. The loans are represented by secured convertible term promissory notes (collectively, the "Notes"). The Loan Agreement amends and restates the Loan and Security Agreement between the Company and the Lenders dated as of June 29, 2011, (the Original Loan Agreement), as noted above. The Company borrowed the first tranche of $15.0 million upon closing of the transaction on December 16, 2013. The Company used approximately $8.6 million of the proceeds from the first tranche to repay its obligations under the Original Loan Agreement.

In accordance with ASC Topic No. 470, "Debt – Modifications and Extinguishments" (Topic No. 470), the amendment noted above was determined to be an extinguishment of the existing debt and an issuance of new debt. The Company reached this conclusion based on a comparison of discounted remaining cash flows of the original loan agreement compared to the amended loan agreement, the result of which was a greater than 10% difference in discounted cash flows. The Company determined this difference to be significant. The Company has recorded the new debt at estimated fair value and, as of December 31, 2013, the balance was $14.3 million.

As a result of the extinguishment, AcelRx recorded a $1.2 million loss on extinguishment of debt which was recorded as other income / expense on the Statement of Comprehensive Loss. The loss on extinguishment was a non-cash write off, consisting of deferred debt charges, the unamortized portion of the original issue discount related to the Original Loan Agreement and other fees associated with extinguishing the debt, including the estimated fair value of warrants issued in connection with the amended loan agreement, facility and legal fees associated with the amended loan agreement and the value of the contingent put option liability associated with the original loan agreement at the time of the amendment.

The second tranche of the amended loan agreement of up to $10.0 million can be drawn, at the Company's option, anytime prior to June 30, 2014. The third tranche, of up to $15.0 million, can be drawn at anytime between December 15, 2014 and March 15, 2015, but only if the Company has obtained approval for Zalviso from the U.S. Food and Drug Administration (the "Milestone"). The interest rate for each tranche will be calculated at a rate equal to the greater of either (i) 9.10% plus the prime rate as reported from time to time in The Wall Street Journal minus 5.25%, and (ii) 9.10%. Payments under the Loan Agreement are interest only until April 1, 2015 (which will be extended until January 1, 2016 if the Company achieves the Milestone on or before April 1, 2015) followed by equal monthly payments of principal and interest through the scheduled maturity date

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on October 1, 2017 (which would be extended until January 1, 2018 if the Company achieves the Milestone on or prior to April 1, 2015) (the "Loan Maturity Date"). In addition, a final payment equal to $1,700,000 will be due on the Loan Maturity Date, or such earlier date specified in the Loan Agreement. The Company's obligations under the Loan Agreement are secured by a security interest in substantially all of its assets, other than its intellectual property.

If the Company prepays the loan prior to maturity, it will pay the Lenders a prepayment charge, based on a percentage of the then outstanding principal balance, equal to 3% if the prepayment occurs prior to December 16, 2014, 2% if the prepayment occurs after December 16, 2014, but prior to December 16, 2015, or 1% if the prepayment occurs after December 16, 2015.

Subject to certain conditions and limitations set forth in the Loan Agreement, the Company has the right to convert up to $5.0 million of scheduled principal installments under the Notes into freely tradeable shares of the Company's common stock ("Common Stock"). The number of shares of Common Stock that would be issued upon conversion of the Notes would be equal to the number determined by dividing (x) the product of (A) the principal amount to be paid in shares of Common Stock and (B) 103%, by (y) $9.30 (subject to certain proportional adjustments as provided for in the Loan Agreement).

The Loan Agreement includes customary affirmative and restrictive covenants, but does not include any financial maintenance covenants, and also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of Lenders' security interest or in the value of the collateral, and events relating to bankruptcy or insolvency. Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the Lenders may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the Loan Agreement.

In connection with the Loan Agreement, the Company issued a warrant to each Lender which together are exercisable for an aggregate of 176,730 shares of Common Stock and each carry an exercise price of $6.79 (the "Warrants"). Each Warrant may be exercised on a cashless basis. The Warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of five years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the Warrants. The number of shares for which the Warrants are exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in the Warrants.

Upon an event of default, including a change of control, Hercules has the option to accelerate repayment of the loan, including payment of any applicable prepayment charges, which range from 1%-3% of the outstanding loan balance and accrued interest, as well as a final payment fee of $1.7 million. This option is considered a contingent put option liability as the holder of the loan may exercise the option in the event of default and, is considered an embedded derivative which must be valued and separately accounted for in the Company's financial statements. As the amendment of the loan agreement was considered an extinguishment, the contingent put option liability associated with the original loan agreement, which had an estimated fair value of $32,000 at the time of the amendment, was written off as a part of the loss on extinguishment, and a new contingent put option liability was established. As of December 31, 2013, 2012 and 2011, the estimated fair value of the contingent put option liability was $334,000, $82,000 and $232,000, respectively which was determined by using a risk-neutral valuation model, wherein the fair value of the underlying debt facility is estimated both with and without the presence of the default provisions, holding all other assumptions constant. The resulting difference between the two estimated fair values is the estimated fair value of the default provisions, or the contingent put option. The fair value of the underlying debt facility is estimated by calculating the expected cash flows in

consideration of an estimated probability of default and expected recovery rate in default, and discounting such cash flows back to the reporting date using a risk-free rate. The contingent put option liability was recorded as a debt discount to the loan and consequently a reduction to the carrying value of the loan. The contingent put option liability will be revalued at the end of each reporting period and any change in the fair value will be recognized in the statement of operations.

As of December 31, 2013, the Company had outstanding borrowings under the amended Hercules loan and security agreement of $15.0 million. Amortization of the debt discount prior to amending the Hercules loan and security agreement in December 2013, which was recorded as interest expense, was $0.4 million for the year ended December 31, 2013.

As of December 31, 2012, the Company had outstanding borrowings under the Hercules loan and security agreement of $16.0 million, net of debt discount of $0.5 million. Amortization of the debt discount, which was recorded as interest expense, was $0.5 million for the year ended December 31, 2012.

Amortization of the debt discount, which was recorded as Interest Expense, was $254,000 for the year ended December 31, 2011.

Pinnacle Loan and Security Agreement

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

Future Payments on Long-Term Debt

The following table summarizes our outstanding future payments associated with the Company's long-term debt as of December 31, 2013 (in thousands):

		Payment by Period			
Obligations:	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Principal Payments	$15,000	$ —	$ 10,106	$ 4,894	—
Interest Payments	3,533	1,327	2,015	$ 191	—
Balloon Payments	1,900	200	—	$ 1,700	—
Total	$ 20,433	$ 1,527	$12,121	$6,785	—

7. Convertible Notes

2010 Convertible Notes

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

Convertible Notes automatically converted into 2,034,438 shares of common stock immediately prior to the closing of the IPO.

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

8. Warrants

Series A Warrants

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

As of December 31, 2013, warrants to purchase 3,425 shares of common stock had not been exercised and were still outstanding. These warrants expire in March 2017.

Series B and Series C Warrants

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

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

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

In February 2013, warrants to purchase 228,264 shares were net exercised, for 58,580 shares of common stock. As of December 31, 2013, no warrants to purchase shares of common stock issued to Pinnacle were outstanding.

2010 Warrants

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

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

Hercules Warrants

In connection with the Amended Loan Agreement, executed in December 2013, the Company issued warrants to Hercules which are exercisable for an aggregate of 176,730 shares of Common Stock and each carry an exercise price of $6.79 (the "Warrants"). Each Warrant may be exercised on a cashless basis. The Warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of five years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the Warrants. The number of shares for which the Warrants are exercisable and the associated exercise price are subject to certain proportional adjustments as set forth in the Warrants. The Company estimated the fair value of these warrants as of the issuance date to be $1.1 million, which was used in the estimating the fair value of the amended debt instrument and was recorded as equity. The fair value of the warrants was calculated using the Black-Scholes option-valuation model, and was based on the strike price of $6.79, the stock price at issuance of $9.67, the five-year contractual term of the warrants, a risk-free interest rate of 1.55%, expected volatility of 71% and 0% expected dividend yield.

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As of December 31, 2013, warrants to purchase 176,730 shares of common stock issued to Hercules had not been exercised and were still outstanding. These warrants expire in December 2018.

In connection with the original loan and security agreement with Hercules, executed in June 2011, the Company issued to Hercules warrants to purchase an aggregate of 274,508 shares of common stock at a price of $3.06 per share. The warrants may be exercised on a cashless basis. The warrants are exercisable for a term beginning on the date of issuance and ending on the earlier to occur of seven years from the date of issuance or the consummation of certain acquisitions of the Company as set forth in the warrants. The Company estimated the fair value of these warrants as of the issuance date to be $967,000, which was recorded as a debt discount to the loan and consequently a reduction to the carrying value of the loan. The fair value of the warrants was calculated using the Black-Scholes option-valuation model, and was based on the seven-year contractual term of the warrants, a risk-free interest rate of 2.44%, expected volatility of 79% and 0% expected dividend yield. During June and July 2013, warrants to purchase 274,508 shares were net exercised, for 183,404 shares of common stock.

2012 Private Placement Warrants

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

Upon execution of the Purchase Agreement, the fair value of the PIPE warrants was estimated to be $5.8 million, which was recorded as a liability. As of December 31, 2013, the fair value of the PIPE warrants was estimated to be $13.1 million. The change in fair value for the year ended December 31, 2013 and December 31, 2012, which was recorded as other expense, was $14.1 million and $1.6 million, respectively.

During the year ended December 31, 2013, warrants to purchase 1,135,589 shares were net exercised, for 808,078 shares of common stock. As of December 31, 2013, PIPE warrants to purchase 1,494,514 shares of common stock issued in connection with the Private Placement had not been exercised and were outstanding. These warrants expire in November 2017.

9. Commitments and Contingencies

Operating Leases

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

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

Rent expense was $0.3 million, $0.3 million and $0.2 million during the years ended December 31, 2013, 2012 and 2011, respectively.

Future minimum payments under the lease agreement as of December 31, 2013 are as follows (in thousands):

Year Ending December 31:	
2014	392
2015	404
2016	142
Total minimum payments	$938

Litigation

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

Manufacturing Agreements

Patheon

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

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

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

The Company also entered into a Capital Expenditure and Equipment Agreement, or the Capital Agreement. Under the terms of the Capital Agreement, the second amendment for which was entered into in January 2014, the Company has made and has the option to make certain future modifications to Patheon's Cincinnati facility, the aggregate cost of which is expected to be less than $4.4 million and which would be the responsibility of the Company. If additional equipment and facility modifications are required to meet the Company's Product needs, the Company may be required to contribute to the cost of such additional equipment and facility modifications. The Capital Agreement also requires that the Company make payments in 2012 and 2013 totaling $480,000,

which the Company made, to Patheon to partially offset taxes incurred and paid by Patheon in connection with facility modifications already completed by Patheon. The Company can seek reimbursement from Patheon for this payment if it receives approval from the U.S. Food and Drug Administration for ARX-01. The Capital Agreement further requires that the Company pay a maximum "overhead fee" of $200,000 annually during the term of the Services Agreement, which amount may be reduced to $0 based on the amount of annual revenues earned by Patheon under the Services Agreement and the pre-existing development agreements. No fee was due in 2013 based on the amount of revenues earned by Patheon from the Company.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for the Company's products, none of which have been approved for commercialization; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

Grünenthal

On December 16, 2013, AcelRx Pharmaceuticals, Inc. (the "Company") and Grünenthal GmbH ("Grünenthal") entered into a Collaboration and License Agreement (the "License Agreement") and related Manufacture and Supply Agreement (the "Manufacturing Agreement" and together with the License Agreement, the "Agreements"). The License Agreement grants Grünenthal rights to commercialize ZalvisoTM (formerly known as ARX-01) the Company's novel sublingual patient-controlled analgesia (PCA) system (the "Product"), in the countries of the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia (the "Territory"), for human use in pain treatment within or dispensed by hospitals hospices, nursing homes and other medically-supervised settings (the "Field").

Under the terms of the Manufacturing Agreement, the Company will manufacture and supply the Product for use in the Field for the Territory exclusively for Grünenthal. Grünenthal shall purchase from AcelRx, during the first five years after the effective date of the Manufacturing Agreement, 100% and thereafter 80% of Grünenthal's and its sublicensees' and distributors' requirements of Product for use in the Field for the Territory. The Product will be supplied at the Company's fully burdened manufacturing cost (as defined in the Manufacturing Agreement). The Manufacturing Agreement requires the Company to use commercially reasonable efforts to enter stand-by contracts with third parties providing significant supply and manufacturing services and under certain specified conditions permits Grünenthal to use a third party back-up manufacturer to manufacture the Product for Grünenthal's commercial sale in the Territory.

Unless earlier terminated, the Manufacturing Agreement continues in effect until the later of the expiration of the obligation of Grünenthal to make royalty and supply and trademark fee payments or the end of any transition period for manufacturing obligations due to the expiration or termination of the License Agreement. The Manufacturing Agreement is subject to earlier termination in connection with certain termination events in the License Agreement, in the event the parties mutually agree, by a party in the event of an uncured material breach by the other party or upon the bankruptcy or insolvency of either party.

Under the Supply Agreement, the Company will exclusively manufacture and supply the Product to Grünenthal for the Field in the Territory.

Expenditures associated with the aforementioned agreements are primarily driven by the potential commercial requirements and demand for the Company's products, none of which are currently approved for commercial use; accordingly, the amounts and timing of such future expenditures cannot be determined at this time.

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10. Stockholders' Equity

Common Stock

Public Offerings

On July 23, 2013, AcelRx completed an underwritten public offering of 4,370,000 shares of common stock, at a price of $11.65 per share to the public. The total gross proceeds of this offering were $50.9 million with net proceeds to AcelRx of $47.9 million after deducting underwriting discounts and commissions and other expenses payable by AcelRx.

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

Private Placement Offering

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

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

2012 ATM Agreement

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

indemnification rights and expense reimbursements for up to $25,000 of expenses. As of December 31, 2013, the Company has not sold any shares of common stock pursuant to the ATM.

Initial Public Offering

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

Convertible Preferred Stock

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

Stock Plans

2011 Equity Incentive Plan

In January 2011, the board of directors adopted, and the Company's stockholders approved, the 2011 Equity Incentive Plan, or 2011 Incentive Plan, as a successor to the 2006 Plan. The 2011 Incentive Plan became effective immediately upon the execution and delivery of the underwriting agreement for the IPO on February 10, 2011. As of February 10, 2011, no more awards may be granted under the 2006 Plan, although all outstanding stock options and other stock awards previously granted under the 2006 Plan will continue to remain subject to the terms of the 2006 Plan. The 51,693 shares reserved under the 2006 Plan that remained available for future grant at the time of the IPO were transferred to the share reserve of the 2011 Incentive Plan.

The initial aggregate number of shares of the Company's common stock that may be issued pursuant to stock awards under the 2011 Incentive Plan is 1,875,000 shares, which number was the sum of (i) 51,693 shares remaining available for future grant under the 2006 Plan at the time of the execution and delivery of the underwriting agreement for the Company's IPO, and (ii) an additional 1,823,307 new shares. Then, the number of shares of common stock reserved for issuance under the 2011 Incentive Plan will automatically increase on January 1st each year, starting on January 1, 2012 and continuing through January 1, 2020, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or such lesser number of shares of common stock as determined by the board of directors. In January 2013 and 2012, an additional 1,482,201 and 782,711 shares, were authorized for issuance under the 2011 Incentive Plan, respectively.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

2011 Employee Stock Purchase Plan

Additionally, in January 2011, the board of directors adopted, and the Company's stockholders approved, the 2011 Employee Stock Purchase Plan, or the ESPP, which also became effective immediately upon the execution and delivery of the underwriting agreement for the IPO.

Initially, 250,000 shares of the Company's common stock were authorized for issuance under the ESPP pursuant to purchase rights granted to the Company's employees or to employees of any of its designated affiliates. The number of shares of the Company's common stock reserved for issuance will automatically increase on January 1st each year, starting January 1, 2012 and continuing through January 1, 2020, in an amount equal to the lower of (1) 2% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or (2) a number of shares of common stock as determined by the board of directors. If a purchase right granted under the ESPP terminates without having been exercised, the shares of the Company's common stock not purchased under such purchase right will be available for issuance under the ESPP. No additional shares were authorized for issuance under the ESPP in 2013, and in January 2012, an additional 391,355 were authorized for issuance under the ESPP.

2006 Stock Plan

In August 2006, the Company established the 2006 Plan in which 342,000 shares of common stock were originally reserved for the issuance of incentive stock options, or ISOs, and nonstatutory stock options, or NSOs, to employees, directors or consultants of the Company. In February 2008, an additional 375,000 shares of common stock were reserved for issuance under the 2006 Plan and, in November 2009, an additional 1,376,059 shares of common stock were reserved for issuance under the 2006 Plan. Per the 2006 Plan, the exercise price of ISOs and NSOs granted to a stockholder who at the time of grant owns stock representing more than 10% of the voting power of all classes of the stock of the Company could not be less than 110% of the fair value per share of the underlying common stock on the date of grant. Effective upon the execution and delivery of the underwriting agreement for the Company's IPO, no additional stock options or other stock awards may be granted under the 2006 Plan.

11. Stock-Based Compensation

The Company recorded total stock-based compensation expense for stock options, stock awards and the ESPP as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Research and development	$1,657	$ 998	$ 785
General and administrative	1,822	1,152	1,048
Total	$ 3,479	$2,150	$1,833

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

The following table summarizes option activity under the 2011 Plan and 2006 Plan:

	Number of Stock Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (Years)	Aggregate Intrinsic Value (in thousands)
December 31, 2010	2,008,797	$ 2.91		
Granted	514,958	3.48		
Forfeited	(58,022)	3.32		
Exercised	(69,765)	1.20		
December 31, 2011	2,395,968	$ 3.08		
Granted	1,213,391	3.36		
Forfeited	(165,781)	3.23		
Exercised	(43,767)	2.32		
December 31, 2012	3,399,811	$ 3.18		
Granted	1,958,727	5.99		
Forfeited	(17,917)	8.82		
Exercised	(431,216)	3.03		
December 31, 2013	4,909,405	$ 4.29	7.9	34,452
Vested and exercisable options—December 31, 2013	2,161,400	$ 3.17	6.7	$ 17,589
Vested and expected to vest—December 31, 2013	4,718,574	$ 4.25	7.8	$ 33,322

As of December 31, 2013, there were 273,290 shares available for future grant under the 2011 Plan. In January 2014, an additional 1,722,023 shares were authorized for issuance under the 2011 Incentive Plan.

Additional information regarding the Company's stock options outstanding and vested and exercisable as of December 31, 2013 is summarized below:

	Options Outstanding			Options Vested and Exercisable	
Exercise Prices	Number of Stock Options Outstanding	Weighted-Average Remaining Contractual Life (Years)	Weighted-Average Exercise Price per Share	Shares Subject to Stock Options	Weighted-Average Exercise Price per Share
$1.20-$2.56	613,875	5.9	$ 2.22	613,874	$ 2.22
$2.5601-$4.00	2,088,053	7.4	$ 3.23	1,299,298	$ 3.16
$4.22-$6.34	1,962,477	8.7	$ 5.31	236,353	$ 5.32
$8.18-$10.55	245,000	9.7	$ 10.40	11,875	$ 10.55
	4,909,405	7.9	$ 4.29	2,161,400	$ 3.17

The weighted average grant-date fair value of options granted during the years ended December 31, 2013, 2012, 2011 was $4.15, $2.25 and $2.45 per share. As of December 31, 2013, total stock-based compensation expense related to unvested options to be recognized in future periods was $8.2 million which is expected to be recognized over a weighted-average period of 2.8 years. The grant date fair value of shares vested during the years ended December 31, 2013, 2012 and 2011 was $1.9 million, $1.3 million and $1.1 million, respectively. The total intrinsic value of options exercised during the years ended December 31, 2013, 2012 and 2011 was $3.6 million, $85,000 and $204,000, respectively.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

The Company used the following assumptions to calculate the fair value of each employee stock option:

	Year Ended December 31,		
	2013	2012	2011
Expected term (in years)	5.75-6.25	5.75-6.25	5.75-6.25
Risk-free interest rate	1.02%-2.96%	0.6%-1.74%	1.1%-2.5%
Expected volatility	80%	80%	79%
Expected dividend rate	0%	0%	0%

Restricted Stock Units

In March 2011, the Company granted 343,815 Restricted Stock Units, or RSUs, to employees and directors under the 2011 Plan at a grant date fair value of $3.45. The fair value of the RSUs was determined on the date of grant based on the market price of the Company's common stock. RSUs are recognized as expense ratably over the vesting period and the Company's RSU's generally vest over three years as follows: 25% on the 6 month anniversary of the vesting commencement date, 25% on the 12 month anniversary of the vesting commencement date, 25% on the 24 month anniversary of the vesting commencement date and 25% on the 36 month anniversary of the vesting commencement date, so long as the RSU recipient continues to provide services to the Company. As of December 31, 2013, there were 65,765 RSUs outstanding. The expense related to RSUs during the years ended December 31, 2013, 2012 and 2011 was $290,000, $315,000 and $492,000, respectively.

12. Net Loss per Share of Common Stock

The following table sets forth the computation of the Company's basic and diluted net loss per share of common stock during the years ended December 31, 2012, 2011 and 2010 (in thousands, except for share and per share amounts):

	Year Ended December 31,		
	2013	2012	2011
Net loss	$ (23,426)	$ (33,363)	$ (20,101)
Shares used in computing net loss per share of common stock, basic and diluted	39,746,678	22,124,637	17,344,727
Net loss per share of common stock, basic and diluted	$ (0.59)	$ (1.51)	$ (1.16)

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

	Year Ended December 31,		
	2013	2012	2011
Stock options to purchase common stock	4,909,405	3,399,811	2,395,968
Restricted Stock Units	65,765	161,096	257,868
Common stock warrants	1,674,669	3,136,300	506,197

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

13. Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities consist of the following (in thousands):

	December 31,	
	2013	2012
Accounts payable	$ 2,341	$ 2,235
Accrued compensation and employee benefits	2,397	1,613
Accrued research and development expenses	248	2,371
Accrued liabilities associated with property and equipment	725	—
Professional fees	230	361
Interest payable	61	119
Other	243	189
Total accounts payable and accrued liabilities	$6,245	$6,888

14. 401(k) Plan

The Company sponsors a 401(k) plan that stipulates that eligible employees can elect to contribute to the 401(k) plan, subject to certain limitations. Pursuant to the 401(k) plan, the Company makes a discretionary safe harbor contribution equal to 3% of the related compensation. Eligible employees are 100% vested in this safe harbor contribution regardless of whether they make salary deferrals into the 401(k) plan. Company contributions were $143,000, $120,000 and $107,000 for the years ended December 31, 2013, 2012 and 2011.

15. Income Taxes

The Company did not record a provision for income taxes during the years ended December 31, 2013, 2012 and 2011. Net deferred tax assets as of December 31, 2013 and 2012 consist of the following (in thousands):

	December 31, 2013	December 31, 2012
Deferred tax assets:		
Accruals and other	$ 2,172	$ 802
Research credits	3,553	2,050
Net operating loss carryforward	36,279	35,730
Section 59(e) R&D expenditures	10,339	8,572
Total deferred tax assets	52,343	47,154
Valuation allowance	$ (52,343)	$ (47,154)
Net deferred tax assets	$ —	$ —

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Reconciliations of the statutory federal income tax to the Company's effective tax during the years ended December 31, 2013, 2012 and 2011 are as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Tax at statutory federal rate	$(7,965)	$(11,343)	$(6,834)
State tax—net of federal benefit	(716)	(1,953)	(1,104)
PIPE Warrant liability	4,898	540	—
General Business credits	(1,326)	—	—
Other	(80)	1,807	161
Change in valuation allowance	5,189	11,949	7,777
Provision (benefit) for income taxes	$ —	$ —	$ —

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is "more likely than not." Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $5.2 million, $11.9 million and $7.8 million during the years ended December 31, 2013, 2012 and 2011, respectively. The amount of the valuation allowance for deferred tax assets associated with excess tax deduction from stock based compensation arrangement that is allocated to contributed capital if the future tax benefits are subsequently recognized is $1.1 million.

As of December 31, 2013, 2012 and 2011, the Company had federal net operating loss carryforwards of $91.1 million, $89.7 million and $82.2 million, respectively, which begin to expire in 2025. As of December 31, 2013, 2012, and 2011, the Company had state net operating loss carryforwards of $91.0 million, $89.7 million and $80.6 million, respectively, which begin to expire in 2015.

As of December 31, 2013, 2012 and 2011, the Company had federal research credit carryovers of $2.6 million, $1.3 million and $1.3 million, respectively, which begin to expire in 2026. As of December 31, 2013, 2012 and 2011, the Company had state research credit carryovers of $1.4 million, $1.1 million and $0.9 million, respectively, which will carryforward indefinitely.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change", generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes, such as research credits, to offset its post-change income may be limited. Based on an analysis performed by the Company as of December 31, 2013, it was determined that two ownership changes have occurred since inception of the Company. The first ownership change occurred in 2006 at the time of the Series A financing and, as a result of the change, $1.4 million in federal and state net operating loss carryforwards will expire unutilized. In addition, $26,000 in federal and state research and development credits will expire unutilized. The second ownership change occurred in July 2013 at the time of the underwritten public offering; however, the Company believes the resulting annual imposed limitation on use of pre-change tax attributes is sufficiently high that the limit itself will not result in unutilized pre-change tax attributes.

AcelRx Pharmaceuticals, Inc.

Notes to Financial Statements

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the unrecognized tax benefits during the years ended December 31, 2013, 2012 and 2011 is as follows (in thousands):

	Year Ended December 31,		
	2013	2012	2011
Unrecognized benefit—beginning of period	$ 810	$748	$ 603
Gross decreases—prior period tax positions	221	(17)	—
Gross increases—current period tax positions	310	79	145
Unrecognized benefit—end of period	$1,341	$810	$ 748

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

Accrued interest and penalties related to unrecognized tax benefits are classified as income tax expense and were immaterial. The Company files income tax returns in the United States and in California. The tax years 2007 through 2013 remain open in both jurisdictions. The Company is not currently under examination by income tax authorities in federal, state or other foreign jurisdictions.

16. Unaudited Quarterly Financial Data (in thousands, except per share amounts)

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2013. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per share data.

	2013				2012			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	$ 940	$ 407	$ 548	$ 27,607	$ 329	$ 224	$ 166	$ 1,675
Operating Expenses	$ 11,509	$ 8,178	$ 8,858	$ 7,624	$ 6,875	$ 7,170	$ 8,358	$ 9,704
Net income / (loss)	$(12,762)	$(17,447)	$(10,986)	$17,769	$(7,065)	$(7,194)	$(8,582)	$(10,522)
Net income / (loss) per share (basic)	$ (0.34)	$ (0.47)	$ (0.26)	$ 0.41	$ (0.36)	$ (0.35)	$ (0.38)	$ (0.41)

Diluted income for the fourth quarter of 2013 was $0.39 per share. For all other periods presented, basic and diluted loss per share were the same.

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EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of the Registrant, currently in effect.	8-K	001-35068	3.1	2/28/2011
3.2	Amended and Restated Bylaws of the Registrant, currently in effect.	S-1	333-170594	3.4	1/7/2011
4.1	Reference is made to Exhibits 3.1 through 3.2.				
4.2	Specimen Common Stock Certificate of the Registrant.	S-1	333-170594	4.2	1/31/2011
4.3	Second Amended and Restated Investors' Rights Agreement, among the Registrant and certain of its security holders, dated as of November 23, 2009.	S-1	333-170594	4.3	11/12/2010
4.4	Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology II, L.P., dated as of December 16, 2013.				
4.5	Warrant to Purchase Common Stock of the Registrant, issued to Hercules Technology Growth Capital, Inc., dated as of December 16, 2013				
4.6	Form of Warrant issued to certain purchasers pursuant to the Securities Purchase Agreement dated May 29, 2012, between the Registrant and the purchasers identified therein.	8-K	001-35068	4.8	5/30/2012
10.1+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers.	S-1	333-170594	10.1	1/7/2011
10.2+	2006 Stock Plan, as amended.	S-1	333-170594	10.2	11/12/2010
10.3+	Forms of Notice of Grant of Stock Option, Stock Option Agreement and Stock Option Exercise Notice under 2006 Stock Plan.	10-K	001-35068	10.3	3/30/2011
10.4+	2011 Equity Incentive Plan.	S-8	333-172409	99.3	2/24/2011
10.5+	Forms of Stock Option Grant Notice, Notice of Exercise and Option Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.5	3/30/2011
10.6+	Forms of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement under 2011 Equity Incentive Plan.	10-K	001-35068	10.6	3/30/2011
10.7+	2011 Employee Stock Purchase Plan.	S-8	333-172409	99.6	2/24/2011
10.8	Lease between Metropolitan Life Insurance Company and the Registrant, dated December 15, 2011.	10-K	001-35068	10.9	3/23/2012
10.9	Note and Warrant Purchase Agreement between Registrant and the Purchasers defined therein, dated September 14, 2010, as amended.	S-1	333-170594	10.10	1/31/2011
10.10	Amended and Restated Loan and Security Agreement among the Registrant, Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., dated as of December 16, 2013.				
10.13	Award/Contract with the U.S. Army Medical Research and Material Command, dated May 26, 2011.	10-Q	001-35068	10.3	8/11/2011
10.15+	Amended and Restated Offer Letter between the Registrant and Larry Hamel, dated December 31, 2010.	S-1	333-170594	10.14	1/7/2011
10.16+	Amended and Restated Offer Letter between the Registrant and Badri (Anil) Dasu, dated December 30, 2010.	S-1	333-170594	10.15	1/7/2011
10.17+	Amended and Restated Offer Letter between the Registrant and Pamela Palmer, dated December 29, 2010.	S-1	333-170594	10.16	1/7/2011

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Exhibit Number	Exhibit Description	Incorporation By Reference			
		Form	SEC File No.	Exhibit	Filing Date
10.18+	Amended and Restated Offer Letter between the Registrant and Richard King, dated December 31, 2010.	S-1	333-170594	10.17	1/7/2011
10.19+	Amended and Restated Offer Letter between the Registrant and James Welch, dated December 29, 2010.	S-1	333-170594	10.18	1/7/2011
10.20+	Offer Letter between the Registrant and David Chung, dated August 7, 2013.				
10.21+	Non-Employee Director Compensation Policy.	10-K	001-35068	Item 11	3/12/2013
10.23+	Summary of 2012 Cash Bonus Plan.	10-K	001-35068	Item 11	3/12/2013
10.24+	Summary of 2103 Cash Bonus Plan.	8-K	001-35068	10.1	5/10/2013
10.25	Securities Purchase Agreement dated May 29, 2012, between the Registrant and the purchasers identified therein.	8-K	001-35068	10.23	5/30/2012
10.26	At Market Issuance Sales Agreement, dated August 31, 2012, by and between the Registrant and MLV & Co. LLC.	8-K	001-35068	10.1	8/31/2012
10.27	Supply Agreement with Mallinckrodt LLC, effective as of May 31, 2013.	10-Q	001-35068	10.1	11/5/2103
10.28#	Manufacture and Supply Agreement with Grunenthal GmbH, effective as of December 16, 2013.				
10.29#	Collaboration and License Agreement with Grunenthal GmbH, effective as of December 16, 2013.				
23.1	Consent of Independent Registered Public Accounting Firm.				
24.1	Power of Attorney (included in signature page).				
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.				
32.1	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.*				
101.INS	XBRL Instance Document				
101.SCH	XBRL Taxonomy Extension Schema Document				
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				

\+ Indicates management contract or compensatory plan.

\# Material in the exhibit marked with a "***" has been omitted pursuant to a request for confidential treatment filed with the SEC. Omitted portions have been filed separately with the SEC.

* The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Exhibit 4.4

THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR ANY STATE SECURITIES LAWS. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED, OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL (WHICH MAY BE COMPANY COUNSEL) REASONABLY SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR ANY APPLICABLE STATE SECURITIES LAWS.

WARRANT AGREEMENT

To Purchase Shares of the Common Stock of

ACELRX PHARMACEUTICALS, INC.

Dated as of December 16, 2013 (the "Effective Date")

WHEREAS, AcelRx Pharmaceuticals, Inc., a Delaware corporation (the " Company"), has entered into a Loan and Security Agreement of even date herewith (the "Loan Agreement") with Hercules Technology Growth Capital, Inc., a Maryland corporation, in its capacity as Lender and Collateral Agent, Hercules Technology II, L.P., a Delaware limited partnership (the "Warrantholder") and the other lender parties thereto;

WHEREAS, the Company desires to grant to Warrantholder, in consideration for, among other things, the financial accommodations provided for in the Loan Agreement, the right to purchase shares of its Common Stock (as defined below) pursuant to this Warrant Agreement (the " Warrant");

NOW, THEREFORE, in consideration of the Warrantholder executing and delivering the Loan Agreement and providing the financial accommodations contemplated therein, and in consideration of the mutual covenants and agreements contained herein, the Company and Warrantholder agree as follows:

SECTION 1. GRANT OF THE RIGHT TO PURCHASE COMMON STOCK.

For value received, the Company hereby grants to the Warrantholder, and the Warrantholder is entitled, upon the terms and subject to the conditions hereinafter set forth, to subscribe for and purchase from the Company, Fifty-Eight Thousand Nine Hundred Ten (58,910) fully paid and non-assessable shares of the Common Stock at the Exercise Price (as defined below). The Exercise Price of such shares is subject to adjustment as provided in Section 8. As used herein, the following terms shall have the following meanings:

"1934 Act" means the Securities Exchange Act of 1934, as amended.

"Acknowledgment of Exercise" has the meaning given to it in Section 3(a).

"Act" means the Securities Act of 1933, as amended, and as the same may be in effect from time to time.

"Charter" means the Company's Certificate of Incorporation or other constitutional document, as the same may be amended from time to time.

"Claims" has the meaning given to it in Section 12(p).

"Common Stock" means the Company's common stock, $0.001 par value per share.

"Company" has the meaning given to it in the preamble to this Warrant.

"Company SEC Reports" means, collectively (a) the Company's most recent Annual Report on Form 10-K (the "Annual Report"), (b) the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2013 and (any other statement, report (including without limitation, Current Reports on Form 8-K) or registration statement filed by the Company with the SEC during the period commencing subsequent to the period covered by such Annual Report (including, in each case, all exhibits thereto and documents incorporated by reference therein).

"Effective Date" has the meaning given to it in the preamble to this Warrant.

"Exercise Price" means $6.79.

"Lender" has the meaning given to it in the Loan Agreement.

"Loan Agreement" has the meaning given to it in the preamble to this Warrant.

"Merger Event" means (a) a merger or consolidation involving the Company in which (i) the Company is not the surviving entity, or (ii) the outstanding shares of the Company's capital stock are otherwise converted into or exchanged for shares of capital of another entity; or (b) the sale of all or substantially all of the assets of the Company.

"Net Issuance" has the meaning given to it in Section 3(a).

"Notice of Exercise" has the meaning given to it in Section 3(a).

"Public Acquisition" means any Merger Event which is effected such that (i) the holders of Common Stock shall be entitled to receive (A) cash and/or (B) shares of stock that are of a publicly traded company listed on a national market or exchange which may be resold without restrictions (other than restrictions to which Warrantholder may separately agree in writing) after the consummation of such Merger Event, and (ii) the Company's stockholders own less than 50% of the voting securities of the surviving entity.

"Purchase Price" means, with respect to any exercise of this Warrant, an amount equal to the Exercise Price as of the relevant time multiplied by the number of shares of Common Stock requested to be exercised under this Warrant pursuant to such exercise.

"Rules" has the meaning given to it in Section 12(q).

"Transfer Notice" has the meaning given to it in Section 11.

"Warrant" has the meaning given to it in the preamble to this Warrant.

"Warrant Term" has the meaning given to it in Section 2.

"Warrantholder" has the meaning given to it in the preamble to this Warrant.

SECTION 2. TERM OF THE AGREEMENT.

Except as otherwise provided for herein, the term of this Warrant (the "Warrant Term") and the right to purchase Common Stock as granted herein shall commence on the Effective Date and shall be exercisable for a period ending upon the earlier to occur of (A) five (5) years from the Effective Date or (B) the consummation of a Public Acquisition.

SECTION 3. EXERCISE OF THE PURCHASE RIGHTS.

(a) Exercise. The purchase rights set forth in this Warrant are exercisable by the Warrantholder, in whole or in part, at any time, or from time to time, during the Warrant Term, by tendering to the Company at its principal office a notice of exercise in the form attached hereto as Exhibit A (the "Notice of Exercise"), duly completed and executed. Promptly upon receipt of the Notice of Exercise and the payment of the Purchase Price in accordance with the terms set forth below, and in no event later than five (5) business days thereafter, the Company shall issue to the Warrantholder a certificate for the number of shares of Common Stock purchased and shall execute the acknowledgment of exercise in the form attached hereto as Exhibit B (the "Acknowledgment of Exercise") indicating the number of shares which remain subject to future purchases, if any.

The Purchase Price may be paid at the Warrantholder's election either (i) by cash or check, or (ii) by surrender of all or a portion of the Warrant for shares of Common Stock to be exercised under this Warrant and, if applicable, an amended Warrant representing the remaining number of shares purchasable hereunder, as determined below ("Net Issuance"). If the Warrantholder elects the Net Issuance method, the Company will issue Common Stock in accordance with the following formula:

$$X = \frac{Y(A-B)}{A}$$

Where: X = the number of shares of Common Stock to be issued to the Warrantholder.

Y = the number of shares of Common Stock requested to be exercised under this Warrant.

A = the fair market value of one (1) share of Common Stock at the time of issuance of such shares of Common Stock.

B = the Exercise Price.

For purposes of the above calculation, the fair market value of one (1) share of Common Stock shall mean:

(i) if the Common Stock is traded on the New York Stock Exchange, the American Stock Exchange, any exchange operated by the NASDAQ Stock Market, LLC or any other securities exchange, the fair market value of one (1) share of Common Stock shall be deemed to be the volume-weighted average of the closing prices over the twenty (20) consecutive trading days ending two (2) trading days before the day the fair market value of one (1) share of Common Stock is being determined; or

(ii) if at any time the Common Stock is not listed on any securities exchange, the fair market value of one (1) share of Common Stock shall be the highest price per share which the Company could obtain from a willing buyer (not a current employee or director) for shares of Common Stock sold by the Company (based upon the valuation by the Board of all shares of Common Stock), from authorized but unissued shares, as determined in good faith by its Board of Directors, unless this Warrant is being exercised in connection with a Merger Event, in which case the fair market value of one (1) share of Common Stock shall be deemed to be the per share value received by the holders of the Common Stock on a Common Stock equivalent basis pursuant to such Merger Event.

Upon partial exercise by either cash or Net Issuance, the Company shall promptly issue an agreement substantially in the form of the Warrant representing the remaining number of shares purchasable hereunder. All other terms and conditions of such agreement shall be identical to those contained herein, including, but not limited to the Effective Date hereof.

(b) Exercise Prior to Expiration. To the extent that the Warrantholder has not exercised its purchase rights under this Warrant to all Common Stock subject hereto, and if the fair market value of one share of the Common Stock is greater than the Exercise Price then in effect, this Warrant shall be deemed automatically exercised pursuant to Section 3(a) (even if not surrendered) immediately before the expiration of the Warrant Term. For purposes of such automatic exercise, the fair market value of one share of the Common Stock upon such expiration shall be determined pursuant to Section 3(a). To the extent this Warrant or any portion thereof is deemed automatically exercised pursuant to this Section 3(b), the Company agrees to promptly notify the Warrantholder of the number of shares of Common Stock, if any, the Warrantholder is to receive by reason of such automatic exercise.

(c) Legend. Each certificate for the shares of Common Stock purchased upon exercise of this Warrant shall bear the restrictive legend set forth on the first page of this Warrant. Such legend shall be removed and the Company shall, or shall instruct its transfer agent to, issue a certificate without such legend or any other legend to the holder of such shares (i) if such shares are sold or transferred pursuant to an effective registration statement under the Act covering the resale of such shares by the holder thereof, (ii) if such shares are sold or transferred pursuant to Rule 144 under the Act, (iii) if, upon advice of counsel to the Company, such shares are eligible for resale without any restrictions under Rule 144 under the Act, or (iv) upon the request of such holder if such request is accompanied (at such holder's expense) by a written opinion of counsel reasonably satisfactory to the Company that registration is not required under the Act or any applicable state securities laws for the resale of the shares of Common Stock purchased upon exercise of this Warrant. The removal of such restrictive legend from any certificates representing the shares of Common Stock purchased upon exercise of this Warrant is predicated upon the Company's reliance that the holder of such shares would sell, transfer, assign, pledge, hypothecate or otherwise dispose of such shares pursuant to either the registration requirements of the Act, including any applicable prospectus delivery requirements, or an exemption therefrom, and that if such shares are sold pursuant to a registration statement, they will be sold in compliance with the plan of distribution set forth therein.

SECTION 4. RESERVATION OF SHARES.

During the Warrant Term, the Company will at all times have authorized and reserved a sufficient number of shares of its Common Stock to provide for the exercise of the rights to purchase Common Stock as provided for herein.

SECTION 5. NO FRACTIONAL SHARES OR SCRIP.

No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant, but in lieu of such fractional shares the Company shall make a cash payment therefor upon the basis of the Exercise Price then in effect.

SECTION 6. NO RIGHTS AS SHAREHOLDER/STOCKHOLDER.

This Warrant does not entitle the Warrantholder to any voting rights or other rights as a shareholder/stockholder of the Company prior to the exercise of this Warrant.

SECTION 7. WARRANTHOLDER REGISTRY.

The Company shall maintain a registry showing the name and address of the registered holder of this Warrant. Warrantholder's initial address, for purposes of such registry, is set forth in Section 12(g). Warrantholder may change such address by giving written notice of such changed address to the Company.

SECTION 8. ADJUSTMENT RIGHTS.

The Exercise Price and the number of shares of Common Stock purchasable hereunder are subject to adjustment, as follows:

(a) Merger Event. If at any time there shall be a Merger Event that is not a Public Acquisition, then, as a part of such Merger Event, lawful provision shall be made so that the Warrantholder shall thereafter be entitled to receive, upon exercise of this Warrant, the kind, amount and value of shares of Common Stock or other securities or property of the successor, surviving or purchasing corporation resulting from, or participating in, such Merger Event that would have been issuable if Warrantholder had exercised this Warrant immediately prior to such Merger Event. In any such case, appropriate adjustment (as determined in good faith by the Company's Board of Directors) shall be made in the application of the provisions of this Warrant with respect to the rights and interests of the Warrantholder after such Merger Event to the end that the provisions of this Warrant (including adjustments of the Exercise Price) shall be applicable in their entirety, and to the greatest extent possible. Without limiting the foregoing, in connection with any Merger Event other than a Public Acquisition, upon the closing thereof, the successor, surviving or purchasing entity shall assume the obligations of this Warrant. The provisions of this Section 8(a) shall similarly apply to successive Merger Events. In connection with a Merger Event and upon Warrantholder's written election to the Company, the Company shall cause this Warrant to be exchanged for the consideration that Warrantholder would have received if Warrantholder chose to exercise its right to have shares issued pursuant to the Net Issuance provisions of this Warrant prior to the Merger Event without actually exercising such right, acquiring such shares and exchanging such shares for such consideration.

(b) Reclassification of Shares. Except as set forth in Section 8(a), if the Company at any time shall, by combination, reclassification, exchange or subdivision of securities or otherwise, change any of the securities as to which purchase rights under this Warrant exist into the same or a different number of securities of any other class or classes, this Warrant shall thereafter represent the right to acquire such number and kind of securities as would have been issuable as the result of such change with respect to the securities which were subject to the purchase rights under this Warrant immediately prior to such combination, reclassification, exchange, subdivision or other change.

(c) Subdivision or Combination of Shares. If the Company at any time shall combine or subdivide its Common Stock, (i) in the case of a subdivision, the Exercise Price shall be proportionately decreased, and the number of shares of Common Stock issuable upon exercise of this Warrant shall be proportionately increased, or (ii) in the case of a combination, the Exercise Price shall be proportionately increased, and the number of shares of Common Stock issuable upon the exercise of this Warrant shall be proportionately decreased.

(d) Stock Dividends. If the Company at any time while this Warrant is outstanding and unexpired shall:

(i) pay a dividend with respect to the Common Stock payable in Common Stock, then the Exercise Price shall be adjusted, from and after the date of determination of stockholders entitled to receive such dividend or distribution, to that price determined by multiplying the Exercise Price in effect immediately prior to such date of determination by a fraction (A) the numerator of which shall be the total number of shares of Common Stock outstanding immediately prior to such dividend or distribution, and (B) the denominator of which shall be the total number of shares of Common Stock outstanding immediately after such dividend or distribution; or

(ii) make any other distribution with respect to the Common Stock, except any distribution specifically provided for in any other clause of this Section 8, then, in each such case, provision shall be made by the Company such that the Warrantholder shall receive upon exercise of this Warrant a proportionate share of any such distribution as though it were the holder of the Common Stock as of the record date fixed for the determination of the stockholders of the Company entitled to receive such distribution.

(e) Antidilution Rights. To the extent that any antidilution rights applicable to the Common Stock purchasable hereunder may be set forth in the Charter, the Company shall promptly provide the Warrantholder with a copy of any restatement, amendment, modification or waiver of the Charter that impairs or reduces such antidilution rights; provided, that no such amendment, modification or waiver shall impair or reduce the antidilution rights, if any, set forth in the Charter with respect to the Common Stock unless such amendment, modification or waiver affects the rights of Warrantholder with respect to the Common Stock issuable hereunder generally in the same manner as it affects all other holders of Common Stock. The Company shall, within ten (10) business days of the end of each fiscal quarter following the Effective Date, provide Warrantholder with written notice of any issuance of its stock or other equity security during such fiscal quarter that triggered an antidilution adjustment under the antidilution rights applicable to the Common Stock purchasable hereunder, if any, as may be set forth in the Charter, which notice shall include (a) the price at which such stock or security was sold, (b) the number of shares issued, and (c) such other information as reasonably necessary for Warrantholder to verify that such antidilution adjustment occurred and the amount of any such adjustment. For the avoidance of doubt, there shall be no duplicate antidilution adjustment pursuant to this subsection (e), the forgoing subsection (d) and the Charter.

(f) Notice of Adjustments. If: (i) the Company shall declare any dividend or distribution upon its Common Stock, whether in stock, cash, property or other securities (assuming Lender consents to a dividend involving cash, property or other securities under the Loan Agreement, if the consent of Lender is then required by the terms of the Loan Agreement); (ii) the Company shall offer for subscription prorata to the holders of Common Stock any additional shares of stock of any class or other rights; (iii) there shall be any Merger Event; (iv) the Company shall sell, lease, license or otherwise transfer all or substantially all of its assets; or (v) there shall be any voluntary dissolution, liquidation or winding up of the Company; then, in connection with each such event, the Company shall send to the Warrantholder: (A) at least ten (10) days' prior written notice of the date on which the books of the Company shall close or a record shall be taken for such dividend, distribution, subscription rights (specifying the date on which the holders of Common Stock shall be entitled thereto) or for determining rights to vote in respect of such Merger Event, sale, lease, license or other transfer of all or substantially all assets, dissolution, liquidation or winding up; and (B) in the case of any such Merger Event, dissolution,

liquidation or winding up, at least ten (10) days' prior written notice of the date when the same shall take place (and specifying the date on which the holders of Common Stock shall be entitled to exchange their Common Stock for securities or other property deliverable upon such Merger Event, dissolution, liquidation or winding up).

Each such written notice shall set forth, in reasonable detail, (i) the event requiring the notice, and (ii) if any adjustment is required to be made, (A) the amount of such adjustment, (B) the method by which such adjustment was calculated, (C) the adjusted Exercise Price (if the Exercise Price has been adjusted), and (D) the number of shares subject to purchase hereunder after giving effect to such adjustment, and shall be given by first class mail, postage prepaid, or by reputable overnight courier with all charges prepaid, addressed to the Warrantholder at the address for Warrantholder set forth in the registry referred to in Section 7.

(g) Timely Notice. Failure to timely provide such notice required by subsection (f) above shall entitle Warrantholder to retain the benefit of the applicable notice period notwithstanding anything to the contrary contained in any insufficient notice received by Warrantholder ; provided, that, notwithstanding anything herein to the contrary, the failure to timely provide such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice.

SECTION 9. REPRESENTATIONS, WARRANTIES AND COVENANTS OF THE COMPANY.

(a) Reservation of Common Stock. The Common Stock issuable upon exercise of the Warrantholder's rights has been duly and validly reserved and, when issued in accordance with the provisions of this Warrant, will be validly issued, fully paid and non-assessable, and will be free of any taxes, liens, charges or encumbrances of any nature whatsoever; provided, that the Common Stock issuable pursuant to this Warrant may be subject to restrictions on transfer under state and/or federal securities laws. The Company has made available to the Warrantholder true, correct and complete copies of its Charter and current bylaws. The issuance of certificates for shares of Common Stock upon exercise of this Warrant shall be made without charge to the Warrantholder for any issuance tax in respect thereof, or other cost incurred by the Company in connection with such exercise and the related issuance of shares of Common Stock; provided, that the Company shall not be required to pay any tax which may be payable in respect of any transfer and the issuance and delivery of any certificate in a name other than that of the Warrantholder.

(b) Due Authority. The execution and delivery by the Company of this Warrant and the performance of all obligations of the Company hereunder, including the issuance to Warrantholder of the right to acquire the shares of Common Stock, have been duly authorized by all necessary corporate action on the part of the Company. This Warrant: (1) does not violate the Company's Charter or current bylaws; (2) does not contravene any law or governmental rule, regulation or order applicable to it; and (3) does not and will not contravene any provision of, or constitute a default under, any indenture, mortgage, contract or other instrument to which it is a party or by which it is bound. This Warrant constitutes a legal, valid and binding agreement of the Company, enforceable in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, fraudulent conveyance, moratorium or other laws affecting the enforcement of creditors' rights in general, and except that the enforceability of this Warrant is subject to general principles of equity.

(c) Consents and Approvals. No consent or approval of, giving of notice to, registration with, or taking of any other action in respect of any state, federal or other governmental authority or agency is required on the part of the Company with respect to the execution, delivery and performance by the Company of its obligations under this Warrant, except for the filing of notices pursuant to Regulation D under the Act and any filing required by applicable state securities law, which filings will be effective by the time required thereby.

(d) Issued Securities. All issued and outstanding shares of Common Stock have been duly authorized and validly issued and are fully paid and nonassessable. All outstanding shares of Common Stock and any other Company securities were issued in compliance with all applicable federal and state securities laws in all material respects. In addition, as of the date immediately preceding the Effective Date:

(i) The authorized capital of the Company consists of (A) 100,000,000 shares of Common Stock, of which 43,039,269 shares are issued and outstanding, and (B) 10,000,000 shares of Preferred Stock, of which no shares are issued and outstanding.

(ii) The Company has reserved an aggregate of 740,562 shares of Common Stock for issuance under its 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan, not including any automatic increases to the shares reserved for issuance under such plans as described in the Company SEC Reports. Stock options or other equity awards to purchase or acquire an aggregate of 4,989,398 shares of Common Stock are outstanding. In addition, there are warrants for the purchase of 1,497,939 shares of Common Stock outstanding. Except as set forth in the Company SEC Reports, there are no other options, warrants, conversion privileges or other rights presently outstanding to purchase or otherwise acquire any authorized but unissued shares of the Company's capital stock or other securities of the Company. The Company has no outstanding loans to any employee, officer or director of the Company, and the Company agrees not to enter into any such loan or otherwise guarantee the payment of any loan made to an employee, officer or director by a third party.

(iii) No stockholder of the Company has preemptive rights to purchase new issuances of the Company's capital stock pursuant to the Charter or the Company's bylaws.

(e) Exempt Transaction. Subject to the accuracy of the Warrantholder's representations in Section 10, the issuance of the Common Stock upon exercise of this Warrant will each constitute a transaction exempt from (i) the registration requirements of Section 5 of the Act, in reliance upon Section 4(2) thereof, and (ii) the qualification requirements of the applicable state securities laws.

(f) Compliance with Rule 144. If the Warrantholder proposes to sell Common Stock issuable upon the exercise of this Warrant in compliance with Rule 144 promulgated by the SEC, then, upon Warrantholder's written request to the Company, the Company shall furnish to the Warrantholder, within five days after receipt of such request, a written statement confirming the Company's compliance with the filing requirements of the SEC as set forth in such Rule, as such Rule may be amended from time to time, and shall issue appropriate instructions to its transfer agent to remove the restrictive legend from any certificates evidencing the Common Stock issuable upon the exercise of this Warrant.

(g) Information Rights. During the Warrant Term, Warrantholder shall be entitled to the information rights contained in Sections 7.1(a), 7.1(b) and 7.1(c) of the Loan Agreement, and Sections 7.1(a), 7.1(b) and 7.1(c) of the Loan Agreement are hereby incorporated into this Warrant by this reference as though fully set forth herein, provided, however, that the Company shall not, once all Indebtedness (as defined in the Loan Agreement) owed by the Company to Lender has been repaid, be required to deliver any information required by Section 7.1 of the

Loan Agreement so long as the Company is subject to SEC reporting obligations under Section 13(a) or Section 15(d) of the 1934 Act. Notwithstanding anything to the contrary in this Section 9(g) or elsewhere herein, to the extent that this Warrant is transferred to a third party that is not then a party to the Loan Agreement as Lender or is not an affiliate of Lender, then this Section 9(g) shall automatically terminate and shall have no further force or effect.

(h) Listing of Shares. The Common Stock is listed for trading on the NASDAQ Global Market as of the Effective Date.

SECTION 10. REPRESENTATIONS AND COVENANTS OF THE WARRANTHOLDER.

This Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Warrantholder:

(a) Investment Purpose. The right to acquire Common Stock or the Common Stock issuable upon exercise of the Warrantholder's rights contained herein has been, and such shares will be, acquired for investment and not with a view to the sale or distribution of any part thereof, and the Warrantholder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration under the Act or an exemption from the registration requirements of the Act. Warrantholder is not a registered broker-dealer under Section 15 of the 1934 Act or an entity engaged in a business that would require it to be so registered as a broker-dealer.

(b) Private Issue. The Warrantholder understands (i) that the Common Stock issuable upon exercise of this Warrant is not registered under the Act or qualified under applicable state securities laws on the ground that the issuance contemplated by this Warrant will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this Section 10.

(c) Financial Risk. The Warrantholder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment, and has the ability to bear the economic risks of its investment.

(d) Risk of No Registration. Without in any way limiting the Company's obligations under this Warrant, the Warrantholder understands that if the Common Stock is not registered with the SEC pursuant to Section 12 of the 1934 Act or the Company is not required to file reports pursuant to Section 13(a) or Section 15(d) of the 1934 Act, or if a registration statement is not effective under the Act covering the resale of the shares of Common Stock issuable upon exercise of the Warrant when it desires to sell (i) the rights to purchase Common Stock pursuant to this Warrant or (ii) the Common Stock issuable upon exercise of the right to purchase, as applicable, it may be required to hold such securities for an indefinite period. The Warrantholder also understands that any sale of (A) its rights hereunder to purchase Common Stock or (B) Common Stock issued or issuable hereunder which might be made by it in reliance upon Rule 144 under the Act may be made only in accordance with the terms and conditions of that Rule.

(e) Accredited Investor. Warrantholder is, and on each date on which it exercises any portion of this Warrant, it will be, an "accredited investor" within the meaning of the Securities and Exchange Rule 501 of Regulation D, as presently in effect.

(f) No Short Sales. Warrantholder has not engaged, and will not engage, in "short sales" of the Common Stock of the Company. The term "short sale" shall mean any sale of a security which the seller does not own or any sale which is consummated by the delivery of a security borrowed by, or for the account of, the seller.

SECTION 11. TRANSFERS.

Subject to compliance with applicable federal and state securities laws, this Warrant and all rights hereunder are transferable, in whole or in part, without charge to the holder hereof (except for transfer taxes) upon surrender of this Warrant properly endorsed. Each taker and holder of this Warrant, by taking or holding the same, consents and agrees that this Warrant, when endorsed in blank, shall be deemed negotiable, and that the holder hereof, when this Warrant shall have been so endorsed and its transfer recorded on the Company's books, shall be treated by the Company and all other persons dealing with this Warrant as the absolute owner hereof for any purpose and as the person entitled to exercise the rights represented by this Warrant. The transfer of this Warrant shall be recorded on the books of the Company upon receipt by the Company of a notice of transfer in the form attached hereto as Exhibit C (the "Transfer Notice"), at its principal offices and the payment to the Company of all transfer taxes and other governmental charges imposed on such transfer. Until the Company receives such Transfer Notice, the Company may treat the registered owner hereof as the owner for all purposes.

SECTION 12. MISCELLANEOUS.

(a) Effective Date. The provisions of this Warrant shall be construed and shall be given effect in all respects as if it had been executed and delivered by the Company on the date hereof. This Warrant shall be binding upon any successors or assigns of the Company and the Warrantholder.

(b) Remedies. In the event of any default hereunder, the non-defaulting party may proceed to protect and enforce its rights either by suit in equity and/or by action at law, including but not limited to an action for damages as a result of any such default, and/or an action for specific performance for any default where Warrantholder will not have an adequate remedy at law and where damages will not be readily ascertainable. The Company expressly agrees that it shall not oppose an application by the Warrantholder or any other person entitled to the benefit of this Warrant requiring specific performance of any or all provisions hereof or enjoining the Company from continuing to commit any such breach of this Warrant.

(c) No Impairment of Rights. The Company will not, by amendment of its Charter or through any other means, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be reasonably necessary or appropriate in order to protect the rights of the Warrantholder against impairment. Notwithstanding the foregoing, nothing in this Section 12(c) shall negate or otherwise restrict or impair the Company's right to effect any changes to the rights, preferences, privileges or restrictions associated with the Common Stock so long as such changes do not adversely affect the rights, preferences, privileges or restrictions associated with the shares of Common Stock issuable upon exercise of this Warrant in a manner different from the effect that such changes have generally on the rights, preferences, privileges or restrictions associated with all other shares of Common Stock.

(d) Additional Documents. The Company, upon execution of this Warrant, shall provide the Warrantholder with certified resolutions with respect to the representations and warranties set forth in the first sentence of Section 9(b).

(e) Attorney's Fees. In any litigation, arbitration or court proceeding between the Company and the Warrantholder relating hereto, the prevailing party shall be entitled to reasonable attorneys' fees and expenses and all reasonable costs of proceedings incurred in enforcing this Warrant. For the purposes of this Section 12(e), attorneys' fees shall include

without limitation reasonable fees incurred in connection with the following: (i) contempt proceedings; (ii) discovery; (iii) any motion, proceeding or other activity of any kind in connection with an insolvency proceeding; (iv) garnishment, levy, and debtor and third party examinations; and (v) post-judgment motions and proceedings of any kind, including without limitation any activity taken to collect or enforce any judgment.

(f) Severability. In the event any one or more of the provisions of this Warrant shall for any reason be held invalid, illegal or unenforceable, the remaining provisions of this Warrant shall be unimpaired, and the invalid, illegal or unenforceable provision shall be replaced by a mutually acceptable valid, legal and enforceable provision, which comes closest to the intention of the parties underlying the invalid, illegal or unenforceable provision.

(g) Notices. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication that is required, contemplated, or permitted under this Warrant or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (i) the day of transmission by facsimile or hand delivery if transmission or delivery occurs on a business day at or before 5:00 pm in the time zone of the recipient, or, if transmission or delivery occurs on a non-business day or after such time, the first business day thereafter, or the first business day after deposit with an overnight express service or overnight mail delivery service; or (ii) the third calendar day after deposit in the United States mails, with proper first class postage prepaid (provided, that any Advance Request shall not be deemed received until Lender's actual receipt thereof), and shall be addressed to the party to be notified as follows:

If to Warrantholder:

HERCULES TECHNOLOGY II, L.P.
Legal Department
Attention: Chief Legal Officer and Manuel Henriquez
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

If to the Company:

ACELRX PHARMACEUTICALS, INC.
Attention: Chief Financial Officer
351 Galveston Drive
Redwood City, CA 94063
Facsimile: 650-216-6500
Telephone: 650-216-3511

With a copy to (which shall not constitute notice hereunder):

Mark. B Weeks
Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304-1130
Facsimile: (650) 849-7400
Telephone: (650) 843-5011

or to such other address as each party may designate for itself by like notice.

(h) Entire Agreement; Amendments . This Warrant constitutes the entire agreement and understanding of the parties hereto in respect of the subject matter hereof, and supersede and replace in their entirety any prior proposals, term sheets, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof (including Lender's proposal letter dated November 19, 2013). None of the terms of this Warrant may be amended except by an instrument executed by each of the parties hereto.

(i) Headings. The various headings in this Warrant are inserted for convenience only and shall not affect the meaning or interpretation of this Warrant or any provisions hereof.

(j) Advice of Counsel. Each of the parties represents to each other party hereto that it has discussed (or had an opportunity to discuss) with its counsel this Warrant and, specifically, the provisions of Sections 12(n), 12(o), 12(p), 12(q) and 12(r).

(k) No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Warrant. In the event an ambiguity or question of intent or interpretation arises, this Warrant shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Warrant.

(l) No Waiver. Except for the requirement that this Warrant be exercised (or be deemed exercised), if at all, during the Warrant Term, no omission or delay by either party hereto at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by the other party hereto at any time designated, shall be a waiver of any such right or remedy to which such party is entitled, nor shall it in any way affect the right of such party to enforce such provisions thereafter.

(m) Survival. All agreements, representations and warranties contained in this Warrant or in any document delivered pursuant hereto shall be for the benefit of Warrantholder and the Company, as the case may be, and shall survive the execution and delivery of this Warrant and the expiration or other termination of this Warrant.

(n) Governing Law. This Warrant has been negotiated and delivered to Warrantholder in the State of California, and shall have been accepted by Warrantholder in the State of California. Delivery of Common Stock to Warrantholder by the Company under this Warrant is due in the State of California. This Warrant shall be governed by, and construed and enforced in accordance with, the laws of the State of California, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

(o) Consent to Jurisdiction and Venue. All judicial proceedings arising in or under or related to this Warrant may be brought in any state or federal court of competent jurisdiction located in the State of California. By execution and delivery of this Warrant, each party hereto generally and unconditionally: (a) consents to personal jurisdiction in Santa Clara County, State of California; (b) waives any objection as to jurisdiction or venue in Santa Clara County, State of California; (c) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (d) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Warrant. Service of process on any party hereto in any action arising out of or relating to this Warrant shall be effective if given in accordance with the requirements for notice set forth in Section 12(g), and shall be deemed effective and received as set forth in Section 12(g). Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

(p) Mutual Waiver of Jury Trial. Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes arising out of this Warrant be resolved by a judge applying such applicable laws. EACH OF THE COMPANY AND WARRANTHOLDER SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, "CLAIMS") ASSERTED BY THE COMPANY AGAINST WARRANTHOLDER OR ITS ASSIGNEE OR BY WARRANTHOLDER OR ITS ASSIGNEE AGAINST THE COMPANY RELATING TO THIS WARRANT. This waiver extends to all such Claims arising out of this Warrant, including Claims that involve persons other than the Company and Warrantholder, and any Claims for damages, breach of contract, specific performance, or any equitable or legal relief of any kind, arising out of this Warrant.

(q) Arbitration. If the Mutual Waiver of Jury Trial set forth in Section 12(p) is ineffective or unenforceable, the parties agree that all Claims shall be resolved by reference to a private judge sitting without a jury, pursuant to Code of Civil Procedure Section 638, before a mutually acceptable referee or, if the parties cannot agree, a referee selected by the Presiding Judge of Santa Clara County, California. Such proceeding shall be conducted in Santa Clara County, California, with California rules of evidence and discovery applicable to such proceeding.

(r) Prejudgment Relief. In the event Claims are to be resolved by judicial reference, either party may seek from a court of competent jurisdiction identified in Section 12(o), any prejudgment order, writ or other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by judicial reference.

(s) Counterparts. This Warrant and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts, and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument.

(t) Specific Performance. The parties hereto hereby declare that it is impossible to measure in money the damages which will accrue to a party hereto by reason of the other party's failure to perform any of the obligations under this Warrant and agree that the terms of this Warrant shall be specifically enforceable by either party hereto. If a party hereto institutes any action or proceeding to specifically enforce the provisions hereof, any person against whom such action or proceeding is brought hereby waives the claim or defense therein that such party has an adequate remedy at law, and such person shall not offer in any such action or proceeding the claim or defense that such remedy at law exists.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have caused this Warrant to be executed by its officers thereunto duly authorized as of the Effective Date.

COMPANY: **ACELRX PHARMACEUTICALS, INC.**

By: /s/ James Welch

Name: James Welch

Title: CFO

WARRANTHOLDER: **HERCULES TECHNOLOGY II, L.P.,**
a Delaware limited partnership

By: Hercules Technology SBIC Management, LLC,
its General Partner

By: Hercules Technology Growth Capital, Inc.,
its Manager

By: /s/ Ben Bang
Name: Ben Bang
Title: Senior Counsel

EXHIBIT A

NOTICE OF EXERCISE

To: ACELRX PHARMACEUTICALS, INC. (the "Company")

(1) The undersigned Warrantholder hereby elects to purchase [_____] shares of the Common Stock of the Company, pursuant to the terms of that certain Warrant Agreement, dated as of December 16, 2013, between the Company and the Warrantholder (the "Warrant"), and [CASH PAYMENT: tenders herewith payment of the Purchase Price in full, together with all applicable transfer taxes, if any.] [NET ISSUANCE: elects pursuant to Section 3(a) of the Warrant to effect a Net Issuance.]

(2) Please issue a certificate or certificates representing said shares of Common Stock in the name of the Warrantholder or in such other name as is specified below:

_____

(Name)

_____

(Address)

WARRANTHOLDER:

HERCULES TECHNOLOGY II, L.P.,
a Delaware limited partnership

By: Hercules Technology SBIC Management, LLC,
its General Partner

By: Hercules Technology Growth Capital, Inc.,
its Manager

By: _____
Name: Ben Bang
Title: Senior Counsel

EXHIBIT B

ACKNOWLEDGMENT OF EXERCISE

The undersigned, as representative of AcelRx Pharmaceuticals, Inc. (the "Company"), hereby acknowledges receipt of the "Notice of Exercise" from Hercules Technology II, L.P. "Warrantholder"), to purchase [_____] shares of the Common Stock of the Company, pursuant to the terms of that certain Warrant Agreement, dated as of December 16, 2013, between the Company and the Warrantholder (the "Warrant"), and further acknowledges that [_____] shares remain subject to purchase under the terms of the Warrant.

COMPANY: ACELRX PHARMACEUTICALS, INC.

By: _____

Title: _____

Date: _____

EXHIBIT C

TRANSFER NOTICE

FOR VALUE RECEIVED, that certain Warrant Agreement, dated as of December 16, 2013, between AcelRx Pharmaceuticals, Inc., as the Company, and Hercules Technology II, L.P., as the Warrantholder (the "Warrant"), and all rights evidenced thereby are hereby transferred and assigned to

_____

(Please Print)

whose address is _____

_____

Dated: _____

Holder's Signature: _____

Holder's Address: _____

_____

Signature Guaranteed: _____

NOTE: The signature to this Transfer Notice must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Exhibit 4.5

THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR ANY STATE SECURITIES LAWS. THEY MAY NOT BE SOLD, OFFERED FOR SALE, PLEDGED, OR HYPOTHECATED IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL (WHICH MAY BE COMPANY COUNSEL) REASONABLY SATISFACTORY TO THE COMPANY THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, OR ANY APPLICABLE STATE SECURITIES LAWS.

WARRANT AGREEMENT

To Purchase Shares of the Common Stock of

ACELRX PHARMACEUTICALS, INC.

Dated as of December 16, 2013 (the "Effective Date")

WHEREAS, AcelRx Pharmaceuticals, Inc., a Delaware corporation (the " Company"), has entered into a Loan and Security Agreement of even date herewith (the "Loan Agreement") with Hercules Technology Growth Capital, Inc., a Maryland corporation, in its capacity as Lender and Collateral Agent (the "Warrantholder") and the other lender parties thereto;

WHEREAS, the Company desires to grant to Warrantholder, in consideration for, among other things, the financial accommodations provided for in the Loan Agreement, the right to purchase shares of its Common Stock (as defined below) pursuant to this Warrant Agreement (the " Warrant");

NOW, THEREFORE, in consideration of the Warrantholder executing and delivering the Loan Agreement and providing the financial accommodations contemplated therein, and in consideration of the mutual covenants and agreements contained herein, the Company and Warrantholder agree as follows:

SECTION 1. GRANT OF THE RIGHT TO PURCHASE COMMON STOCK.

For value received, the Company hereby grants to the Warrantholder, and the Warrantholder is entitled, upon the terms and subject to the conditions hereinafter set forth, to subscribe for and purchase from the Company, One Hundred Seventeen Thousand Eight Hundred Twenty (117,820) fully paid and non-assessable shares of the Common Stock at the Exercise Price (as defined below). The Exercise Price of such shares is subject to adjustment as provided in Section 8. As used herein, the following terms shall have the following meanings:

"1934 Act" means the Securities Exchange Act of 1934, as amended.

"Acknowledgment of Exercise" has the meaning given to it in Section 3(a).

"Act" means the Securities Act of 1933, as amended, and as the same may be in effect from time to time.

"Charter" means the Company's Certificate of Incorporation or other constitutional document, as the same may be amended from time to time.

"Claims" has the meaning given to it in Section 12(p).

"Common Stock" means the Company's common stock, $0.001 par value per share.

"Company" has the meaning given to it in the preamble to this Warrant.

"Company SEC Reports" means, collectively (a) the Company's most recent Annual Report on Form 10-K (the "Annual Report"), (b) the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2013 and (any other statement, report (including without limitation, Current Reports on Form 8-K) or registration statement filed by the Company with the SEC during the period commencing subsequent to the period covered by such Annual Report (including, in each case, all exhibits thereto and documents incorporated by reference therein).

"Effective Date" has the meaning given to it in the preamble to this Warrant.

"Exercise Price" means $6.79.

"Lender" has the meaning given to it in the Loan Agreement.

"Loan Agreement" has the meaning given to it in the preamble to this Warrant.

"Merger Event" means (a) a merger or consolidation involving the Company in which (i) the Company is not the surviving entity, or (ii) the outstanding shares of the Company's capital stock are otherwise converted into or exchanged for shares of capital of another entity; or (b) the sale of all or substantially all of the assets of the Company.

"Net Issuance" has the meaning given to it in Section 3(a).

"Notice of Exercise" has the meaning given to it in Section 3(a).

"Public Acquisition" means any Merger Event which is effected such that (i) the holders of Common Stock shall be entitled to receive (A) cash and/or (B) shares of stock that are of a publicly traded company listed on a national market or exchange which may be resold without restrictions (other than restrictions to which Warrantholder may separately agree in writing) after the consummation of such Merger Event, and (ii) the Company's stockholders own less than 50% of the voting securities of the surviving entity.

"Purchase Price" means, with respect to any exercise of this Warrant, an amount equal to the Exercise Price as of the relevant time multiplied by the number of shares of Common Stock requested to be exercised under this Warrant pursuant to such exercise.

"Rules" has the meaning given to it in Section 12(q).

"Transfer Notice" has the meaning given to it in Section 11.

"Warrant" has the meaning given to it in the preamble to this Warrant.

"Warrant Term" has the meaning given to it in Section 2.

"Warrantholder" has the meaning given to it in the preamble to this Warrant.

SECTION 2. TERM OF THE AGREEMENT.

Except as otherwise provided for herein, the term of this Warrant (the "Warrant Term") and the right to purchase Common Stock as granted herein shall commence on the Effective Date and shall be exercisable for a period ending upon the earlier to occur of (A) five (5) years from the Effective Date or (B) the consummation of a Public Acquisition.

SECTION 3. EXERCISE OF THE PURCHASE RIGHTS.

(a) Exercise. The purchase rights set forth in this Warrant are exercisable by the Warrantholder, in whole or in part, at any time, or from time to time, during the Warrant Term, by tendering to the Company at its principal office a notice of exercise in the form attached hereto as Exhibit A (the "Notice of Exercise"), duly completed and executed. Promptly upon receipt of the Notice of Exercise and the payment of the Purchase Price in accordance with the terms set forth below, and in no event later than five (5) business days thereafter, the Company shall issue to the Warrantholder a certificate for the number of shares of Common Stock purchased and shall execute the acknowledgment of exercise in the form attached hereto as Exhibit B (the "Acknowledgment of Exercise") indicating the number of shares which remain subject to future purchases, if any.

The Purchase Price may be paid at the Warrantholder's election either (i) by cash or check, or (ii) by surrender of all or a portion of the Warrant for shares of Common Stock to be exercised under this Warrant and, if applicable, an amended Warrant representing the remaining number of shares purchasable hereunder, as determined below ("Net Issuance"). If the Warrantholder elects the Net Issuance method, the Company will issue Common Stock in accordance with the following formula:

$$X = \frac{Y(A-B)}{A}$$

Where: X = the number of shares of Common Stock to be issued to the Warrantholder.

Y = the number of shares of Common Stock requested to be exercised under this Warrant.

A = the fair market value of one (1) share of Common Stock at the time of issuance of such shares of Common Stock.

B = the Exercise Price.

For purposes of the above calculation, the fair market value of one (1) share of Common Stock shall mean:

(i) if the Common Stock is traded on the New York Stock Exchange, the American Stock Exchange, any exchange operated by the NASDAQ Stock Market, LLC or any other securities exchange, the fair market value of one (1) share of Common Stock shall be deemed to be the volume-weighted average of the closing prices over the twenty (20) consecutive trading days ending two (2) trading days before the day the fair market value of one (1) share of Common Stock is being determined; or

(ii) if at any time the Common Stock is not listed on any securities exchange, the fair market value of one (1) share of Common Stock shall be the highest price per share which the Company could obtain from a willing buyer (not a current employee or director) for shares of Common Stock sold by the Company (based upon the valuation by the Board of all shares of Common Stock), from authorized but unissued shares, as determined in good faith by its Board of Directors, unless this Warrant is being exercised in connection with a Merger Event, in which case the fair market value of one (1) share of Common Stock shall be deemed to be the per share value received by the holders of the Common Stock on a Common Stock equivalent basis pursuant to such Merger Event.

Upon partial exercise by either cash or Net Issuance, the Company shall promptly issue an agreement substantially in the form of the Warrant representing the remaining number of shares purchasable hereunder. All other terms and conditions of such agreement shall be identical to those contained herein, including, but not limited to the Effective Date hereof.

(b) Exercise Prior to Expiration. To the extent that the Warrantholder has not exercised its purchase rights under this Warrant to all Common Stock subject hereto, and if the fair market value of one share of the Common Stock is greater than the Exercise Price then in effect, this Warrant shall be deemed automatically exercised pursuant to Section 3(a) (even if not surrendered) immediately before the expiration of the Warrant Term. For purposes of such automatic exercise, the fair market value of one share of the Common Stock upon such expiration shall be determined pursuant to Section 3(a). To the extent this Warrant or any portion thereof is deemed automatically exercised pursuant to this Section 3(b), the Company agrees to promptly notify the Warrantholder of the number of shares of Common Stock, if any, the Warrantholder is to receive by reason of such automatic exercise.

(c) Legend. Each certificate for the shares of Common Stock purchased upon exercise of this Warrant shall bear the restrictive legend set forth on the first page of this Warrant. Such legend shall be removed and the Company shall, or shall instruct its transfer agent to, issue a certificate without such legend or any other legend to the holder of such shares (i) if such shares are sold or transferred pursuant to an effective registration statement under the Act covering the resale of such shares by the holder thereof, (ii) if such shares are sold or transferred pursuant to Rule 144 under the Act, (iii) if, upon advice of counsel to the Company, such shares are eligible for resale without any restrictions under Rule 144 under the Act, or (iv) upon the request of such holder if such request is accompanied (at such holder's expense) by a written opinion of counsel reasonably satisfactory to the Company that registration is not required under the Act or any applicable state securities laws for the resale of the shares of Common Stock purchased upon exercise of this Warrant. The removal of such restrictive legend from any certificates representing the shares of Common Stock purchased upon exercise of this Warrant is predicated upon the Company's reliance that the holder of such shares would sell, transfer, assign, pledge, hypothecate or otherwise dispose of such shares pursuant to either the registration requirements of the Act, including any applicable prospectus delivery requirements, or an exemption therefrom, and that if such shares are sold pursuant to a registration statement, they will be sold in compliance with the plan of distribution set forth therein.

SECTION 4. RESERVATION OF SHARES.

During the Warrant Term, the Company will at all times have authorized and reserved a sufficient number of shares of its Common Stock to provide for the exercise of the rights to purchase Common Stock as provided for herein.

SECTION 5. NO FRACTIONAL SHARES OR SCRIP.

No fractional shares or scrip representing fractional shares shall be issued upon the exercise of this Warrant, but in lieu of such fractional shares the Company shall make a cash payment therefor upon the basis of the Exercise Price then in effect.

SECTION 6. NO RIGHTS AS SHAREHOLDER/STOCKHOLDER.

This Warrant does not entitle the Warrantholder to any voting rights or other rights as a shareholder/stockholder of the Company prior to the exercise of this Warrant.

SECTION 7. WARRANTHOLDER REGISTRY.

The Company shall maintain a registry showing the name and address of the registered holder of this Warrant. Warrantholder's initial address, for purposes of such registry, is set forth in Section 12(g). Warrantholder may change such address by giving written notice of such changed address to the Company.

SECTION 8. ADJUSTMENT RIGHTS.

The Exercise Price and the number of shares of Common Stock purchasable hereunder are subject to adjustment, as follows:

(a) Merger Event. If at any time there shall be a Merger Event that is not a Public Acquisition, then, as a part of such Merger Event, lawful provision shall be made so that the Warrantholder shall thereafter be entitled to receive, upon exercise of this Warrant, the kind, amount and value of shares of Common Stock or other securities or property of the successor, surviving or purchasing corporation resulting from, or participating in, such Merger Event that would have been issuable if Warrantholder had exercised this Warrant immediately prior to such Merger Event. In any such case, appropriate adjustment (as determined in good faith by the Company's Board of Directors) shall be made in the application of the provisions of this Warrant with respect to the rights and interests of the Warrantholder after such Merger Event to the end that the provisions of this Warrant (including adjustments of the Exercise Price) shall be applicable in their entirety, and to the greatest extent possible. Without limiting the foregoing, in connection with any Merger Event other than a Public Acquisition, upon the closing thereof, the successor, surviving or purchasing entity shall assume the obligations of this Warrant. The provisions of this Section 8(a) shall similarly apply to successive Merger Events. In connection with a Merger Event and upon Warrantholder's written election to the Company, the Company shall cause this Warrant to be exchanged for the consideration that Warrantholder would have received if Warrantholder chose to exercise its right to have shares issued pursuant to the Net Issuance provisions of this Warrant prior to the Merger Event without actually exercising such right, acquiring such shares and exchanging such shares for such consideration.

(b) Reclassification of Shares. Except as set forth in Section 8(a), if the Company at any time shall, by combination, reclassification, exchange or subdivision of securities or otherwise, change any of the securities as to which purchase rights under this Warrant exist into the same or a different number of securities of any other class or classes, this Warrant shall thereafter represent the right to acquire such number and kind of securities as would have been issuable as the result of such change with respect to the securities which were subject to the purchase rights under this Warrant immediately prior to such combination, reclassification, exchange, subdivision or other change.

(c) Subdivision or Combination of Shares. If the Company at any time shall combine or subdivide its Common Stock, (i) in the case of a subdivision, the Exercise Price shall be proportionately decreased, and the number of shares of Common Stock issuable upon exercise of this Warrant shall be proportionately increased, or (ii) in the case of a combination, the Exercise Price shall be proportionately increased, and the number of shares of Common Stock issuable upon the exercise of this Warrant shall be proportionately decreased.

(d) Stock Dividends. If the Company at any time while this Warrant is outstanding and unexpired shall:

(i) pay a dividend with respect to the Common Stock payable in Common Stock, then the Exercise Price shall be adjusted, from and after the date of determination of stockholders entitled to receive such dividend or distribution, to that price determined by multiplying the Exercise Price in effect immediately prior to such date of determination by a fraction (A) the numerator of which shall be the total number of shares of Common Stock outstanding immediately prior to such dividend or distribution, and (B) the denominator of which shall be the total number of shares of Common Stock outstanding immediately after such dividend or distribution; or

(ii) make any other distribution with respect to the Common Stock, except any distribution specifically provided for in any other clause of this Section 8, then, in each such case, provision shall be made by the Company such that the Warrantholder shall receive upon exercise of this Warrant a proportionate share of any such distribution as though it were the holder of the Common Stock as of the record date fixed for the determination of the stockholders of the Company entitled to receive such distribution.

(e) Antidilution Rights. To the extent that any antidilution rights applicable to the Common Stock purchasable hereunder may be set forth in the Charter, the Company shall promptly provide the Warrantholder with a copy of any restatement, amendment, modification or waiver of the Charter that impairs or reduces such antidilution rights; provided, that no such amendment, modification or waiver shall impair or reduce the antidilution rights, if any, set forth in the Charter with respect to the Common Stock unless such amendment, modification or waiver affects the rights of Warrantholder with respect to the Common Stock issuable hereunder generally in the same manner as it affects all other holders of Common Stock. The Company shall, within ten (10) business days of the end of each fiscal quarter following the Effective Date, provide Warrantholder with written notice of any issuance of its stock or other equity security during such fiscal quarter that triggered an antidilution adjustment under the antidilution rights applicable to the Common Stock purchasable hereunder, if any, as may be set forth in the Charter, which notice shall include (a) the price at which such stock or security was sold, (b) the number of shares issued, and (c) such other information as reasonably necessary for Warrantholder to verify that such antidilution adjustment occurred and the amount of any such adjustment. For the avoidance of doubt, there shall be no duplicate antidilution adjustment pursuant to this subsection (e), the forgoing subsection (d) and the Charter.

(f) Notice of Adjustments. If: (i) the Company shall declare any dividend or distribution upon its Common Stock, whether in stock, cash, property or other securities (assuming Lender consents to a dividend involving cash, property or other securities under the Loan Agreement, if the consent of Lender is then required by the terms of the Loan Agreement); (ii) the Company shall offer for subscription prorata to the holders of Common Stock any additional shares of stock of any class or other rights; (iii) there shall be any Merger Event; (iv) the Company shall sell, lease, license or otherwise transfer all or substantially all of its assets; or (v) there shall be any voluntary dissolution, liquidation or winding up of the Company; then, in connection with each such event, the Company shall send to the Warrantholder: (A) at least ten (10) days' prior written notice of the date on which the books of the Company shall close or a record shall be taken for such dividend, distribution, subscription rights (specifying the date on which the holders of Common Stock shall be entitled thereto) or for determining rights to vote in respect of such Merger Event, sale, lease, license or other transfer of all or substantially all assets, dissolution, liquidation or winding up; and (B) in the case of any such Merger Event, dissolution, liquidation or winding up, at least ten (10) days' prior written notice of the date when the same shall take place (and specifying the date on which the holders of Common Stock shall be entitled to exchange their Common Stock for securities or other property deliverable upon such Merger Event, dissolution, liquidation or winding up).

Each such written notice shall set forth, in reasonable detail, (i) the event requiring the notice, and (ii) if any adjustment is required to be made, (A) the amount of such adjustment, (B) the method by which such adjustment was calculated, (C) the adjusted Exercise Price (if the Exercise Price has been adjusted), and (D) the number of shares subject to purchase hereunder after giving effect to such adjustment, and shall be given by first class mail, postage prepaid, or by reputable overnight courier with all charges prepaid, addressed to the Warrantholder at the address for Warrantholder set forth in the registry referred to in Section 7.

(g) Timely Notice. Failure to timely provide such notice required by subsection (f) above shall entitle Warrantholder to retain the benefit of the applicable notice period notwithstanding anything to the contrary contained in any insufficient notice received by Warrantholder ; provided, that, notwithstanding anything herein to the contrary, the failure to timely provide such notice or any defect therein shall not affect the validity of the corporate action required to be described in such notice.

SECTION 9. REPRESENTATIONS, WARRANTIES AND COVENANTS OF THE COMPANY.

(a) Reservation of Common Stock. The Common Stock issuable upon exercise of the Warrantholder's rights has been duly and validly reserved and, when issued in accordance with the provisions of this Warrant, will be validly issued, fully paid and non-assessable, and will be free of any taxes, liens, charges or encumbrances of any nature whatsoever; provided, that the Common Stock issuable pursuant to this Warrant may be subject to restrictions on transfer under state and/or federal securities laws. The Company has made available to the Warrantholder true, correct and complete copies of its Charter and current bylaws. The issuance of certificates for shares of Common Stock upon exercise of this Warrant shall be made without charge to the Warrantholder for any issuance tax in respect thereof, or other cost incurred by the Company in connection with such exercise and the related issuance of shares of Common Stock; provided, that the Company shall not be required to pay any tax which may be payable in respect of any transfer and the issuance and delivery of any certificate in a name other than that of the Warrantholder.

(b) Due Authority. The execution and delivery by the Company of this Warrant and the performance of all obligations of the Company hereunder, including the issuance to Warrantholder of the right to acquire the shares of Common Stock, have been duly authorized by all necessary corporate action on the part of the Company. This Warrant: (1) does not violate the Company's Charter or current bylaws; (2) does not contravene any law or governmental rule, regulation or order applicable to it; and (3) does not and will not contravene any provision of, or constitute a default under, any indenture, mortgage, contract or other instrument to which it is a party or by which it is bound. This Warrant constitutes a legal, valid and binding agreement of the Company, enforceable in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, fraudulent conveyance, moratorium or other laws affecting the enforcement of creditors' rights in general, and except that the enforceability of this Warrant is subject to general principles of equity.

(c) Consents and Approvals. No consent or approval of, giving of notice to, registration with, or taking of any other action in respect of any state, federal or other governmental authority or agency is required on the part of the Company with respect to the execution, delivery and performance by the Company of its obligations under this Warrant, except for the filing of notices pursuant to Regulation D under the Act and any filing required by applicable state securities law, which filings will be effective by the time required thereby.

(d) Issued Securities. All issued and outstanding shares of Common Stock have been duly authorized and validly issued and are fully paid and nonassessable. All outstanding shares of Common Stock and any other Company securities were issued in compliance with all applicable federal and state securities laws in all material respects. In addition, as of the date immediately preceding the Effective Date:

(i) The authorized capital of the Company consists of (A) 100,000,000 shares of Common Stock, of which 43,039,269 shares are issued and outstanding, and (B) 10,000,000 shares of Preferred Stock, of which no shares are issued and outstanding.

(ii) The Company has reserved an aggregate of 740,562 shares of Common Stock for issuance under its 2011 Equity Incentive Plan and 2011 Employee Stock Purchase Plan, not including any automatic increases to the shares reserved for issuance under such plans as described in the Company SEC Reports. Stock options or other equity awards to purchase or acquire an aggregate of 4,989,398 shares of Common Stock are outstanding. In addition, there are warrants for the purchase of 1,497,939 shares of Common Stock outstanding. Except as set forth in the Company SEC Reports, there are no other options, warrants, conversion privileges or other rights presently outstanding to purchase or otherwise acquire any authorized but unissued shares of the Company's capital stock or other securities of the Company. The Company has no outstanding loans to any employee, officer or director of the Company, and the Company agrees not to enter into any such loan or otherwise guarantee the payment of any loan made to an employee, officer or director by a third party.

(iii) No stockholder of the Company has preemptive rights to purchase new issuances of the Company's capital stock pursuant to the Charter or the Company's bylaws.

(e) Exempt Transaction. Subject to the accuracy of the Warrantholder's representations in Section 10, the issuance of the Common Stock upon exercise of this Warrant will each constitute a transaction exempt from (i) the registration requirements of Section 5 of the Act, in reliance upon Section 4(2) thereof, and (ii) the qualification requirements of the applicable state securities laws.

(f) Compliance with Rule 144. If the Warrantholder proposes to sell Common Stock issuable upon the exercise of this Warrant in compliance with Rule 144 promulgated by the SEC, then, upon Warrantholder's written request to the Company, the Company shall furnish to the Warrantholder, within five days after receipt of such request, a written statement confirming the Company's compliance with the filing requirements of the SEC as set forth in such Rule, as such Rule may be amended from time to time, and shall issue appropriate instructions to its transfer agent to remove the restrictive legend from any certificates evidencing the Common Stock issuable upon the exercise of this Warrant.

(g) Information Rights. During the Warrant Term, Warrantholder shall be entitled to the information rights contained in Sections 7.1(a), 7.1(b) and 7.1(c) of the Loan Agreement, and Sections 7.1(a), 7.1(b) and 7.1(c) of the Loan Agreement are hereby incorporated into this Warrant by this reference as though fully set forth herein, provided, however, that the Company shall not, once all Indebtedness (as defined in the Loan Agreement) owed by the Company to Lender has been repaid, be required to deliver any information required by Section 7.1 of the Loan Agreement so long as the Company is subject to SEC reporting obligations under Section 13(a) or Section 15(d) of the 1934 Act. Notwithstanding anything to the contrary in this Section 9(g) or elsewhere herein, to the extent that this Warrant is transferred to a third party that is not then a party to the Loan Agreement as Lender or is not an affiliate of Lender, then this Section 9(g) shall automatically terminate and shall have no further force or effect.

(h) Listing of Shares. The Common Stock is listed for trading on the NASDAQ Global Market as of the Effective Date.

SECTION 10. REPRESENTATIONS AND COVENANTS OF THE WARRANTHOLDER.

This Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Warrantholder:

(a) Investment Purpose. The right to acquire Common Stock or the Common Stock issuable upon exercise of the Warrantholder's rights contained herein has been, and such shares will be, acquired for investment and not with a view to the sale or distribution of any part thereof, and the Warrantholder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration under the Act or an exemption from the registration requirements of the Act. Warrantholder is not a registered broker-dealer under Section 15 of the 1934 Act or an entity engaged in a business that would require it to be so registered as a broker-dealer.

(b) Private Issue. The Warrantholder understands (i) that the Common Stock issuable upon exercise of this Warrant is not registered under the Act or qualified under applicable state securities laws on the ground that the issuance contemplated by this Warrant will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this Section 10.

(c) Financial Risk. The Warrantholder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment, and has the ability to bear the economic risks of its investment.

(d) Risk of No Registration. Without in any way limiting the Company's obligations under this Warrant, the Warrantholder understands that if the Common Stock is not registered with the SEC pursuant to Section 12 of the 1934 Act or the Company is not required to file reports pursuant to Section 13(a) or Section 15(d) of the 1934 Act, or if a registration statement is not effective under the Act covering the resale of the shares of Common Stock issuable upon exercise of the Warrant when it desires to sell (i) the rights to purchase Common Stock pursuant to this Warrant or (ii) the Common Stock issuable upon exercise of the right to purchase, as applicable, it may be required to hold such securities for an indefinite period. The Warrantholder also understands that any sale of (A) its rights hereunder to purchase Common Stock or (B) Common Stock issued or issuable hereunder which might be made by it in reliance upon Rule 144 under the Act may be made only in accordance with the terms and conditions of that Rule.

(e) Accredited Investor. Warrantholder is, and on each date on which it exercises any portion of this Warrant, it will be, an "accredited investor" within the meaning of the Securities and Exchange Rule 501 of Regulation D, as presently in effect.

(f) No Short Sales. Warrantholder has not engaged, and will not engage, in "short sales" of the Common Stock of the Company. The term "short sale" shall mean any sale of a security which the seller does not own or any sale which is consummated by the delivery of a security borrowed by, or for the account of, the seller.

SECTION 11. TRANSFERS.

Subject to compliance with applicable federal and state securities laws, this Warrant and all rights hereunder are transferable, in whole or in part, without charge to the holder hereof (except for transfer taxes) upon surrender of this Warrant properly endorsed. Each taker and

holder of this Warrant, by taking or holding the same, consents and agrees that this Warrant, when endorsed in blank, shall be deemed negotiable, and that the holder hereof, when this Warrant shall have been so endorsed and its transfer recorded on the Company's books, shall be treated by the Company and all other persons dealing with this Warrant as the absolute owner hereof for any purpose and as the person entitled to exercise the rights represented by this Warrant. The transfer of this Warrant shall be recorded on the books of the Company upon receipt by the Company of a notice of transfer in the form attached hereto as Exhibit C (the "Transfer Notice"), at its principal offices and the payment to the Company of all transfer taxes and other governmental charges imposed on such transfer. Until the Company receives such Transfer Notice, the Company may treat the registered owner hereof as the owner for all purposes.

SECTION 12. MISCELLANEOUS.

(a) Effective Date. The provisions of this Warrant shall be construed and shall be given effect in all respects as if it had been executed and delivered by the Company on the date hereof. This Warrant shall be binding upon any successors or assigns of the Company and the Warrantholder.

(b) Remedies. In the event of any default hereunder, the non-defaulting party may proceed to protect and enforce its rights either by suit in equity and/or by action at law, including but not limited to an action for damages as a result of any such default, and/or an action for specific performance for any default where Warrantholder will not have an adequate remedy at law and where damages will not be readily ascertainable. The Company expressly agrees that it shall not oppose an application by the Warrantholder or any other person entitled to the benefit of this Warrant requiring specific performance of any or all provisions hereof or enjoining the Company from continuing to commit any such breach of this Warrant.

(c) No Impairment of Rights. The Company will not, by amendment of its Charter or through any other means, avoid or seek to avoid the observance or performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such actions as may be reasonably necessary or appropriate in order to protect the rights of the Warrantholder against impairment. Notwithstanding the foregoing, nothing in this Section 12(c) shall negate or otherwise restrict or impair the Company's right to effect any changes to the rights, preferences, privileges or restrictions associated with the Common Stock so long as such changes do not adversely affect the rights, preferences, privileges or restrictions associated with the shares of Common Stock issuable upon exercise of this Warrant in a manner different from the effect that such changes have generally on the rights, preferences, privileges or restrictions associated with all other shares of Common Stock.

(d) Additional Documents. The Company, upon execution of this Warrant, shall provide the Warrantholder with certified resolutions with respect to the representations and warranties set forth in the first sentence of Section 9(b).

(e) Attorney's Fees. In any litigation, arbitration or court proceeding between the Company and the Warrantholder relating hereto, the prevailing party shall be entitled to reasonable attorneys' fees and expenses and all reasonable costs of proceedings incurred in enforcing this Warrant. For the purposes of this Section 12(e), attorneys' fees shall include without limitation reasonable fees incurred in connection with the following: (i) contempt proceedings; (ii) discovery; (iii) any motion, proceeding or other activity of any kind in connection with an insolvency proceeding; (iv) garnishment, levy, and debtor and third party examinations; and (v) post-judgment motions and proceedings of any kind, including without limitation any activity taken to collect or enforce any judgment.

(f) Severability. In the event any one or more of the provisions of this Warrant shall for any reason be held invalid, illegal or unenforceable, the remaining provisions of this Warrant shall be unimpaired, and the invalid, illegal or unenforceable provision shall be replaced by a mutually acceptable valid, legal and enforceable provision, which comes closest to the intention of the parties underlying the invalid, illegal or unenforceable provision.

(g) Notices. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication that is required, contemplated, or permitted under this Warrant or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (i) the day of transmission by facsimile or hand delivery if transmission or delivery occurs on a business day at or before 5:00 pm in the time zone of the recipient, or, if transmission or delivery occurs on a non-business day or after such time, the first business day thereafter, or the first business day after deposit with an overnight express service or overnight mail delivery service; or (ii) the third calendar day after deposit in the United States mails, with proper first class postage prepaid (provided, that any Advance Request shall not be deemed received until Lender's actual receipt thereof), and shall be addressed to the party to be notified as follows:

If to Warrantholder:

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.
Legal Department
Attention: Chief Legal Officer and Manuel Henriquez
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

If to the Company:

ACELRX PHARMACEUTICALS, INC.
Attention: Chief Financial Officer
351 Galveston Drive
Redwood City, CA 94063
Facsimile: 650-216-6500
Telephone: 650-216-3511

With a copy to (which shall not constitute notice hereunder):

Mark. B Weeks
Cooley LLP
3175 Hanover Street
Palo Alto, CA 94304-1130
Facsimile: (650) 849-7400
Telephone: (650) 843-5011

or to such other address as each party may designate for itself by like notice.

(h) Entire Agreement; Amendments. This Warrant constitutes the entire agreement and understanding of the parties hereto in respect of the subject matter hereof, and supersede and replace in their entirety any prior proposals, term sheets, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof (including Lender's proposal letter dated November 19, 2013). None of the terms of this Warrant may be amended except by an instrument executed by each of the parties hereto.

(i) Headings. The various headings in this Warrant are inserted for convenience only and shall not affect the meaning or interpretation of this Warrant or any provisions hereof.

(j) Advice of Counsel. Each of the parties represents to each other party hereto that it has discussed (or had an opportunity to discuss) with its counsel this Warrant and, specifically, the provisions of Sections 12(n), 12(o), 12(p), 12(q) and 12(r).

(k) No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Warrant. In the event an ambiguity or question of intent or interpretation arises, this Warrant shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Warrant.

(l) No Waiver. Except for the requirement that this Warrant be exercised (or be deemed exercised), if at all, during the Warrant Term, no omission or delay by either party hereto at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by the other party hereto at any time designated, shall be a waiver of any such right or remedy to which such party is entitled, nor shall it in any way affect the right of such party to enforce such provisions thereafter.

(m) Survival. All agreements, representations and warranties contained in this Warrant or in any document delivered pursuant hereto shall be for the benefit of Warrantholder and the Company, as the case may be, and shall survive the execution and delivery of this Warrant and the expiration or other termination of this Warrant.

(n) Governing Law. This Warrant has been negotiated and delivered to Warrantholder in the State of California, and shall have been accepted by Warrantholder in the State of California. Delivery of Common Stock to Warrantholder by the Company under this Warrant is due in the State of California. This Warrant shall be governed by, and construed and enforced in accordance with, the laws of the State of California, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

(o) Consent to Jurisdiction and Venue. All judicial proceedings arising in or under or related to this Warrant may be brought in any state or federal court of competent jurisdiction located in the State of California. By execution and delivery of this Warrant, each party hereto generally and unconditionally: (a) consents to personal jurisdiction in Santa Clara County, State of California; (b) waives any objection as to jurisdiction or venue in Santa Clara County, State of California; (c) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (d) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Warrant. Service of process on any party hereto in any action arising out of or relating to this Warrant shall be effective if given in accordance with the requirements for notice set forth in Section 12(g), and shall be deemed effective and received as set forth in Section 12(g). Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

(p) Mutual Waiver of Jury Trial. Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes arising out of this Warrant be resolved by a judge applying such applicable laws. EACH OF THE COMPANY AND WARRANTHOLDER SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY

CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, "CLAIMS") ASSERTED BY THE COMPANY AGAINST WARRANTHOLDER OR ITS ASSIGNEE OR BY WARRANTHOLDER OR ITS ASSIGNEE AGAINST THE COMPANY RELATING TO THIS WARRANT. This waiver extends to all such Claims arising out of this Warrant, including Claims that involve persons other than the Company and Warrantholder, and any Claims for damages, breach of contract, specific performance, or any equitable or legal relief of any kind, arising out of this Warrant.

(q) Arbitration. If the Mutual Waiver of Jury Trial set forth in Section 12(p) is ineffective or unenforceable, the parties agree that all Claims shall be resolved by reference to a private judge sitting without a jury, pursuant to Code of Civil Procedure Section 638, before a mutually acceptable referee or, if the parties cannot agree, a referee selected by the Presiding Judge of Santa Clara County, California. Such proceeding shall be conducted in Santa Clara County, California, with California rules of evidence and discovery applicable to such proceeding.

(r) Prejudgment Relief. In the event Claims are to be resolved by judicial reference, either party may seek from a court of competent jurisdiction identified in Section 12(o), any prejudgment order, writ or other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by judicial reference.

(s) Counterparts. This Warrant and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts, and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument.

(t) Specific Performance. The parties hereto hereby declare that it is impossible to measure in money the damages which will accrue to a party hereto by reason of the other party's failure to perform any of the obligations under this Warrant and agree that the terms of this Warrant shall be specifically enforceable by either party hereto. If a party hereto institutes any action or proceeding to specifically enforce the provisions hereof, any person against whom such action or proceeding is brought hereby waives the claim or defense therein that such party has an adequate remedy at law, and such person shall not offer in any such action or proceeding the claim or defense that such remedy at law exists.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have caused this Warrant to be executed by its officers thereunto duly authorized as of the Effective Date.

COMPANY: **ACELRX PHARMACEUTICALS, INC.**

By: /s/ James Welch

Name: James Welch

Title: CFO

WARRANTHOLDER: **HERCULES TECHNOLOGY GROWTH CAPITAL, INC.**

By: /s/ Ben Bang

Name: Ben Bang

Title:

EXHIBIT A

NOTICE OF EXERCISE

To: ACELRX PHARMACEUTICALS, INC. (the "Company")

(1) The undersigned Warrantholder hereby elects to purchase [_____] shares of the Common Stock of the Company, pursuant to the terms of that certain Warrant Agreement, dated as of December 16, 2013, between the Company and the Warrantholder (the "Warrant"), and [CASH PAYMENT: tenders herewith payment of the Purchase Price in full, together with all applicable transfer taxes, if any.] [NET ISSUANCE: elects pursuant to Section 3(a) of the Warrant to effect a Net Issuance.]

(2) Please issue a certificate or certificates representing said shares of Common Stock in the name of the Warrantholder or in such other name as is specified below:

_____

(Name)

_____

(Address)

WARRANTHOLDER:

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

By: _____

Name: _____

Title: _____

EXHIBIT B

ACKNOWLEDGMENT OF EXERCISE

The undersigned, as representative of AcelRx Pharmaceuticals, Inc. (the "Company"), hereby acknowledges receipt of the "Notice of Exercise" from Hercules Technology Growth Capital, Inc., ("Warrantholder"), to purchase [_____] shares of the Common Stock of the Company, pursuant to the terms of that certain Warrant Agreement, dated as of December 16, 2013, between the Company and the Warrantholder (the "Warrant"), and further acknowledges that [_____] shares remain subject to purchase under the terms of the Warrant.

COMPANY: ACELRX PHARMACEUTICALS, INC.

By: _____

Title: _____

Date: _____

EXHIBIT C

TRANSFER NOTICE

FOR VALUE RECEIVED, that certain Warrant Agreement, dated as of December 16, 2013, between AcelRx Pharmaceuticals, Inc., as the Company, and Hercules Technology Growth Capital, Inc., as the Warrantholder (the "Warrant"), and all rights evidenced thereby are hereby transferred and assigned to

_____

(Please Print)

whose address is _____

_____

Dated: _____

Holder's Signature: _____

Holder's Address: _____

_____

Signature Guaranteed: _____

NOTE: The signature to this Transfer Notice must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Exhibit 10.10

AMENDED AND RESTATED
LOAN AND SECURITY AGREEMENT

THIS LOAN AND SECURITY AGREEMENT is made and dated as of December 16, 2013 and is entered into by and between ACELRX PHARMACEUTICALS, INC., a Delaware corporation, and each of its subsidiaries, (hereinafter collectively referred to as the "Borrower"), HERCULES TECHNOLOGY II, L.P., a Delaware limited partnership, and HERCULES TECHNOLOGY GROWTH CAPITAL, INC., a Maryland corporation (collectively, "Lender") and amends and restates in its entirety that certain Loan and Security Agreement between Borrower, as the borrower and Hercules Technology II, L.P., a Delaware limited partnership, and Hercules Technology Growth Capital, Inc., collectively as the lender, dated June 29, 2011 (the "Original Agreement").

RECITALS

A. Borrower has requested Lender to make available to Borrower a loan in an aggregate principal amount of up to Forty Million Dollars ($40,000,000) (the "Term Loan");

B. Part of the proceeds of the Term Loan will be used to refinance loans funded under the Original Agreement and for general corporate purposes; and

C. Lender is willing to make the Term Loan on the terms and conditions set forth in this Agreement.

AGREEMENT

NOW, THEREFORE, Borrower and Lender agree as follows:

SECTION 1. DEFINITIONS AND RULES OF CONSTRUCTION

1.1 Unless otherwise defined herein, the following capitalized terms shall have the following meanings:

"Account Control Agreement(s)" means any agreement entered into by and among the Lender, Borrower and a third party Bank or other institution (including a Securities Intermediary) in which Borrower maintains a Deposit Account or an account holding Investment Property and which grants Lender a perfected first priority security interest in the subject account or accounts.

"ACH Authorization" means the ACH Debit Authorization Agreement in substantially the form of Exhibit I.

"Advance(s)" means a Term Loan Advance.

"Advance Date" means the funding date of any Advance.

"Advance Request" means a request for an Advance submitted by Borrower to Lender in substantially the form of Exhibit A.

"Agreement" means this Loan and Security Agreement, as amended from time to time.

"Assignee" has the meaning given to it in Section 11.13.

"Borrower Products" means all products, software, service offerings, technical data or technology currently being designed, manufactured or sold by Borrower or which Borrower intends to sell, license, or distribute in the future including any products or service offerings under development, collectively, together with all products, software, service offerings, technical data or technology that have been sold, licensed or distributed by Borrower since its incorporation.

"Cap" shall have the meaning assigned to such term in Section 2.2(e)(iii).

"Cash" means all cash and liquid funds.

"Change in Control" means any reorganization, recapitalization, consolidation or merger (or similar transaction or series of related transactions) of Borrower or any Subsidiary, sale or exchange of outstanding shares (or similar transaction or series of related transactions) of Borrower or any Subsidiary in which the holders of Borrower or Subsidiary's outstanding shares immediately before consummation of such transaction or series of related transactions do not, immediately after consummation of such transaction or series of related transactions, retain shares representing more than fifty percent (50%) of the voting power of the surviving entity of such transaction or series of related transactions (or the parent of such surviving entity if such surviving entity is wholly owned by such parent), in each case without regard to whether Borrower or Subsidiary is the surviving entity.

"Claims" has the meaning given to it in Section 11.10.

"Closing Date" means the date of this Agreement.

"Collateral" means the property described in Section 3.

"Collateral Agent" means Hercules Technology II, L.P..

"Commitment Fee" means $25,000, which fee was paid to Lender upon countersignature of Lender's proposal letter dated November 19, 2013, and shall be deemed fully earned on such date regardless of the early termination of this Agreement.

"Common Stock" means the Common Stock, $0.001 par value per share, of the Company.

"Confidential Information" has the meaning given to it in Section 11.12.

"Contingent Obligation" means, as applied to any Person, any direct or indirect liability, contingent or otherwise, of that Person with respect to (i) any indebtedness, lease, dividend, letter of credit or other obligation of another, including any such obligation directly or indirectly guaranteed, endorsed, co-made or discounted or sold with recourse by that Person, or in respect of which that Person is otherwise directly or indirectly liable; (ii) any obligations with respect to undrawn letters of credit, corporate credit cards or merchant services issued for the account of that Person; and (iii) all obligations arising under any interest rate, currency or commodity swap agreement, interest rate cap agreement, interest rate collar agreement, or other agreement or arrangement designated to protect a Person against fluctuation in interest rates, currency exchange rates or commodity prices; provided, however, that the term "Contingent Obligation" shall not include endorsements for collection or deposit in the ordinary course of business. The amount of any Contingent Obligation shall be deemed to be an amount equal to the stated or determined amount of the primary obligation in respect of which such Contingent Obligation is made or, if not stated or determinable, the maximum reasonably anticipated liability in respect thereof as determined by such Person in good faith; provided, however, that such amount shall not in any event exceed the maximum amount of the obligations under the guarantee or other support arrangement.

"Copyright License" means any written agreement granting any right to use any Copyright or Copyright registration, now owned or hereafter acquired by Borrower or in which Borrower now holds or hereafter acquires any interest.

"Copyrights" means all copyrights, whether registered or unregistered, held pursuant to the laws of the United States, any State thereof, or of any other country.

"Delivery Date" has the meaning given to it in Section 2.2(e)(i).

"Deposit Accounts" means any "deposit accounts," as such term is defined in the UCC, and includes any checking account, savings account, or certificate of deposit.

"ERISA" is the Employee Retirement Income Security Act of 1974, and its regulations.

"Event of Default" has the meaning given to it in Section 9.

"Facility Charge" means one percent (1.00%) of the Maximum Term Loan Amount.

"FDA" means the U.S. Food and Drug Administration or any successor entity performing similar functions.

"Financial Statements" has the meaning given to it in Section 7.1.

"Fixed Conversion Price" has the meaning given to it in Section 2.2(e)(i).

"GAAP" means generally accepted accounting principles in the United States of America, as in effect from time to time.

"Indebtedness" means indebtedness of any kind, including (a) all indebtedness for borrowed money or the deferred purchase price of property or services (excluding trade credit entered into in the ordinary course of business due within sixty (60) days), including reimbursement and other obligations with respect to surety bonds and letters of credit, (b) all obligations evidenced by notes, bonds, debentures or similar instruments, (c) all capital lease obligations, and (d) all Contingent Obligations.

"Insolvency Proceeding" is any proceeding by or against any Person under the United States Bankruptcy Code, or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other relief.

"Intellectual Property" means all of Borrower's Copyrights; Trademarks; Patents; Licenses; trade secrets and inventions; mask works; Borrower's applications therefor and reissues, extensions, or renewals thereof; and Borrower's goodwill associated with any of the foregoing, together with Borrower's rights to sue for past, present and future infringement of Intellectual Property and the goodwill associated therewith.

"Investment" means any beneficial ownership (including stock, partnership or limited liability company interests) of or in any Person, or any loan, advance or capital contribution to any Person.

"Joinder Agreements" means for each Subsidiary, a completed and executed Joinder Agreement in substantially the form attached hereto as Exhibit G.

"Lender" has the meaning given to it in the preamble to this Agreement.

"Lender Expenses" are all audit fees and expenses, costs, and expenses (including reasonable attorneys' fees and expenses) for preparing, negotiating, administering, defending and enforcing the Loan Documents (including, without limitation, those incurred in connection with appeals or Insolvency Proceedings) or otherwise incurred with respect to Borrower.

"License" means any Copyright License, Patent License, Trademark License or other license of rights or interests.

"Lien" means any mortgage, deed of trust, pledge, hypothecation, assignment for security, security interest, encumbrance, levy, lien or charge of any kind, whether voluntarily incurred or arising by operation of law or otherwise, against any property, any conditional sale or other title retention agreement, and any lease in the nature of a security interest.

"Loan" means the Advances made under this Agreement.

"Loan Documents" means this Agreement, the Notes, the ACH Authorization, the Account Control Agreements, the Joinder Agreements, all UCC Financing Statements, the Warrant, and any other documents executed in connection with the Secured Obligations or the transactions contemplated hereby, as the same may from time to time be amended, modified, supplemented or restated.

"Material Adverse Effect" means a material adverse effect upon: (i) the business, operations, properties, assets, or condition (financial or otherwise) of Borrower; or (ii) the ability of Borrower to perform the Secured Obligations in accordance with the terms of the Loan Documents, or the ability of Lender to enforce any of its rights or remedies with respect to the Secured Obligations; or (iii) the Collateral or Lender's Liens on the Collateral or the priority of such Liens.

"Maximum Term Loan Amount" means Forty Million and No/100 Dollars ($40,000,000).

"Maximum Rate" shall have the meaning assigned to such term in Section 2.3.

"Note" means Secured Convertible Term Promissory Notes in substantially the form of Exhibit B-1 and Exhibit B-2.

"Optional Prepayment" has the meaning given to it in Section 2.2(e)(i).

"Optional Prepayment Date" has the meaning given to it in Section 2.2(e)(i).

"Patent License" means any written agreement granting any right with respect to any invention on which a Patent is in existence or a Patent application is pending, in which agreement Borrower now holds or hereafter acquires any interest.

"Patents" means all letters patent of, or rights corresponding thereto, in the United States or in any other country, all registrations and recordings thereof, and all applications for letters patent of, or rights corresponding thereto, in the United States or any other country.

"Performance Milestone" means the date upon which the FDA approves Zalviso.

"Permitted Indebtedness" means: (i) Indebtedness of Borrower in favor of Lender arising under this Agreement or any other Loan Document; (ii) Indebtedness existing on the Closing Date which is disclosed in Schedule 1A; (iii) Indebtedness of up to $200,000 outstanding at any time secured by a lien described in clause (vii) of the defined term "Permitted Liens," provided such Indebtedness does not exceed the lesser of the cost or fair market value of the Equipment financed with such Indebtedness; (iv) Indebtedness to trade creditors incurred in the ordinary course of business, including Indebtedness incurred in the ordinary course of business with corporate credit cards; (v) Indebtedness that also constitutes a Permitted Investment; (vi) Subordinated Indebtedness; (vii) reimbursement obligations in connection with letters of credit that are secured by cash or cash equivalents and issued on behalf of the Borrower or a Subsidiary thereof in an amount not to exceed $200,000 at any time outstanding, (viii) other Indebtedness in an amount not to exceed $500,000 at any time outstanding, and (ix) extensions, refinancings and renewals of any items of Permitted Indebtedness, provided that the principal amount is not increased or the terms modified to impose materially more burdensome terms upon Borrower or its Subsidiary, as the case may be.

"Permitted Investment" means: (i) Investments existing on the Closing Date which are disclosed in Schedule 1B; (ii) (a) marketable direct obligations issued or unconditionally guaranteed by the United States of America or any agency or any State thereof maturing within one year from the date of acquisition thereof, (b) commercial paper maturing no more than one year from the date of creation thereof and currently having a rating of at least A-2 or P-2 from either Standard & Poor's Corporation or Moody's Investors Service, (c) certificates of deposit issued by any bank with assets of at least $500,000,000 maturing no more than one year from the date of investment therein, and (d) money market accounts; (iii) Investments consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of business; (iv) repurchases of stock from former employees, directors, or consultants of Borrower under the terms of applicable repurchase agreements at the original issuance price of such securities in an aggregate amount not to exceed $250,000 in any fiscal year, provided that no Event of Default has occurred, is continuing or would exist after giving effect to the repurchases; (v) Investments accepted in connection with Permitted Transfers; (vi) Investments (including debt obligations) received in connection with the bankruptcy or reorganization of customers or suppliers and in settlement of delinquent obligations of, and other disputes with, customers or suppliers arising in the ordinary course of Borrower's business; (vii) Investments consisting of notes receivable of, or prepaid royalties and other credit extensions, to customers and suppliers who are not affiliates, in the ordinary course of business, provided that this subparagraph (vii) shall not apply to Investments of Borrower in any Subsidiary; (viii) Investments consisting of loans not involving the net transfer on a substantially contemporaneous basis of cash proceeds to employees, officers or directors relating to the purchase of capital stock of Borrower pursuant to employee stock purchase plans or other similar agreements approved by Borrower's Board of Directors; (ix) Investments consisting of travel advances, employee relocation loans and other employee loans and advances in the ordinary course of business and not in excess of $500,000 in the aggregate; (x) Investments in newly-formed Subsidiaries organized in the United States, provided that such Subsidiaries enter into a Joinder Agreement promptly after their formation by Borrower and execute such other documents as shall be reasonably requested by Lender; (xi) Investments in subsidiaries organized outside of the United States approved in advance in writing by Lender; (xii) joint ventures or strategic alliances in the ordinary course of Borrower's business consisting of the nonexclusive licensing of technology, the development of technology or the providing of technical support, provided that any cash Investments by Borrower do not exceed $100,000 in the aggregate in any fiscal year; (xiii) Investments constituting mergers or acquisitions permitted by Section 7.10; and (xiv) additional Investments that do not exceed $500,000 in the aggregate.

"Permitted Liens" means any and all of the following: (i) Liens in favor of Lender; (ii) Liens existing on the Closing Date which are disclosed in Schedule 1C; (iii) Liens for taxes, fees, assessments or other governmental charges or levies, either not delinquent or being contested in good faith by appropriate proceedings; provided, that Borrower maintains adequate reserves therefor in accordance with GAAP to the extent required thereby; (iv) Liens securing claims or demands of materialmen, artisans, mechanics, carriers, warehousemen, landlords and other like Persons arising in the ordinary course of Borrower's business and imposed without action of such parties; provided, that the payment thereof is not overdue; (v) Liens arising from judgments, decrees or attachments in circumstances which do not constitute an Event of Default hereunder; (vi) the following deposits, to the extent made in the ordinary course of business: deposits under worker's compensation, unemployment insurance, social security and other similar laws, or to

secure the performance of bids, tenders or contracts (other than for the repayment of borrowed money) or to secure indemnity, performance or other similar bonds for the performance of bids, tenders or contracts (other than for the repayment of borrowed money) or to secure statutory obligations (other than liens arising under ERISA or environmental liens) or surety or appeal bonds, or to secure indemnity, performance or other similar bonds; (vii) Liens on Equipment or software or other intellectual property constituting purchase money liens and liens in connection with capital leases securing Indebtedness permitted in clause (iii) of "Permitted Indebtedness"; (viii) Liens incurred in connection with Subordinated Indebtedness; (ix) leasehold interests in leases or subleases and licenses granted in the ordinary course of business and not interfering in any material respect with the business of the licensor; (x) Liens in favor of customs and revenue authorities arising as a matter of law to secure payment of custom duties that are promptly paid on or before the date they become due; (xi) Liens on insurance proceeds securing the payment of financed insurance premiums that are promptly paid on or before the date they become due (provided that such Liens extend only to such insurance proceeds and not to any other property or assets); (xii) statutory and common law rights of set-off and other similar rights as to deposits of cash and securities in favor of banks, other depository institutions and brokerage firms; (xiii) easements, zoning restrictions, rights-of-way and similar encumbrances on real property imposed by law or arising in the ordinary course of business so long as they do not materially impair the value or marketability of the related property; (xiv) Liens on cash or cash equivalents securing obligations permitted under clause (vii) of the definition of Permitted Indebtedness; and (xv) Liens incurred in connection with the extension, renewal or refinancing of the indebtedness secured by Liens of the type described in clauses (i) through (xi) above; provided, that any extension, renewal or replacement Lien shall be limited to the property encumbered by the existing Lien and the principal amount of the indebtedness being extended, renewed or refinanced (as may have been reduced by any payment thereon) does not increase.

"Permitted Transfers" means (i) sales of Inventory in the normal course of business, (ii) non-exclusive licenses and similar arrangements for the use of Intellectual Property in the ordinary course of business and licenses that could not result in a legal transfer of title of the licensed property but that may be exclusive in respects other than territory and that may be exclusive as to territory only as to discrete geographical areas outside of the United States in the ordinary course of business, or (iii) dispositions of worn-out, obsolete or surplus Equipment at fair market value in the ordinary course of business, (iv) dispositions expressly permitted under Section 7.7, 7.8 or 7.10 hereof, (v) dispositions arising from the abandonment of fixtures and other similar tenant improvements in connection with office relocations, and (vi) other Transfers of assets having a fair market value of not more than $250,000 in the aggregate in any fiscal year.

"Person" means any individual, sole proprietorship, partnership, joint venture, trust, unincorporated organization, association, corporation, limited liability company, institution, other entity or government.

"Preferred Stock" means at any given time any equity security issued by Borrower that has any rights, preferences or privileges senior to Borrower's Common Stock.

"Prepayment Charge" shall have the meaning assigned to such term in Section 2.5.

"Principal Installment Due Date" has the meaning given to it in Section 2.2(e)(i).

"Principal Installment Payment" has the meaning given to it in Section 2.2(e)(i).

"Receivables" means (i) all of Borrower's Accounts, Instruments, Documents, Chattel Paper, Supporting Obligations, letters of credit, proceeds of any letter of credit, and Letter of Credit Rights, and (ii) all customer lists, software, and business records related thereto.

"Repayment Election Notice" has the meaning given to it in Section 2.2(e)(i).

"Rule 144" means Rule 144 under the Securities Act.

"SBA" shall have the meaning assigned to such term in Section 7.15.

"SBIC" shall have the meaning assigned to such term in Section 7.15.

"SBIC Act" shall have the meaning assigned to such term in Section 7.15.

"SEC" has the meaning given to it in Section 2.2(e)(iv).

"Secured Obligations" means Borrower's obligations under this Agreement and any Loan Document, including any obligation to pay any amount now owing or later arising. Notwithstanding the foregoing, the Secured Obligations shall not include any of Borrower's obligations, liabilities or duties under the Warrant.

"Securities Act" means the Securities Act of 1933, as amended.

"Stock Payment Conditions" shall have the meaning assigned to such term in Section 2.2(e)(ii).

"Stock Payment Option" has the meaning given to it in Section 2.2(e)(i).

"Subordinated Indebtedness" means Indebtedness subordinated to the Secured Obligations in amounts and on terms and conditions satisfactory to Lender in its sole discretion.

"Subsidiary" means an entity, whether corporate, partnership, limited liability company, joint venture or otherwise, in which Borrower owns or controls 50% or more of the outstanding voting securities, including each entity listed on Schedule 1 hereto.

"Term Commitment" means as to any Lender, the obligation of such Lender, if any, to make a Term Loan Advance to the Borrower in a principal amount not to exceed the amount set forth under the heading "Term Commitment" opposite such Lender's name on Schedule 1.1.

"Term Loan Advance" means any Term Loan funds advanced under this Agreement.

"Term Loan Interest Rate" means for any day a per annum rate of interest equal to the greater of either (i) 9.1% plus the prime rate as reported in The Wall Street Journal minus 5.25%, and (ii) 9.10%.

"Term Loan Maturity Date" means October 1, 2017, or, if the Performance Milestone has occurred on or before April 1, 2015, January 1, 2018.

"Trademark License" means any written agreement granting any right to use any Trademark or Trademark registration, now owned or hereafter acquired by Borrower or in which Borrower now holds or hereafter acquires any interest.

"Trademarks" means all trademarks (registered, common law or otherwise) and any applications in connection therewith, including registrations, recordings and applications in the United States Patent and Trademark Office or in any similar office or agency of the United States, any State thereof or any other country or any political subdivision thereof.

"UCC" means the Uniform Commercial Code as the same is, from time to time, in effect in the State of California; provided, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection or priority of, or remedies with respect to, Lender's Lien on any Collateral is governed by the Uniform Commercial Code as the same is, from time to time, in effect in a jurisdiction other than the State of California, then the term "UCC" shall mean the Uniform Commercial Code as in effect, from time to time, in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority or remedies and for purposes of definitions related to such provisions.

"Warrant" means the warrant entered into in connection with the Loan.

"1934 Act" has the meaning given to it in Section 2.2(e)(iii).

Unless otherwise specified, all references in this Agreement or any Annex or Schedule hereto to a "Section," "subsection," "Exhibit," "Annex," or "Schedule" shall refer to the corresponding Section, subsection, Exhibit, Annex, or Schedule in or to this Agreement. Unless otherwise specifically provided herein, any accounting term used in this Agreement or the other Loan Documents shall have the meaning customarily given such term in accordance with GAAP, and all financial computations hereunder shall be computed in accordance with GAAP, consistently applied. Unless otherwise defined herein or in the other Loan Documents, terms that are used herein or in the other Loan Documents and defined in the UCC shall have the meanings given to them in the UCC.

SECTION 2. THE LOAN

2.1 Reserved.

2.2 Term Loan.

(a) Advances. Subject to the terms and conditions of this Agreement, Lender will make, and Borrower agrees to draw, a Term Loan Advance of $15,000,000 on the Closing Date. Beginning at any time on or after the Closing Date through June 30, 2014, Borrower may request a second Term Loan Advance of up to $10,000,000. Subject to Borrower's achievement of the Performance Milestone, from December 15, 2014 through March 15, 2015, Borrower may request a third Term Loan Advance of up to $15,000,000. Each Term Loan Advance shall be subject to the conditions precedent set forth in Sections 4.2 and 4.3. The aggregate outstanding Term Loan Advances may be up to the Maximum Term Loan Amount.

(b) Advance Request. To obtain a Term Loan Advance, Borrower shall complete, sign and deliver an Advance Request (at least five business days before the Advance Date). Lender shall fund the Term Loan Advance in the manner requested by the Advance Request provided that each of the conditions precedent to such Term Loan Advance is satisfied as of the requested Advance Date.

(c) Interest. The principal balance of each Term Loan Advance shall bear interest thereon from such Advance Date at the Term Loan Interest Rate based on a year consisting of 360 days, with interest computed daily based on the actual number of days elapsed. The Term Loan Interest Rate will float and change on the day the Prime Rate changes from time to time.

(d) Payment. Borrower will pay interest on each Term Loan Advance on the first day of each month, beginning the month after the Advance Date. Borrower shall repay the aggregate Term Loan principal balance in thirty (30) equal monthly installments of principal and interest beginning April 1, 2015, or, if the Performance Milestone has occurred on or before April 1, 2015, Borrower shall repay the aggregate Term Loan principal balance in twenty-four (24) equal monthly installments of principal and interest beginning January 1, 2016, and continuing on the first business day of each month thereafter. The entire Term Loan principal balance and all accrued but unpaid interest hereunder, shall be due and payable on the Term Loan Maturity Date. Borrower shall make all payments under this Agreement without setoff, recoupment or deduction and regardless of any counterclaim or defense. Except to the extent Borrower pays any regularly scheduled installments of principal and/or optional prepayments of principal in Common stock in accordance with, and subject to the limitations set forth in, Section 2.2(e), Lender will initiate debit entries to the Borrower's account as authorized on the ACH Authorization on each payment date of all periodic obligations payable to Lender under each Note or Term Loan Advance.

(e) Payment in Cash or Common Stock of Monthly Amount or Prepayment Principal Amount.

(i) Payment in Cash or Common Stock. Subject to satisfaction of the Stock Payment Conditions and compliance with the other terms and conditions of this Section 2.2(e), Borrower may elect to pay, in whole or in part, any regularly scheduled installment of principal (a "Principal Installment Payment") or any

optional prepayment of principal (an "Optional Prepayment") by converting the Notes into shares of Common Stock in lieu of payment in cash (such option, the "Stock Payment Option"). In order to validly exercise a Stock Payment Option, Borrower (A) must deliver written notice thereof, in the form attached hereto as Exhibit J, to Lender (a "Repayment Election Notice") five (5) days prior to (i) the applicable due date of the Principal Installment Payment (the "Principal Installment Due Date") or (ii) the Optional Prepayment (such date, the "Optional Prepayment Date") and (B) shall either (i) (provided that Borrower's transfer agent is participating in the Fast Automated Securities Transfer Program of the Depository Trust Company) credit to Lender by no later than the first trading day following the applicable Principal Installment Due Date or Optional Prepayment Date (such date, the "Delivery Date") such aggregate number of shares of Common Stock to be issued to Lender with respect to such Repayment Election Notice, as determined in accordance with this Section 2.2(e) (which shares shall be free of any restrictions on transfer), or (ii) deliver to Collateral Agent, on behalf of Lender, stock certificates, without restrictive legend, evidencing the number of shares of Common Stock with respect to such Repayment Election Notice, as determined in accordance with this Section 2.2(e), by no later than the first trading day following the applicable Delivery Date. All payments in respect of a Principal Installment Payment and Optional Prepayment shall be made in cash, unless (i) Borrower timely delivers a Repayment Election Notice in accordance with the immediately preceding sentence, (ii) Borrower timely delivers the requisite stock certificates or credits the shares of Common Stock to Lender, free of restrictive legends, in accordance with this Section 2.2(e) and (iii) the Stock Payment Conditions are satisfied in respect of such payment. A Repayment Election Notice, once delivered by Borrower, shall be irrevocable unless otherwise agreed, in writing, by Collateral Agent, on behalf of Lender. If Borrower elects to convert the Notes to repay a Principal Installment Payment or make an Optional Prepayment, in whole or in part, in shares of Common Stock, the number of such shares of Common Stock to be issued in respect of such Principal Installment Payment or Optional Prepayment shall be equal to the number determined by dividing (x) the product of (A) the principal amount to be paid in shares of Common Stock and (B) 103%, by (y) the Fixed Conversion Price. For purposes hereof, the "Fixed Conversion Price" shall be $9.30; provided, however, that upon the occurrence of any stock split, stock dividend, combination of shares or reverse stock split pertaining to the Common Stock, the Fixed Conversion Price shall be proportionately increased or decreased as necessary to reflect the proportionate change in the shares of Common Stock issued and outstanding as a result of such stock split, stock dividend, combination of shares or reverse stock split. Any shares of Common Stock issued pursuant to a Repayment Election Notice shall be deemed to be issued upon conversion of the Notes.

(ii) Stock Payment Conditions. Notwithstanding the foregoing, Borrower's right to deliver, and Lender's obligation to accept, shares of Common Stock in lieu of payment in cash of a Principal Installment Payment or Optional Prepayment, as applicable, is conditioned on the satisfaction of each of the following conditions (the "Stock Payment Conditions") as of such Delivery Date: (A) the closing price of the shares of Common Stock as reported by Bloomberg, L.P. on the NASDAQ market for each of the seven (7) consecutive trading days immediately preceding the Delivery Date shall be greater than or equal to 115% of the Fixed Conversion Price; (B) the Common Stock issued in connection with any such payment does not exceed 15% of the total trading volume of the Common Stock for the twenty-two (22) consecutive trading days immediately prior to and including such Delivery Date; (C) only one Repayment Election Notice may be given in any calendar month; (D) the aggregate principal amount to be paid in shares of Common Stock pursuant to Section 2.2 of this Agreement shall not exceed Five Million Dollars ($5,000,000); (E) the Common Stock is (and was on each of the twenty-two (22) consecutive trading days immediately preceding such Delivery Date) quoted or listed on the NASDAQ market; (F) a registration statement is effective and available for the resale of all of the shares of Common Stock to be delivered on such Delivery Date, or such shares of Common Stock are eligible for resale to the public pursuant to Rule 144 without any limitation; (G) after giving effect to the issuance of such shares of Common Stock to Lender, Lender would not (A) beneficially own, together with its affiliates, Common Stock in excess of the limitations specified in subsection (e)(iii) below and (B) have been issued shares of Common Stock pursuant to all Repayment Election Notices in an aggregate amount in excess of the Cap; (H) as of such Delivery Date, there is no outstanding Event of Default and there is no breach or default that, if left uncured, would result in an Event of Default; and (I) Borrower shall have sufficient authorized but unissued shares of Common Stock to provide for the issuance of the shares of Common Stock pursuant to the Repayment Election Notice. If any of the Stock Payment Conditions are not satisfied as of a Delivery Date, Borrower shall not be permitted to pay, and the Lender shall not be obligated to accept, the Principal Installment Payment or Optional Prepayment, as applicable, in shares of Common Stock, and Borrower shall instead pay such principal amount in cash; provided, however , that the Stock Payment Conditions set forth in clauses (A), (B), (C), (E), (F) and (H) above may be waived by a writing executed by both Borrower and Lender. In the event the Company is relying upon an effective registration statement to satisfy clause (F) of the Stock Payment Conditions, each of the Company and Lender shall provide customary indemnification to one another with respect to such registration statement in a form acceptable to the Company and Lender. By no later than the first trading day following the Delivery Date, Borrower shall either (i) (provided that Borrower's transfer agent is participating in the Fast Automated Securities Transfer Program of the Depository Trust Company) credit to Lender the shares of Common Stock to be delivered by Borrower with respect to the portion of the Principal Installment Payment or Optional Prepayment being paid in shares of Common Stock or (ii) deliver to Collateral Agent, on behalf of each Lender, certificates, free of restrictive legends, evidencing the shares of Common Stock to be delivered by Borrower with respect to the portion of the Principal Installment Payment or Optional Prepayment being paid in shares of Common Stock, which shares of Common Stock, in the case of clauses (i) and (ii), shall be allocated among each Lender in the manner specified to Borrower by the Collateral Agent.

(iii) Beneficial Ownership Limitation. Notwithstanding any provision herein to the contrary, Lender, together with its affiliates, shall not be permitted to beneficially own a number of shares of Common Stock (other than shares that may be deemed beneficially owned except for being subject to a limitation analogous to the limitation contained in this Section 2.2(e)(iii)) in excess of 9.99% of the number of shares of Common Stock then issued and outstanding, it being the intent of Borrower and Lender that Lender, together with its affiliates, not be deemed at any time to have the power to vote or dispose of greater than 9.99% of the number of shares of Common Stock issued and outstanding at any time; *provided*, *however*, that Lender shall have the right, upon 61 days' prior written notice to Borrower, to waive the 9.99% limitation of this subsection (e)(iii). Notwithstanding anything contained herein to the contrary, Borrower shall not be permitted to issue to Lender, and Lender shall not be required to accept, shares of Common Stock pursuant to a Repayment Election Notice if and to the extent such issuance, when taking together with all other issuances pursuant to prior Repayment Election Notices, would result in (A) the issuance of more than 19.99% of the Common Stock outstanding as of the date of this Agreement or (B) Lender, together with its affiliates, beneficially owning in excess of 19.99% of the outstanding Common Stock (each of clauses (A) and (B) are referred to herein as the "Cap"). As used herein, beneficial ownership shall be determined in accordance with Section 13(d) of the Securities Exchange Act of 1934, as amended (the "1934 Act"). For any reason at any time, upon written or oral request of Lender, Borrower shall within one business day confirm orally and in writing to Lender the number of shares of Common Stock then issued and outstanding as of any given date.

(iv) With a view to making available to Lender the benefits of Rule 144 (or its successor rule) and any other rule or regulation of the Securities and Exchange Commission (the "SEC") that may at any time permit Lender to sell shares of Common Stock issued pursuant to Section 2.2(e) of this Agreement to the public without registration, Borrower covenants and agrees to: (i) make and keep public information available, as those terms are understood and defined in Rule 144, until six (6) months after such date as all of the shares of Common Stock issued pursuant to Section 2.2(e) of this Agreement may be sold without restriction by Lender pursuant to Rule 144 or any other rule of similar effect; (ii) file with the SEC in a timely manner all reports and other documents required of Borrower under the 1934 Act; and (iii) furnish to Lender upon request, as long as Lender owns any shares of Common Stock issued pursuant to Section 2.2(e) of this Agreement, such information as may be reasonably requested in order to avail Lender of any rule or regulation of the SEC that permits the selling of any such shares of Common Stock without registration.

(v) Borrower covenants and agrees to reserve from its duly authorized capital stock not less than the number of shares of Common Stock that may be issuable upon payment of any Principal Installment Payment or Optional Prepayment pursuant to Section 2.2(e) of this Agreement. Borrower further represents, warrants and covenants that, upon issuance of any shares of Common Stock pursuant to Section 2.2(e) of this Agreement, such shares of Common Stock shall be validly issued, fully paid and non-assessable and free from all preemptive or similar rights, taxes, liens and charges with respect to the issue thereof.

(vi) For so long as Lender holds any shares of Common Stock issued pursuant to Section 2.2(e) of this Agreement, Borrower shall maintain the Common Stock's authorization for listing on NASDAQ and Borrower shall not take any action which would reasonably be executed to result in the delisting or suspension of the Common Stock on NASDAQ.

2.3 Maximum Interest. Notwithstanding any provision in this Agreement, the Notes, or any other Loan Document, it is the parties' intent not to contract for, charge or receive interest at a rate that is greater than the maximum rate permissible by law that a court of competent jurisdiction shall deem applicable hereto (which under the laws of the State of California shall be deemed to be the laws relating to permissible rates of interest on commercial loans) (the "Maximum Rate"). If a court of competent jurisdiction shall finally determine that Borrower has actually paid to Lender an amount of interest in excess of the amount that would have been payable if all of the Secured Obligations had at all times borne interest at the Maximum Rate, then such excess interest actually paid by Borrower shall be deemed retroactively applied as of the date of receipt of such payment as follows: first, to the payment of the Secured Obligations, consisting of the outstanding principal; second, after all principal is repaid, to the payment of Lender's accrued interest, costs, expenses, professional fees and any other Secured Obligations; and third, after all Secured Obligations are repaid, the excess (if any) shall be refunded to Borrower.

2.4 Default Interest. In the event any payment is not paid on the scheduled payment date, an amount equal to five percent (5%) of the past due amount shall be payable on demand. In addition, upon the occurrence and during the continuation of an Event of Default hereunder, all Secured Obligations, including principal, interest, compounded interest, and Lender's fees and expenses in accordance with Section 11.11 hereof, shall bear interest at a rate per annum equal to the rate set forth in Section 2.2(c) plus five percent (5%) per annum. In the event any interest is not paid when due hereunder, delinquent interest shall be added to principal and shall bear interest on interest, compounded at the rate set forth in Section 2.2(c) or this Section 2.4, as applicable.

2.5 Prepayment. At its option upon at least 7 business days prior notice to Lender, Borrower may prepay all, but not less than all, of the outstanding Advances by paying the entire principal balance and all accrued and unpaid interest, together with a prepayment charge equal to the following percentage of the Advance amount being prepaid: if such Advance amounts are prepaid in any of the first twelve (12) months following the Closing Date, 3.0%; after twelve (12) months but prior to twenty four (24) months, 2.0%;

and thereafter, 1.0% (each, a "Prepayment Charge"). Borrower agrees that the Prepayment Charge is a reasonable calculation of Lender's lost profits in view of the difficulties and impracticality of determining actual damages resulting from an early repayment of the Advances. Borrower shall prepay the outstanding amount of all principal and accrued interest through the prepayment date and the Prepayment Charge upon the occurrence of a Change in Control. Notwithstanding the above, no Prepayment Charge shall be due in connection with term loan advances funded under the Original Agreement.

2.6 End of Term Charge.

(a) On the earliest to occur of (i) the Term Loan Maturity Date, (ii) the date that Borrower prepays the outstanding Secured Obligations, or (iii) the date that the Secured Obligations become due and payable, Borrower shall pay Lender a charge of $1,700,000. Notwithstanding the required payment date of such charge, it shall be deemed earned by Lender as of the Closing Date.

(b) On December 1, 2014, Borrower shall pay Lender a charge of $200,000 as scheduled in connection with the term loan advances funded in connection with the Original Agreement. Notwithstanding the required payment date of such charge, it shall be deemed earned by Lender as of the Closing Date.

2.7 Lender Investment Representations. The Note is being issued to Lender in reliance upon the following representations and covenants of Lender (which, for the avoidance of doubt, are being made severally, but not jointly, by each Lender):

(a) Investment Purpose. The Note has been, and the Common Stock issuable upon conversion of the Note by Borrower in accordance with Section 2.2(e) of this Agreement will be, acquired by Lender for investment and not with a view to the sale or distribution of any part thereof, and Lender has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration under the Securities Act or an exemption from the registration requirements of the Securities Act. Lender is not a registered broker-dealer under Section 15 of the 1934 Act or an entity engaged in a business that would require it to be so registered as a broker-dealer.

(b) Private Issue. The Lender understands (i) that the Common Stock issuable upon conversion of the Note by Borrower in accordance with Section 2.2(e) of this Agreement is not registered under the Securities Act or qualified under applicable state securities laws on the ground that the issuance contemplated upon conversion of the Note will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this Section 2.7.

(c) Financial Risk. The Lender has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment in the Note, and has the ability to bear the economic risks of its investment.

(d) Risk of No Registration. Without in any way limiting the Company's obligations under this Agreement, the Lender understands that if the Common Stock is not registered with the SEC pursuant to Section 12 of the 1934 Act or the Company is not required to file reports pursuant to Section 13(a) or Section 15(d) of the 1934 Act, or if a registration statement is not effective under the Securities Act covering the resale of the shares of Common Stock issued to Lender upon conversion of the Note when it desires to sell such shares of Common Stock it may be required to hold such securities for an indefinite period. The Lender also understands that any sale of Common Stock issuable by Borrower to Lender upon conversion of the Note in accordance with Section 2.2(e) of this Agreement which might be made by it in reliance upon Rule 144 under the Securities Act may be made only in accordance with the terms and conditions of Rule 144.

(e) Accredited Investor. The Lender is an "accredited investor" within the meaning of Rule 501 of Regulation D promulgated under the Securities Act.

(f) No Short Sales. The Lender has not engaged, and will not engage, in "short sales" of the Common Stock of the Company. The term "short sale" shall mean any sale of a security which the seller does not own or any sale which is consummated by the delivery of a security borrowed by, or for the account of, the seller.

(g) Legends. The Lender understands and agrees that each Note issued pursuant to this Agreement may bear the following legend.

THIS SECURED CONVERTIBLE TERM PROMISSORY NOTE HAS NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND, ACCORDINGLY, MAY NOT BE TRANSFERRED UNLESS (I) THIS NOTE HAS BEEN REGISTERED FOR SALE PURSUANT TO THE SECURITIES ACT OF 1933, AS AMENDED, (II) THIS NOTE MAY BE SOLD PURSUANT TO RULE 144, OR (III) THE BORROWER HAS RECEIVED AN OPINION OF COUNSEL REASONABLY SATISFACTORY TO IT THAT SUCH TRANSFER MAY LAWFULLY BE MADE WITHOUT REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

Lender acknowledges and agrees that the issuance of a certificate or certificates without restrictive legend for, or deposit with the Depositary Trust Company via book-entry of, any shares of Common Stock that may be issued upon conversion of the Notes is predicated upon the Company's reliance that the holder of such shares would sell, transfer, assign, pledge, hypothecate or otherwise dispose of such shares pursuant to either the registration requirements of the Act, including any applicable prospectus delivery requirements, or an exemption therefrom, and that if such shares are sold pursuant to a registration statement, they will be sold in compliance with the plan of distribution set forth therein. Lender acknowledges that the foregoing representations, warranties and covenants will be relied upon by the Company, the Company's transfer agent, and by the Company's counsel in delivering an opinion to such transfer agent, in connection with not including restrictive legends on the certificates representing the shares, in order to facilitate the sale of the shares pursuant Rule 144 or an effective registration statement.

The foregoing representations and covenants of Lender do not imply any period of time that Lender will hold any shares of Common Stock issuable to Lender in accordance with Section 2.2(e) of this Agreement, and any shares of Common Stock issuable to Lender in accordance with Section 2.2(e) of this Agreement shall (i) not contain any restrictions on transfer and (ii) either be subject to an effective resale registration statement or be eligible for resale to the public pursuant to Rule 144 without any limitation.

2.8 Pro Rata Treatment. Each payment (including prepayment) on account of any fee and any reduction of the Term Loans shall be made pro rata according to the Term Commitments of the relevant Lender.

SECTION 3. SECURITY INTEREST

3.1 As security for the prompt, complete and indefeasible payment when due (whether on the payment dates or otherwise) of all the Secured Obligations, Borrower grants to Lender a security interest in all of Borrower's personal property now owned or hereafter acquired, including the following (collectively, the "Collateral"): (a) Receivables; (b) Equipment; (c) Fixtures; (d) General Intangibles (other than Intellectual Property); (e) Inventory; (f) Investment Property (but excluding thirty-five percent (35%) of the capital stock of any foreign Subsidiary that constitutes a Permitted Investment); (g) Deposit Accounts; (h) Cash; (i) Goods; and other tangible and intangible personal property of Borrower whether now or hereafter owned or existing, leased, consigned by or to, or acquired by, Borrower and wherever located; and, to the extent not otherwise included, all Proceeds of each of the foregoing and all accessions to, substitutions and replacements for, and rents, profits and products of each of the foregoing; provided, however, that the Collateral shall include all Accounts and General Intangibles that consist of rights to payment and proceeds from the sale, licensing or disposition of all or any part, or rights in, the Intellectual Property (the "Rights to Payment"). Notwithstanding the foregoing, if a judicial authority (including a U.S. Bankruptcy Court) holds that a security interest in the underlying Intellectual Property is necessary to have a security interest in the Rights to Payment, then the Collateral shall automatically, and effective as of the date of this Agreement, include the Intellectual Property to the extent necessary to permit perfection of Lender's security interest in the Rights to Payment. Upon payment in full in cash of the Secured Obligations (other than inchoate indemnity obligations and any other obligations which, by their terms, are to survive the termination of this Agreement) and at such time as this Agreement has been terminated, the Collateral Agent shall, at Borrower's sole cost and expense, release its Liens in the Collateral and all rights therein shall revert to Borrower.

SECTION 4. CONDITIONS PRECEDENT TO LOAN

The obligations of Lender to make the Loan hereunder are subject to the satisfaction by Borrower of the following conditions:

4.1 Initial Advance. On or prior to the Closing Date, Borrower shall have delivered to Lender the following:

(a) executed originals of the Loan Documents, Account Control Agreements, and all other documents and instruments reasonably required by Lender to effectuate the transactions contemplated hereby or to create and perfect the Liens of Lender with respect to all Collateral, in all cases in form and substance reasonably acceptable to Lender;

(b) certified copy of resolutions of Borrower's board of directors evidencing approval of (i) the Loan and other transactions evidenced by the Loan Documents; and (ii) the Warrant and transactions evidenced thereby;

(c) certified copies of the Certificate of Incorporation and the Bylaws, as amended through the Closing Date, of Borrower;

(d) a certificate of good standing for Borrower from its state of incorporation and similar certificates from all other jurisdictions in which it does business and where the failure to be qualified would have a Material Adverse Effect;

(e) payment of the Facility Charge and reimbursement of Lender's current expenses reimbursable pursuant to this Agreement, which amounts may be deducted from the initial Advance; and

(f) such other documents as Lender may reasonably request.

4.2 All Advances. On each Advance Date:

(a) Lender shall have received (i) an Advance Request for the relevant Advance as required by Section 2.2(b), each duly executed by Borrower's Chief Executive Officer or Chief Financial Officer, and (ii) any other documents Lender may reasonably request.

(b) The representations and warranties set forth in this Agreement and in Section 5 and in the Warrant shall be true and correct in all material respects on and as of the Advance Date with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date.

(c) Borrower shall be in compliance with all the terms and provisions set forth herein and in each other Loan Document on its part to be observed or performed, and at the time of and immediately after such Advance no Event of Default shall have occurred and be continuing.

(d) Each Advance Request shall be deemed to constitute a representation and warranty by Borrower on the relevant Advance Date as to the matters specified in paragraphs (b) and (c) of this Section 4.2 and as to the matters set forth in the Advance Request.

4.3 No Default. As of the Closing Date and each Advance Date, (i) no fact or condition exists that would (or would, with the passage of time, the giving of notice, or both) constitute an Event of Default and (ii) no event that has had or could reasonably be expected to have a Material Adverse Effect has occurred and is continuing.

SECTION 5. REPRESENTATIONS AND WARRANTIES OF BORROWER

Borrower represents and warrants that:

5.1 Corporate Status. Borrower is a corporation duly organized, legally existing and in good standing under the laws of the State of Delaware, and is duly qualified as a foreign corporation in all jurisdictions in which the nature of its business or location of its properties require such qualifications and where the failure to be qualified could reasonably be expected to have a Material Adverse Effect. Borrower's present name, former names (if any), locations, place of formation, tax identification number, organizational identification number and other information are correctly set forth in Exhibit C, as may be updated by Borrower in a written notice (including any Compliance Certificate) provided to Lender after the Closing Date.

5.2 Collateral. Borrower owns the Collateral and the Intellectual Property, free of all Liens, except for Permitted Liens. Borrower has the power and authority to grant to Lender a Lien in the Collateral as security for the Secured Obligations.

5.3 Consents. Borrower's execution, delivery and performance of the Notes, this Agreement and all other Loan Documents, and Borrower's execution of the Warrant, (i) have been duly authorized by all necessary corporate action of Borrower, (ii) will not result in the creation or imposition of any Lien upon the Collateral, other than Permitted Liens and the Liens created by this Agreement and the other Loan Documents, (iii) do not violate any provisions of Borrower's Certificate or Articles of Incorporation (as applicable), bylaws, or any, law, regulation, order, injunction, judgment, decree or writ to which Borrower is subject and (iv) except as described on Schedule 5.3, do not violate any contract or agreement or require the consent or approval of any other Person. The individual or individuals executing the Loan Documents and the Warrant are duly authorized to do so.

5.4 Material Adverse Effect. Since September 30, 2013, no event that has had or could reasonably be expected to have a Material Adverse Effect has occurred and is continuing. Borrower is not aware of any event likely to occur that is reasonably expected to result in a Material Adverse Effect.

5.5 Actions Before Governmental Authorities. Except as described on Schedule 5.5, there are no actions, suits or proceedings at law or in equity or by or before any governmental authority now pending or, to the knowledge of Borrower, threatened against or affecting Borrower or its property.

5.6 Laws. Borrower is not in violation of any law, rule or regulation, or in default with respect to any judgment, writ, injunction or decree of any governmental authority, where such violation or default is reasonably expected to result in a Material Adverse Effect. Borrower is not in default in any manner under any provision of any agreement or instrument evidencing indebtedness, or any other material agreement to which it is a party or by which it is bound.

5.7 Information Correct and Current. No information, report, Advance Request, financial statement, exhibit or schedule furnished, by or on behalf of Borrower to Lender in connection with any Loan Document or included therein or delivered pursuant thereto contained, contains or will contain any material misstatement of fact or omitted, omits or will omit to state any material fact necessary to make the statements therein, in the light of the circumstances under which they were, are or will be made, not misleading at the time such statement was made or deemed made. Additionally, any and all financial or business projections provided by Borrower to Lender shall be (i) provided in good faith and based on the most current data and information available to Borrower, and (ii) the most current of such projections approved by Borrower's Board of Directors.

5.8 Tax Matters. Except as described on Schedule 5.8, (a) Borrower has filed all federal, and all material state and local tax returns that it is required to file, (b) Borrower has duly paid or fully reserved for all taxes or installments thereof (including any interest or penalties) as and when due, which have or may become due pursuant to such returns, and (c) Borrower has paid or fully reserved for any tax assessment received by Borrower for the three (3) years preceding the Closing Date, if any (including any taxes being contested in good faith and by appropriate proceedings).

5.9 Intellectual Property Claims. Borrower is the sole owner of, or otherwise has the right to use, the Intellectual Property. Except as described on Schedule 5.9,(i) each of the material Copyrights, Trademarks and Patents is valid and enforceable, (ii) no material part of the Intellectual Property has been judged invalid or unenforceable, in whole or in part, and (iii) no claim has been made to Borrower that any material part of the Intellectual Property violates the rights of any third party. Exhibit D is a true, correct and complete list of each of Borrower's Patents, registered Trademarks, registered Copyrights, and material agreements under which Borrower licenses Intellectual Property from third parties (other than shrink-wrap software licenses), together with application or registration numbers, as applicable, owned by Borrower or any Subsidiary, in each case as of the Closing Date. Borrower is not in material breach of, nor has Borrower failed to perform any material obligations under, any of the foregoing contracts, licenses or agreements and, to Borrower's knowledge, no third party to any such contract, license or agreement is in material breach thereof or has failed to perform any material obligations thereunder.

5.10 Intellectual Property. Except as described on Schedule 5.10, Borrower has, or in the case of any proposed business, will have, all material rights with respect to Intellectual Property necessary in the operation or conduct of Borrower's business as currently conducted and proposed to be conducted by Borrower. Without limiting the generality of the foregoing, and in the case of Licenses, except for restrictions that are

unenforceable under Division 9 of the UCC, Borrower has the right, to the extent required to operate Borrower's business, to freely transfer, license or assign Intellectual Property without condition, restriction or payment of any kind (other than license payments in the ordinary course of business) to any third party, and Borrower owns or has the right to use, pursuant to valid licenses, all software development tools, library functions, compilers and all other third-party software and other items that are used in the design, development, promotion, sale, license, manufacture, import, export, use or distribution of Borrower Products.

5.11 Borrower Products. Except as described on Schedule 5.11, no Intellectual Property owned by Borrower and no Borrower Product has been or is subject to any actual or, to the knowledge of Borrower, threatened litigation, proceeding (including any proceeding in the United States Patent and Trademark Office or any corresponding foreign office or agency) or outstanding decree, order, judgment, settlement agreement or stipulation that restricts in any manner Borrower's use, transfer or licensing thereof or that may affect the validity, use or enforceability thereof. There is no decree, order, judgment, agreement, stipulation, arbitral award or other provision entered into in connection with any litigation or proceeding that obligates Borrower to grant licenses or ownership interest in any future Intellectual Property related to the operation or conduct of the business of Borrower or Borrower Products. Borrower has not received any written notice or claim, or, to the knowledge of Borrower, oral notice or claim, challenging or questioning Borrower's ownership in any Intellectual Property (or written notice of any claim challenging or questioning the ownership in any licensed Intellectual Property of the owner thereof) or suggesting that any third party has any claim of legal or beneficial ownership with respect thereto nor, to Borrower's knowledge, is there a reasonable basis for any such claim. Neither Borrower's use of its Intellectual Property nor the production and sale of Borrower Products infringes the Intellectual Property or other rights of others.

5.12 Financial Accounts. Exhibit E, as may be updated by the Borrower in a written notice provided to Lender after the Closing Date, is a true, correct and complete list of (a) all banks and other financial institutions at which Borrower or any Subsidiary maintains Deposit Accounts and (b) all institutions at which Borrower or any Subsidiary maintains an account holding Investment Property, and such exhibit correctly identifies the name, address and telephone number of each bank or other institution, the name in which the account is held, a description of the purpose of the account, and the complete account number therefor.

5.13 Employee Loans. Borrower has no outstanding loans to any employee, officer or director of the Borrower nor has Borrower guaranteed the payment of any loan made to an employee, officer or director of the Borrower by a third party.

5.14 Capitalization and Subsidiaries. Borrower's capitalization as of the Closing Date is set forth on Schedule 5.14 annexed hereto. Borrower does not own any stock, partnership interest or other securities of any Person, except for Permitted Investments. Attached as Schedule 5.14, as may be updated by Borrower in a written notice provided after the Closing Date, is a true, correct and complete list of each Subsidiary.

SECTION 6. INSURANCE; INDEMNIFICATION

6.1 Coverage. Borrower shall cause to be carried and maintained commercial general liability insurance, on an occurrence form, against risks customarily insured against in Borrower's line of business. Such risks shall include the risks of bodily injury, including death, property damage, personal injury, advertising injury, and contractual liability per the terms of the indemnification agreement found in Section 6.3. Borrower must maintain a minimum of $2,000,000 of commercial general liability insurance for each occurrence. Borrower has and agrees to maintain a minimum of $10,000,000 of directors and officers' insurance for each occurrence and $10,000,000 in the aggregate. So long as there are any Secured Obligations (other than inchoate indemnity obligations) outstanding, Borrower shall also cause to be carried and maintained insurance upon the Collateral, insuring against all risks of physical loss or damage, in an amount not less than the full replacement cost of the Collateral, provided that such insurance may be subject to standard exceptions and deductibles. Borrower shall also carry and maintain a fidelity insurance policy in an amount not less than $25,000.

6.2 Certificates. Borrower shall deliver to Lender certificates of insurance that evidence Borrower's compliance with its insurance obligations in Section 6.1 and the obligations contained in this Section 6.2. Borrower's insurance certificate shall state Lender is an additional insured for commercial general liability, loss payee for all risk property damage insurance, subject to the insurer's approval, and a loss payee for property insurance. Attached to the certificates of insurance will be additional insured endorsements for liability and lender's loss payable endorsements, or copies of policy forms evidencing such coverages. Any failure of Lender to scrutinize such insurance certificates for compliance is not a waiver of any of Lender's rights, all of which are reserved.

6.3 Indemnity. Borrower agrees to indemnify and hold Lender and its officers, directors, employees, agents, in-house attorneys, representatives and shareholders harmless from and against any and all claims, costs, expenses, damages and liabilities (including such claims, costs, expenses, damages and liabilities based on liability in tort, including strict liability in tort), including reasonable attorneys' fees and disbursements and other costs of investigation or defense (including those incurred upon any appeal), that may be instituted or asserted against or incurred by Lender or any such Person as the result of credit having been extended, suspended or terminated under this Agreement and the other Loan Documents or the administration of such credit, or in connection with or arising out of the transactions contemplated hereunder and thereunder, or any actions or failures to act in connection therewith, or arising out of the disposition or utilization of the Collateral, excluding in all cases claims resulting solely from the Collateral Agent's or the Lender's gross negligence or willful misconduct. Borrower agrees to pay, and to save Lender harmless from, any and all liabilities with respect to, or resulting from any delay in paying, any and all excise, sales or other similar taxes (excluding taxes imposed on or measured by the net income of Lender) that may be payable or determined to be payable with respect to any of the Collateral or this Agreement.

SECTION 7. COVENANTS OF BORROWER

Borrower agrees as follows:

7.1 Financial Reports. Borrower shall furnish to Lender the financial statements and reports listed hereinafter (the "Financial Statements"):

(a) as soon as practicable (and in any event within 30 days) after the end of each month, unaudited interim and year-to-date financial statements as of the end of such month (prepared on a consolidated and consolidating basis, if applicable), including balance sheet and related statements of income and cash flows accompanied by a report detailing any material contingencies (including the commencement of any material litigation by or against Borrower) or any other occurrence that would reasonably be expected to have a Material Adverse Effect, all certified by Borrower's Chief Executive Officer or Chief Financial Officer to the effect that they have been prepared in accordance with GAAP, except (i) for the absence of footnotes, (ii) that they are subject to normal year end adjustments, (iii) they do not contain certain non-cash items that are customarily included in quarterly and annual financial statements, and (iv) for the first two months of each quarter only the balance sheet and income statement will be required;

(b) as soon as practicable (and in any event within 45 days) after the end of each of the first three fiscal quarters of any fiscal year of Borrower, unaudited interim and year-to-date financial statements as of the end of such fiscal quarter (prepared on a consolidated and consolidating basis, if applicable), including balance sheet and related statements of income and cash flows accompanied by a report detailing any material contingencies (including the commencement of any material litigation by or against Borrower) or any other occurrence that would reasonably be expected to have a Material Adverse Effect, certified by Borrower's Chief Executive Officer or Chief Financial Officer to the effect that they have been prepared in accordance with GAAP, except (i) for the absence of footnotes, and (ii) that they are subject to normal year end adjustments; as well as the most recent capitalization table for Borrower, including the weighted average exercise price of employee stock options;

(c) as soon as practicable (and in any event within 90 days) after the end of each fiscal year, unqualified audited financial statements as of the end of such year (prepared on a consolidated and consolidating basis, if applicable), including balance sheet and related statements of income and cash flows, and setting forth in comparative form the corresponding figures for the preceding fiscal year, certified by a firm of independent certified public accountants selected by Borrower and reasonably acceptable to Lender, accompanied by any management report from such accountants;

(d) as soon as practicable (and in any event within 30 days) after the end of each month, a Compliance Certificate in the form of Exhibit F;

(e) promptly after the sending or filing thereof, as the case may be, copies of any proxy statements, financial statements or reports that Borrower has made available to holders of its Preferred Stock and copies of any regular, periodic and special reports or registration statements that Borrower files with the SEC or any governmental authority that may be substituted therefor, or any national securities exchange;

(f) [reserved]; and

(g) financial and business projections promptly following their approval by Borrower's Board of Directors, as well as other financial information reasonably requested by Lender.

Borrower shall not make any change in its (a) accounting policies or reporting practices, except in accordance with GAAP or with the consent of Lender, or (b) fiscal years or fiscal quarters. The fiscal year of Borrower shall end on December 31.

The executed Compliance Certificate may be sent via facsimile to Lender at (650) 473-9194 or via e-mail to cnorman@herculestech.com. All Financial Statements required to be delivered pursuant to clauses (a), (b) and (c) shall be sent via e-mail to financialstatements@herculestech.com with a copy to cnorman@herculestech.com provided, that if e-mail is not available or sending such Financial Statements via e-mail is not possible, they shall be sent via facsimile to Lender at: (866) 468-8916, attention Chief Credit Officer. Notwithstanding anything herein to the contrary, documents required to be delivered pursuant to this Section 7.1 may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date on which Borrower posts such documents, or provides a link thereto, on Borrower's website on the Internet at www.acelrx.com, and notifies Lender via email or facsimile as provided in the immediately preceding sentence.

7.2 Management Rights. Borrower shall permit any representative that Lender authorizes, including its attorneys and accountants, to inspect the Collateral and examine and make copies and abstracts of the books of account of Borrower at reasonable times and upon reasonable notice during normal business hours. Such inspections or examinations shall be conducted no more often than once every six months unless an Event of Default has occurred and is continuing. In addition, any such representative shall have the right to meet with management and officers of Borrower to discuss such books of account and records. In addition, Lender shall be entitled at reasonable times and intervals to consult with and advise the management and officers of Borrower concerning significant business issues affecting Borrower. Such consultations shall not unreasonably interfere with Borrower's business operations. The parties intend that the rights granted Lender shall constitute "management rights" within the meaning of 29 C.F.R Section 2510.3-101(d)(3)(ii), but that any advice, recommendations or participation by Lender with respect to any business issues shall not be deemed to give Lender, nor be deemed an exercise by Lender of, control over Borrower's management or policies.

7.3 Further Assurances. Borrower shall from time to time execute, deliver and file, alone or with Lender, any financing statements, security agreements, collateral assignments, notices, control agreements, or other documents to perfect or give the highest priority to Lender's Lien on the Collateral. Borrower shall from time to time procure any instruments or documents as may be requested by Lender, and take all further action that may be necessary or desirable, or that Lender may reasonably request, to perfect and protect the Liens granted hereby and thereby. In addition, and for such purposes only, Borrower hereby authorizes Lender to execute and deliver on behalf of Borrower and to file such financing statements, collateral assignments, notices, control agreements, security agreements and other documents without the signature of Borrower either in Lender's name or in the name of Lender as agent and attorney-in-fact for Borrower. Borrower shall protect and defend Borrower's title to the Collateral and Lender's Lien thereon against all Persons claiming any interest adverse to Borrower or Lender other than Permitted Liens.

7.4 Post-Closing Items. Borrower shall use its commercially reasonable efforts to deliver or cause to be delivered the documents listed on Schedule 7.4 on or before the corresponding dates set forth on Schedule 7.4. Within three (3) business days of the Closing Date, Borrower shall deliver to Lender a legal opinion of Borrower's counsel and certified incumbency signatures.

7.5 Indebtedness. Borrower shall not create, incur, assume, guarantee or be or remain liable with respect to any Indebtedness, or permit any Subsidiary so to do, other than Permitted Indebtedness, or prepay any Indebtedness or take any actions which impose on Borrower an obligation to prepay any Indebtedness, except for the conversion of Indebtedness into equity securities and the payment of cash in lieu of fractional shares in connection with such conversion.

7.6 Collateral. Borrower shall at all times keep the Collateral, the Intellectual Property and all other property and assets used in Borrower's business or in which Borrower now or hereafter holds any interest free and clear from any legal process or Liens whatsoever (except for Permitted Liens), and shall give Lender prompt written notice of any legal process affecting the Collateral, the Intellectual Property, such other property and assets, or any Liens thereon. Borrower shall cause its Subsidiaries to protect and defend such Subsidiary's title to its assets from and against all Persons claiming any interest adverse to such Subsidiary, and Borrower shall cause its Subsidiaries at all times to keep such Subsidiary's property and assets free and clear from any legal process or Liens whatsoever (except for Permitted Liens), and shall give Lender prompt written notice of any legal process affecting such Subsidiary's assets. Except with respect to (i) specific property encumbered to secure payment of particular Indebtedness incurred to finance the acquisition of such property, and (ii) restrictions by reason of customary provisions restricting assignment, subletting or other transfers contained in leases, licenses and similar agreements entered into in the ordinary course of business (provided that such restrictions are limited to the property or assets secured by such Liens or the property or assets subject to such leases, licenses or similar agreements, as the case may be), Borrower shall not agree with any Person other than Lender not to encumber its property.

7.7 Investments. Borrower shall not directly or indirectly acquire or own, or make any Investment in or to any Person, or permit any of its Subsidiaries so to do, other than Permitted Investments.

7.8 Distributions. Borrower shall not, and shall not allow any Subsidiary to, (a) repurchase or redeem any class of stock or other equity interest other than pursuant to employee, director or consultant stock purchase or repurchase plans or other similar agreements, provided, however, in each case the repurchase or redemption price does not exceed the original consideration paid for such stock or equity interest, or (b) declare or pay any cash dividend or make a cash distribution on any class of stock or other equity interest, except that a Subsidiary may pay dividends or make distributions to Borrower, or (c) lend money to any employees, officers or directors except as expressly permitted by clause (ix) of the definition of Permitted Investments.

7.9 Transfers. Except for Permitted Transfers, neither Borrower nor its Subsidiaries shall voluntarily or involuntarily transfer, sell, lease, license, lend or in any other manner convey any equitable, beneficial or legal interest in any material portion of their assets.

7.10 Mergers or Acquisitions. Borrower shall not merge or consolidate, or permit any of its Subsidiaries to merge or consolidate, with or into any other business organization (other than mergers or consolidations of a Subsidiary into another Subsidiary or into Borrower), or acquire, or permit any of its Subsidiaries to acquire, all or substantially all of the capital stock or property of another Person.

7.11 Taxes. Borrower and its Subsidiaries shall pay when due all taxes, fees or other charges of any nature whatsoever (together with any related interest or penalties) now or hereafter imposed or assessed against Borrower, Lender (to the extent assessed in connection with the making of the Loan hereunder but excluding taxes on Lender's net income) or the Collateral or upon Borrower's ownership, possession, use, operation or disposition thereof or upon Borrower's rents, receipts or earnings arising therefrom. Borrower shall file on or before the due date therefor all personal property tax returns in respect of the Collateral. Notwithstanding the foregoing, Borrower may contest, in good faith and by appropriate proceedings, taxes for which Borrower maintains adequate reserves therefor in accordance with GAAP.

7.12 Corporate Changes. Neither Borrower nor any Subsidiary shall change its corporate name, legal form or jurisdiction of formation without twenty (20) days' prior written notice to Lender. Neither Borrower nor any Subsidiary shall suffer a Change in Control. Neither Borrower nor any Subsidiary shall relocate its chief executive office or its principal place of business unless: (i) it has provided prior written notice to Lender; and (ii) such relocation shall be within the continental United States. Neither Borrower nor any Subsidiary shall relocate any item of Collateral (other than (w) sales of Inventory in the ordinary course of business, (x) relocations of mobile Equipment, (y) relocations of other Equipment having an aggregate value of up to $150,000 in any fiscal year, and (z) relocations of Collateral from a location described on Exhibit C to another location described on Exhibit C) unless (i) it has provided prompt written notice to Lender, (ii) such relocation is within the continental United States or to such other jurisdiction as designated in writing by Borrower from time to time, and (iii), if such relocation is to a third party bailee, it has delivered a bailee agreement in form and substance reasonably acceptable to Lender.

7.13 Deposit Accounts. Neither Borrower nor any Subsidiary shall maintain any Deposit Accounts, or accounts holding Investment Property, except with respect to which Lender has an Account Control Agreement.

7.14 Borrower shall notify Lender of each Subsidiary formed subsequent to the Closing Date and, within 30 days of formation, shall cause any such Subsidiary organized under the laws of any State within the United States to execute and deliver to Lender a Joinder Agreement.

7.15 Notification of Event of Default. Borrower shall notify Lender promptly upon becoming aware of the occurrence of any Event of Default, such notice to be sent via facsimile to Lender.

7.16 Hercules Technology II, L.P. has received a license from the U.S. Small Business Administration ("SBA") to extend loans as a small business investment company ("SBIC") pursuant to the Small Business Investment Act of 1958, as amended, and the associated regulations (collectively, the "SBIC Act"). Portions of the loan to Borrower will be made under the SBA license and the SBIC Act. Addendum 1 to this Agreement outlines various responsibilities of Lender and Borrower associated with an SBA loan, and such Addendum 1 is hereby incorporated in this Agreement.

SECTION 8. [RESERVED]

SECTION 9. EVENTS OF DEFAULT

The occurrence of any one or more of the following events shall be an Event of Default:

9.1 Payments. Borrower fails to pay any amount due under this Agreement, the Notes or any of the other Loan Documents on the due date; or

9.2 Covenants. Borrower breaches or defaults in the performance of any covenant or Secured Obligation under this Agreement, the Notes, or any of the other Loan Documents, and (a) with respect to a default under any covenant under this Agreement (other than under Sections 6, 7.5, 7.6, 7.7, 7.8, 7.9, 7.10 or 7.16) such default continues for more than ten (10) days after the earlier of the date on which (i) Lender has given notice of such default to Borrower and (ii) Borrower has actual knowledge of such default or (b) with respect to a default under any of Sections 6, 7.5, 7.6, 7.7, 7.8, 7.9, 7.10 or 7.16, the occurrence of such default; or

9.3 Material Adverse Effect. A circumstance has occurred that would reasonably be expected to have a Material Adverse Effect; or

9.4 Other Loan Documents. The occurrence of any default under any Loan Document or any other agreement between Borrower and Lender and such default continues for more than ten (10) days after the earlier of the date on which (a) Lender has given notice of such default to Borrower, or (b) Borrower has actual knowledge of such default; or

9.5 Representations. Any representation or warranty made by Borrower in any Loan Document or in the Warrant shall have been false or misleading in any material respect; or

9.6 Insolvency. Borrower (A) (i) shall make an assignment for the benefit of creditors; or (ii) shall be unable to pay its debts as they become due, or be unable to pay or perform under the Loan Documents, or shall become insolvent; or (iii) shall file a voluntary petition in bankruptcy; or (iv) shall file any petition, answer, or document seeking for itself any reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation pertinent to such circumstances; or (v) shall seek or consent to or acquiesce in the appointment of any trustee, receiver, or liquidator of Borrower or of all or any substantial part (i.e., 33-1/3% or more) of the assets or property of Borrower; or (vi) shall cease operations of its business as its business has normally been conducted, or terminate substantially all of its employees; or (vii) Borrower or its directors or majority shareholders shall take any action initiating any of the foregoing actions described in clauses (i) through (vi); or (B) either (i) forty-five (45) days shall have expired after the commencement of an involuntary action against Borrower seeking reorganization, arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, without such action being dismissed or all orders or proceedings thereunder affecting the operations or the business of Borrower being stayed; or (ii) a stay of any such order or proceedings shall thereafter be set aside and the action setting it aside shall not be timely appealed; or (iii) Borrower shall file any answer admitting or not contesting the material allegations of a petition filed against Borrower in any such proceedings; or (iv) the court in which such proceedings are pending shall enter a decree or order granting the relief sought in any such proceedings; or (v) forty-five (45) days shall have expired after the appointment, without the consent or acquiescence of Borrower, of any trustee, receiver or liquidator of Borrower or of all or any substantial part of the properties of Borrower without such appointment being vacated; or

9.7 Attachments; Judgments. Any portion of Borrower's assets is attached or seized, or a levy is filed against any such assets, or a judgment or judgments is/are entered for the payment of money, individually or in the aggregate, of at least $500,000, and such judgment remains unstayed for a period of ten (10) days, or Borrower is enjoined or in any way prevented by court order from conducting any part of its business; or

9.8 Other Obligations. The occurrence of any default under any agreement or obligation of Borrower involving any Indebtedness which results in a right by a third party or parties, whether or not exercised, to accelerate the maturity of such Indebtedness in excess of $250,000, or the occurrence of any default under any agreement or obligation of Borrower that could reasonably be expected to have a Material Adverse Effect; or

9.9 Stop Trade. At any time after Lender has received shares of Common Stock pursuant to the terms set forth in Section 2.3(e), an SEC stop trade order or NASDAQ market trading suspension of the Common Stock shall be in effect for five (5) consecutive days or five (5) days during a period of ten (10) consecutive days, excluding in all cases a suspension of all trading on a public market, provided that Borrower shall not have been able to cure such trading suspension within thirty (30) days of the notice thereof or list the Common Stock on another public market within sixty (60) days of such notice.

SECTION 10. REMEDIES

10.1 General. Upon and during the continuance of any one or more Events of Default, (i) Lender may, at its option, accelerate and demand payment of all or any part of the Secured Obligations together with a Prepayment Charge and declare them to be immediately due and payable (provided, that upon the occurrence of an Event of Default of the type described in Section 9.6, the Notes and all of the Secured Obligations shall automatically be accelerated and made due and payable, in each case without any further notice or act), and (ii) Lender may notify any of Borrower's account debtors to make payment directly to Lender, compromise the amount of any such account on Borrower's behalf and endorse Lender's name without recourse on any such payment for deposit directly to Lender's account. Lender may exercise all rights and remedies with respect to the Collateral under the Loan Documents or otherwise available to it under the UCC and other applicable law, including the right to release, hold, sell, lease, liquidate, collect, realize upon, or otherwise dispose of all or any part of the Collateral and the right to occupy, utilize, process and commingle the Collateral. All Lender's rights and remedies shall be cumulative and not exclusive.

10.2 Collection; Foreclosure. Upon the occurrence and during the continuance of any Event of Default, Lender may, at any time or from time to time, apply, collect, liquidate, sell in one or more sales, lease or otherwise dispose of, any or all of the Collateral, in its then condition or following any commercially reasonable preparation or processing, in such order as Lender may elect. Any such sale may be made either at public or private sale at its place of business or elsewhere. Borrower agrees that any such public or private sale may occur upon ten (10) calendar days' prior written notice to Borrower. Lender may require Borrower to assemble the Collateral and make it available to Lender at a place designated by Lender that is reasonably convenient to Lender and Borrower. The proceeds of any sale, disposition or other realization upon all or any part of the Collateral shall be applied by Lender in the following order of priorities:

First, to Lender in an amount sufficient to pay in full Lender's costs and professionals' and advisors' fees and expenses as described in Section 11.11;

Second, to Lender in an amount equal to the then unpaid amount of the Secured Obligations (including principal, interest, and the Default Rate interest), in such order and priority as Lender may choose in its sole discretion; and Finally, after the full, final, and indefeasible payment in Cash of all of the Secured Obligations, to any creditor holding a junior Lien on the Collateral, or to Borrower or its representatives or as a court of competent jurisdiction may direct.

Lender shall be deemed to have acted reasonably in the custody, preservation and disposition of any of the Collateral if it complies with the obligations of a secured party under the UCC.

10.3 No Waiver. Lender shall be under no obligation to marshal any of the Collateral for the benefit of Borrower or any other Person, and Borrower expressly waives all rights, if any, to require Lender to marshal any Collateral.

10.4 Cumulative Remedies. The rights, powers and remedies of Lender hereunder shall be in addition to all rights, powers and remedies given by statute or rule of law and are cumulative. The exercise of any one or more of the rights, powers and remedies provided herein shall not be construed as a waiver of or election of remedies with respect to any other rights, powers and remedies of Lender.

SECTION 11. MISCELLANEOUS

11.1 Severability. Whenever possible, each provision of this Agreement shall be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement shall be prohibited by or invalid under such law, such provision shall be ineffective only to the extent and duration of such prohibition or invalidity, without invalidating the remainder of such provision or the remaining provisions of this Agreement.

11.2 Notice. Except as otherwise provided herein, any notice, demand, request, consent, approval, declaration, service of process or other communication (including the delivery of Financial Statements) that is required, contemplated, or permitted under the Loan Documents or with respect to the subject matter hereof shall be in writing, and shall be deemed to have been validly served, given, delivered, and received upon the earlier of: (i) the day of transmission by facsimile or hand delivery or delivery by an overnight express service or overnight mail delivery service; or (ii) the third calendar day after deposit in the United States mails, with proper first class postage prepaid, in each case addressed to the party to be notified as follows:

(a) If to either Lender:

HERCULES TECHNOLOGY II, L.P.
Legal Department
Attention: Chief Legal Officer and Chad Norman
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

(b) If to Borrower:

ACELRX PHARMACEUTICALS, INC.

Attention: Chief Financial Officer
351 Galveston Drive
Redwood City, CA 94063
Facsimile: 650-216-6500
Telephone: 650-216-3511

or to such other address as each party may designate for itself by like notice.

11.3 Entire Agreement; Amendments. This Agreement, the Notes, and the other Loan Documents constitute the entire agreement and understanding of the parties hereto in respect of the subject matter hereof and thereof, and supersede and replace in their entirety any prior proposals, term sheets, letters, negotiations or other documents or agreements, whether written or oral, with respect to the subject matter hereof or thereof (including Lender's proposal letter dated November 19, 2013). None of the terms of this Agreement, the Notes or any of the other Loan Documents may be amended except by an instrument executed by each of the parties hereto.

11.4 No Strict Construction. The parties hereto have participated jointly in the negotiation and drafting of this Agreement. In the event an ambiguity or question of intent or interpretation arises, this Agreement shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Agreement.

11.5 No Waiver. The powers conferred upon Lender by this Agreement are solely to protect its rights hereunder and under the other Loan Documents and its interest in the Collateral and shall not impose any duty upon Lender to exercise any such powers. No omission or delay by Lender at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof by Borrower at any time designated, shall be a waiver of any such right or remedy to which Lender is entitled, nor shall it in any way affect the right of Lender to enforce such provisions thereafter.

11.6 Survival. All agreements, representations and warranties contained in this Agreement, the Notes and the other Loan Documents or in any document delivered pursuant hereto or thereto shall be for the benefit of Lender and shall survive the execution and delivery of this Agreement and the expiration or other termination of this Agreement.

11.7 Successors and Assigns. The provisions of this Agreement and the other Loan Documents shall inure to the benefit of and be binding on Borrower and its permitted assigns (if any). Borrower shall not assign its obligations under this Agreement, the Notes or any of the other Loan Documents without Lender's express prior written consent, and any such attempted assignment without such consent shall be void and of no effect. Subject to Section 11.13, Lender may assign, transfer, or endorse its rights hereunder and under the other Loan Documents without prior notice to Borrower, and all of such rights shall inure to the benefit of Lender's successors and assigns.

11.8 Governing Law. This Agreement, the Notes and the other Loan Documents have been negotiated and delivered to Lender in the State of California, and shall have been accepted by Lender in the State of California. Payment to Lender by Borrower of the Secured Obligations is due in the State of California. This Agreement, the Notes and the other Loan Documents shall be governed by, and construed and enforced in accordance with, the laws of the State of California, excluding conflict of laws principles that would cause the application of laws of any other jurisdiction.

11.9 Consent to Jurisdiction and Venue. All judicial proceedings (to the extent that the reference requirement of Section 11.10 is not applicable) arising in or under or related to this Agreement, the Notes or any of the other Loan Documents may be brought in any state or federal court located in the State of California. By execution and delivery of this Agreement, each party hereto generally and unconditionally: (a) consents to nonexclusive personal jurisdiction in Santa Clara County, State of California; (b) waives any objection as to jurisdiction or venue in Santa Clara County, State of California; (c) agrees not to assert any defense based on lack of jurisdiction or venue in the aforesaid courts; and (d) irrevocably agrees to be bound by any judgment rendered thereby in connection with this Agreement, the Notes or the other Loan Documents. Service of process on any party hereto in any action arising out of or relating to this Agreement shall be effective if given in accordance with the requirements for notice set forth in Section 11.2, and shall be deemed effective and received as set forth in Section 11.2. Nothing herein shall affect the right to serve process in any other manner permitted by law or shall limit the right of either party to bring proceedings in the courts of any other jurisdiction.

11.10 Mutual Waiver of Jury Trial / Judicial Reference.

(a) Because disputes arising in connection with complex financial transactions are most quickly and economically resolved by an experienced and expert person and the parties wish applicable state and federal laws to apply (rather than arbitration rules), the parties desire that their disputes be resolved by a judge applying such applicable laws. EACH OF BORROWER AND LENDER SPECIFICALLY WAIVES ANY RIGHT IT MAY HAVE TO TRIAL BY JURY OF ANY CAUSE OF ACTION, CLAIM, CROSS-CLAIM, COUNTERCLAIM, THIRD PARTY CLAIM OR ANY OTHER CLAIM (COLLECTIVELY, “CLAIMS”) ASSERTED BY BORROWER AGAINST LENDER OR ITS ASSIGNEE OR BY LENDER OR ITS ASSIGNEE AGAINST BORROWER. This waiver extends to all such Claims, including Claims that involve Persons other than Borrower and Lender; Claims that arise out of or are in any way connected to the relationship between Borrower and Lender; and any Claims for damages, breach of contract, tort, specific performance, or any equitable or legal relief of any kind, arising out of this Agreement, any other Loan Document.

(b) If the waiver of jury trial set forth in Section 11.10(a) is ineffective or unenforceable, the parties agree that all Claims shall be resolved by reference to a private judge sitting without a jury, pursuant to Code of Civil Procedure Section 638, before a mutually acceptable referee or, if the parties cannot agree, a referee selected by the Presiding Judge of the Santa Clara County, California. Such proceeding shall be conducted in Santa Clara County, California, with California rules of evidence and discovery applicable to such proceeding.

(c) In the event Claims are to be resolved by judicial reference, either party may seek from a court identified in Section 11.9, any prejudgment order, writ or other relief and have such prejudgment order, writ or other relief enforced to the fullest extent permitted by law notwithstanding that all Claims are otherwise subject to resolution by judicial reference.

11.11 Professional Fees. Borrower promises to pay Lender's fees and expenses necessary to finalize the loan documentation, including but not limited to reasonable attorneys fees, UCC searches, filing costs, and other miscellaneous expenses. In addition, Borrower promises to pay any and all reasonable attorneys' and other professionals' fees and expenses (including fees and expenses of in-house counsel) incurred by Lender after the Closing Date in connection with or related to: (a) the Loan; (b) the administration, collection, or enforcement of the Loan; (c) the amendment or modification of the Loan Documents; (d) any waiver, consent, release, or termination under the Loan Documents; (e) the protection, preservation, sale, lease, liquidation, or disposition of Collateral or the exercise of remedies with respect to the Collateral; (f) any legal, litigation, administrative, arbitration, or out of court proceeding in connection with or related to Borrower or the Collateral, and any appeal or review thereof; and (g) any bankruptcy, restructuring, reorganization, assignment for the benefit of creditors, workout, foreclosure, or other action related to Borrower, the Collateral, the Loan Documents, including representing Lender in any adversary proceeding or contested matter commenced or continued by or on behalf of Borrower's estate, and any appeal or review thereof.

11.12 Confidentiality. Lender acknowledges that certain items of Collateral and information provided to Lender by Borrower are confidential and proprietary information of Borrower, if and to the extent such information either (x) is marked as confidential by Borrower at the time of disclosure, or (y) should reasonably be understood to be confidential (the "Confidential Information"). Accordingly, Lender agrees that any Confidential Information it may obtain in the course of acquiring, administering, or perfecting Lender's security interest in the Collateral shall not be disclosed to any other person or entity in any manner whatsoever, in whole or in part, without the prior written consent of Borrower, except that Lender may disclose any such information: (a) to its own directors, officers, employees, accountants, counsel and other professional advisors and to its affiliates if Lender in its sole discretion determines that any such party should have access to such information in connection with such party's responsibilities in connection with the Loan or this Agreement and, provided that such recipient of such Confidential Information either (i) agrees to be bound by the confidentiality provisions of this paragraph or (ii) is otherwise subject to confidentiality restrictions that reasonably protect against the disclosure of Confidential Information; (b) if such information is generally available to the public through no fault of Collateral Agent or Lender; (c) if required or appropriate in any report, statement or testimony submitted to any governmental authority having or claiming to have jurisdiction over Lender; (d) if required or appropriate in response to any summons

or subpoena or in connection with any litigation, to the extent permitted or deemed advisable by Lender's counsel; (e) to comply with any legal requirement or law applicable to Lender; (f) to the extent reasonably necessary in connection with the exercise of any right or remedy under any Loan Document, including Lender's sale, lease, or other disposition of Collateral after default; (g) to any participant or assignee of Lender or any prospective participant or assignee; provided, that such participant or assignee or prospective participant or assignee agrees in writing to be bound by this Section prior to disclosure; or (h) otherwise with the prior consent of Borrower; provided, that any disclosure made in violation of this Agreement shall not affect the obligations of Borrower or any of its affiliates or any guarantor under this Agreement or the other Loan Documents.

11.13 Assignment of Rights. Borrower acknowledges and understands that Lender may sell and assign all or part of its interest hereunder and under the Note(s) and Loan Documents to any person or entity (an "Assignee"), provided, however, that (i) Lender shall not sell or assign any of its rights pursuant to Section 8 of this Agreement without the express written consent of Borrower, which consent may be withheld by Borrower in its sole discretion, and any such attempted assignment without such consent shall be void and of no effect and (ii) any transfer by Lender of the Note shall be subject to compliance with applicable federal and state securities laws. After such assignment the term "Lender" as used in the Loan Documents shall mean and include such Assignee, and such Assignee shall be vested with all rights, powers and remedies of Lender hereunder with respect to the interest so assigned; but with respect to any such interest not so transferred, Lender shall retain all rights, powers and remedies hereby given. No such assignment by Lender shall relieve Borrower of any of its obligations hereunder. Lender agrees that in the event of any transfer by it of the Note(s), it will endorse thereon a notation as to the portion of the principal of the Note(s), which shall have been paid at the time of such transfer and as to the date to which interest shall have been last paid thereon.

11.14 Revival of Secured Obligations. This Agreement and the Loan Documents shall remain in full force and effect and continue to be effective if any petition is filed by or against Borrower for liquidation or reorganization, if Borrower becomes insolvent or makes an assignment for the benefit of creditors, if a receiver or trustee is appointed for all or any significant part of Borrower's assets, or if any payment or transfer of Collateral is recovered from Lender. The Loan Documents and the Secured Obligations and Collateral security shall continue to be effective, or shall be revived or reinstated, as the case may be, if at any time payment and performance of the Secured Obligations or any transfer of Collateral to Lender, or any part thereof is rescinded, avoided or avoidable, reduced in amount, or must otherwise be restored or returned by, or is recovered from, Lender or by any obligee of the Secured Obligations, whether as a "voidable preference," "fraudulent conveyance," or otherwise, all as though such payment, performance, or transfer of Collateral had not been made. In the event that any payment, or any part thereof, is rescinded, reduced, avoided, avoidable, restored, returned, or recovered, the Loan Documents and the Secured Obligations shall be deemed, without any further action or documentation, to have been revived and reinstated except to the extent of the full, final, and indefeasible payment to Lender in Cash.

11.15 Counterparts. This Agreement and any amendments, waivers, consents or supplements hereto may be executed in any number of counterparts, and by different parties hereto in separate counterparts, each of which when so delivered shall be deemed an original, but all of which counterparts shall constitute but one and the same instrument.

11.16 No Third Party Beneficiaries. No provisions of the Loan Documents are intended, nor will be interpreted, to provide or create any third-party beneficiary rights or any other rights of any kind in any person other than Lender and Borrower unless specifically provided otherwise herein, and, except as otherwise so provided, all provisions of the Loan Documents will be personal and solely between the Lender and the Borrower.

11.17 Publicity. Lender may use Borrower's name and logo, and include a brief description of the relationship between Borrower and Lender, in Lender's marketing materials.

SECTION 12. COLLATERAL AGENT

12.1 Appointment of Agent. Hercules Technology II, L.P. is hereby appointed as Collateral Agent hereunder and under the other Loan Documents and each Lender hereby authorizes Hercules Technology II, L.P. to act as Collateral Agent in accordance with the terms hereof and the other Loan Documents. Collateral Agent hereby agrees to act in its capacity as such upon the express conditions contained herein and the other Loan Documents, as applicable. The provisions of this Section 12 are solely for the benefit of Collateral Agent and each Lender and Borrower shall have any rights as a third party beneficiary of any of the provisions thereof.

12.2 Powers and Duties. Each Lender irrevocably authorizes Collateral Agent to take such action on such Lender's behalf and to exercise such powers, rights and remedies hereunder and under the other Loan Documents as are specifically delegated or granted to Collateral Agent by the terms hereof and thereof, together with such powers, rights and remedies as are reasonably incidental thereto. Collateral Agent may exercise such powers, rights and remedies and perform such duties by or through its agents or employees. Collateral Agent may accept payments of principal, interest, fees and expenses due under the Loan Documents from and deposits from Borrower on the account or benefit for any Lender.

(SIGNATURES TO FOLLOW)

IN WITNESS WHEREOF, Borrower and Lender have duly executed and delivered this Loan and Security Agreement as of the day and year first above written.

BORROWER:

ACELRX PHARMACEUTICALS, INC.

Signature: /s/ James Welch

Print Name: James Welch

Title: CFO

Accepted in Palo Alto, California:

LENDER:

HERCULES TECHNOLOGY II, L.P.

By: Hercules Technology SBIC Management, LLC, its General Partner

By: Hercules Technology Growth Capital, Inc., its Manager

Signature: /s/ Ben Bang

Print Name: Ben Bang

Title: Senior Counsel

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

Signature: /s/ Ben Bang

Print Name: Ben Bang

Title: Senior Counsel

Table of Addenda, Exhibits and Schedules

ADDENDUM 1 to LOAN AND SECURITY AGREEMENT

(a) *Borrower's Business.* For purposes of this Addendum 1, Borrower shall be deemed to include its "affiliates" as defined in Title 13 Code of Federal Regulations Section 121.103. Borrower represents and warrants to Hercules Technology II, L.P. ("Hercules II") as of the Closing Date, and covenants to Hercules II

(b) for a period of one year after the Closing Date with respect to subsections 2, 3, 4, 5, 6 and 7 below, as follows:

1. Size Status. As of the Closing Date, Borrower's NAIC is 325412, and Borrower has fewer than 750 employees;

2. No Relender. Borrower's primary business activity does not involve, directly or indirectly, providing funds to others, purchasing debt obligations, factoring, or long-term leasing of equipment with no provision for maintenance or repair;

3. No Passive Business. Borrower is engaged in a regular and continuous business operation (excluding the mere receipt of payments such as dividends, rents, lease payments, or royalties). Borrower's employees are carrying on the majority of day to day operations. Borrower will not pass through substantially all of the proceeds of the Loan to another entity;

4. No Real Estate Business. Borrower is not classified under Major Group 65 (Real Estate) or Industry No. 1531 (Operative Builders) of the SIC Manual. The proceeds of the Loan will not be used to acquire or refinance real property unless Borrower (x) is acquiring an existing property and will use at least 51 percent of the usable square footage for its business purposes; (y) is building or renovating a building and will use at least 67 percent of the usable square footage for its business purposes; or (z) occupies the subject property and uses at least 67 percent of the usable square footage for its business purposes.

5. No Project Finance. Borrower's assets are not intended to be reduced or consumed, generally without replacement, as the life of its business progresses, and the nature of Borrower's business does not require that a stream of cash payments be made to the business's financing sources, on a basis associated with the continuing sale of assets (e.g., real estate development projects and oil and gas wells). The primary purpose of the Loan is not to fund production of a single item or defined limited number of items, generally over a defined production period, where such production will constitute the majority of the activities of Borrower (e.g., motion pictures and electric generating plants).

6. No Farm Land Purchases. Borrower will not use the proceeds of the Loan to acquire farm land which is or is intended to be used for agricultural or forestry purposes, such as the production of food, fiber, or wood, or is so taxed or zoned.

7. No Foreign Investment. The proceeds of the Loan will not be used substantially for a foreign operation. At the time of the Loan, Borrower will not have more than 49 percent of its employees or tangible assets located outside the United States. The representation in this subsection (7) is made only as of the date hereof and shall not continue for one year as contemplated in the first sentence of this Section 1.

(c) *Small Business Administration Documentation*. Hercules II acknowledges that Borrower completed, executed and delivered to Hercules II SBA Forms 480, 652 and 1031 (Parts A and B) together with a business plan showing Borrower's financial projections (including balance sheets and income and cash flows statements) for the period described therein and a written statement (whether included in the purchase agreement or pursuant to a separate statement) from Hercules II regarding its intended use of proceeds from the sale of securities to Hercules II (the "Use of Proceeds Statement"). Borrower represents and warrants to Hercules II that the information regarding Borrower and its affiliates set forth in the SBA Form 480, Form 652 and Form 1031 and the Use of Proceeds Statement delivered as of the Closing Date is accurate and complete.

(d) *Inspection*. The following covenants contained in this Section (c) are intended to supplement and not to restrict the related provisions of the Loan Documents. Subject to the preceding sentence, Borrower will permit, for so long as Hercules II holds any debt or equity securities of Borrower, Hercules II or its representative, at Hercules II's expense, and examiners of the SBA to visit and inspect the properties and assets of Borrower, to examine its books of account and records, and to discuss Borrower's affairs, finances and accounts with Borrower's officers, senior management and accountants, all at such reasonable times as may be requested by Hercules II or the SBA.

(e) *Annual Assessment*. Promptly after the end of each calendar year (but in any event prior to February 28 of each year) and at such other times as may be reasonably requested by Hercules II, Borrower will deliver to Hercules II a written assessment of the economic impact of Hercules II's investment in Borrower, specifying the full-time equivalent jobs created or retained in connection with the investment, the impact of the investment on the businesses of Borrower in terms of expanded revenue and taxes, other economic benefits resulting from the investment (such as technology development or commercialization, minority business development, or expansion of exports) and such other information as may be required regarding Borrower in connection with the filing of

Hercules II's SBA Form 468. Hercules II will assist Borrower with preparing such assessment. In addition to any other rights granted hereunder, Borrower will grant Hercules II and the SBA access to Borrower's books and records for the purpose of verifying the use of such proceeds. Borrower also will furnish or cause to be furnished to Hercules II such other information regarding the business, affairs and condition of Borrower as Hercules II may from time to time reasonably request.

(f) *Use of Proceeds.* Borrower will deliver to Hercules II from time to time promptly following Hercules II's request, a written report, certified as correct by Borrower's Chief Financial Officer, verifying the purposes and amounts for which proceeds from the Loan have been disbursed. Borrower will supply to Hercules II such additional information and documents as Hercules II reasonably requests with respect to its use of proceeds and will permit Hercules II and the SBA to have access to any and all Borrower records and information and personnel as Hercules II deems necessary to verify how such proceeds have been or are being used.

(g) *Activities and Proceeds*. Neither Borrower nor any of its affiliates (if any) will engage in any activities or use directly or indirectly the proceeds from the Loan for any purpose for which a small business investment company is prohibited from providing funds by the SBIC Act, including 13 C.F.R. §107.720. Without obtaining the prior written approval of Hercules II, Borrower will not change within 1 year of the date hereof, Borrower's current business activity to a business activity which a licensee under the SBIC Act is prohibited from providing funds by the SBIC Act.

(h) *Redemption Provisions.* Notwithstanding any provision to the contrary contained in the Certificate of Incorporation of Borrower, as amended from time to time (the "Charter"), if, pursuant to the redemption provisions contained in the Charter, Hercules II is entitled to a redemption of its Warrant, such redemption (in the case of Hercules II) will be at a price equal to the redemption price set forth in the Charter (the "Existing Redemption Price"). If, however, Hercules II delivers written notice to Borrower that the then current regulations promulgated under the SBIC Act prohibit payment of the Existing Redemption Price in the case of an SBIC (or, if applied, the Existing Redemption Price would cause the Series C Preferred Stock to lose its classification as an "equity security" and Hercules II has determined that such classification is unadvisable), the amount Hercules II will be entitled to receive shall be the greater of (i) fair market value of the securities being redeemed taking into account the rights and preferences of such securities plus any costs and expenses of Hercules II incurred in making or maintaining the Warrant, and (ii) the Existing Redemption Price where the amount of accrued but unpaid dividends payable to Hercules II is limited to Borrower's earnings plus any costs and expenses of Hercules II incurred in making or maintaining the Warrant; provided, however, the amount calculated in subsections (i) or (ii) above shall not exceed the Existing Redemption Price.

(i) *Cost of Money.* Notwithstanding any provision to the contrary contained in the Loan Documents, all interest and fees charged pursuant to the Loan Documents shall comply with the provisions of 13 C.F.R. § 107.855, including, without limitation, that such amounts shall not exceed the Cost of Money ceiling (as defined hereafter). The current Cost of Money ceiling for this Loan is fourteen percent.

(j) *Compliance and Resolution.* Borrower agrees that a failure to comply with Borrower's obligations under this Addendum, or any other set of facts or circumstances where it has been asserted by any governmental regulatory agency (or Hercules II believes that there is a substantial risk of such assertion) that Hercules II and its affiliates are not entitled to hold, or exercise any significant right with respect to, any securities issued to Hercules II by Borrower, will constitute a breach of the obligations of Borrower under the financing agreements between Borrower and Hercules II. In the event of (i) a failure to comply with Borrower's obligations under this Addendum; or (ii) an assertion by any governmental regulatory agency (or Hercules II believes that there is a substantial risk of such assertion) of a failure to comply with Borrower's obligations under this Addendum, then (i) Hercules II and Borrower will meet and resolve any such issue in good faith to the satisfaction of Borrower, Hercules II, and any governmental regulatory agency, and (ii) upon request of Hercules II, Borrower will cooperate and assist with any assignment of the financing agreements from Hercules II to Hercules Technology Growth Capital, Inc.

EXHIBIT A

ADVANCE REQUEST

To: Lender: Date: _____, 20__

Hercules Technology II, L.P.
Hercules Technology Growth Capital, Inc.
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Attn:

AcelRx Pharmaceuticals, Inc. ("Borrower") hereby requests from Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc. (collectively, "Lender") an Advance in the amount of Fifteen Million Dollars ($15,000,000.00) on December 16, 2013 (the "Advance Date") pursuant to the Loan and Security Agreement between Borrower and Lender dated as of December 16, 2013 (the "Agreement"). In addition, Borrower directs Lender to (i) retain the Facility Charge and reimbursement of Lender's current expenses and (ii) payoff loans funded under the Original Agreement. Capitalized words and other terms used but not otherwise defined herein are used with the same meanings as defined in the Agreement.

Please:

(a) Issue a check payable to Borrower _____

or

(b) Wire Funds to Borrower's account _____

Bank: _____
Address: _____
_____
ABA Number: _____
Account Number: _____
Account Name: _____

Borrower represents that the conditions precedent to the Advance set forth in the Agreement are satisfied and shall be satisfied upon the making of such Advance, including but not limited to: (i) that no event that has had or could reasonably be expected to have a Material Adverse Effect has occurred and is continuing; (ii) that the representations and warranties set forth in the Agreement and in the Warrants are and shall be true and correct in all material respects on and as of the Advance Date with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date; (iii) that Borrower is in compliance with all the terms and provisions set forth in each Loan Document on its part to be observed or performed; and (iv) that as of the Advance Date, no fact or condition exists that would (or would, with the passage of time, the giving of notice, or both) constitute an Event of Default under the Loan Documents. Borrower understands and acknowledges that Lender has the right to review the financial information supporting this representation and, based upon such review in its sole discretion, Lender may decline to fund the requested Advance.

Borrower hereby represents that Borrower's corporate status and locations have not changed since the date of the Agreement or, if the Attachment to this Advance Request is completed, are as set forth in the Attachment to this Advance Request.

Borrower agrees to notify Lender promptly before the funding of the Loan if any of the matters which have been represented above shall not be true and correct on the Borrowing Date and if Lender has received no such notice before the Advance Date then the statements set forth above shall be deemed to have been made and shall be deemed to be true and correct as of the Advance Date.

Executed as of _____, 20__.

BORROWER: AcelRx Pharmaceuticals, Inc.

SIGNATURE: _____
TITLE: _____
PRINT NAME: _____

[Signature Page to Advance Request]

ATTACHMENT TO ADVANCE REQUEST

Dated: _____

Borrower hereby represents and warrants to Lender that Borrower's current name and organizational status is as follows:

Name:	AcelRx Pharmaceuticals, Inc.
Type of organization:	Corporation
State of organization:	Delaware
Organization file number:	3998627

Borrower hereby represents and warrants to Lender that the street addresses, cities, states and postal codes of its current locations are as follows:

EXHIBIT B-1

THIS SECURED CONVERTIBLE TERM PROMISSORY NOTE HAS NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND, ACCORDINGLY, MAY NOT BE TRANSFERRED UNLESS (I) THIS NOTE HAS BEEN REGISTERED FOR SALE PURSUANT TO THE SECURITIES ACT OF 1933, AS AMENDED, (II) THIS NOTE MAY BE SOLD PURSUANT TO RULE 144, OR (III) THE BORROWER HAS RECEIVED AN OPINION OF COUNSEL REASONABLY SATISFACTORY TO IT THAT SUCH TRANSFER MAY LAWFULLY BE MADE WITHOUT REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

SECURED CONVERTIBLE TERM PROMISSORY NOTE

$13,333,333.33 Advance Date: December 16, 2013

FOR VALUE RECEIVED, AcelRx Pharmaceuticals, Inc., a Delaware corporation, for itself and each of its Subsidiaries (the "Borrower") hereby promises to pay to the order of Hercules Technology II, L.P., a Delaware limited partnership or the holder of this Note (the "Lender") at 400 Hamilton Avenue, Suite 310, Palo Alto, CA 94301 or such other place of payment as the holder of this Secured Term Promissory Note (this "Promissory Note") may specify from time to time in writing, in lawful money of the United States of America, the principal amount of Thirteen Million Three Hundred Thirty-Three Thousand Three Hundred Thirty-Three and 33/100 Dollars ($13,333,333.33) or such other principal amount as Lender has advanced to Borrower, together with interest at a floating rate as set forth in that certain Loan and Security Agreement dated December 16, 2013, by and between Borrower and Lender (as the same may from time to time be amended, modified or supplemented in accordance with its terms, the "Loan Agreement").

This Promissory Note is one of the Notes referred to in, and is executed and delivered in connection with, the Loan Agreement, and is entitled to the benefit and security of the Loan Agreement and the other Loan Documents (as defined in the Loan Agreement), to which reference is made for a statement of all of the terms and conditions thereof. All payments shall be made in accordance with the Loan Agreement, including the right of Borrower to pay a portion of the amounts due and owing under this Promissory Note in shares of Common Stock in accordance with, and subject to the limitations set forth in, Section 2.2(e) of the Loan Agreement (including the requirement that any shares of Common Stock issuable by Borrower upon conversion of this Note are subject to an effective resale registration statement or are eligible for resale to the public pursuant to Rule 144 without any limitation). All terms defined in the Loan Agreement shall have the same definitions when used herein, unless otherwise defined herein. An Event of Default under the Loan Agreement shall constitute a default under this Promissory Note.

Borrower waives presentment and demand for payment, notice of dishonor, protest and notice of protest under the UCC or any applicable law. Borrower agrees to make all payments under this Promissory Note without setoff, recoupment or deduction and regardless of any counterclaim or defense. This Promissory Note has been negotiated and delivered to Lender and is payable in the State of California. This Promissory Note shall be governed by and construed and enforced in accordance with, the laws of the State of California, excluding any conflicts of law rules or principles that would cause the application of the laws of any other jurisdiction.

BORROWER:

ACELRX PHARMACEUTICALS, INC.

By:
Title:

EXHIBIT B-2

THIS SECURED CONVERTIBLE TERM PROMISSORY NOTE, AND ANY SECURITIES ISSUED UPON CONVERSION PURSUANT TO THIS SECURED CONVERTIBLE TERM PROMISSORY NOTE, HAVE NOT BEEN REGISTERED WITH THE SECURITIES AND EXCHANGE COMMISSION OR THE SECURITIES COMMISSION OF ANY STATE IN RELIANCE UPON AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND, ACCORDINGLY, MAY NOT BE TRANSFERRED UNLESS (I) SUCH SECURITIES HAVE BEEN REGISTERED FOR SALE PURSUANT TO THE SECURITIES ACT OF 1933, AS AMENDED, (II) SUCH SECURITIES MAY BE SOLD PURSUANT TO RULE 144, OR (III) THE BORROWER HAS RECEIVED AN OPINION OF COUNSEL REASONABLY SATISFACTORY TO IT THAT SUCH TRANSFER MAY LAWFULLY BE MADE WITHOUT REGISTRATION UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

SECURED CONVERTIBLE TERM PROMISSORY NOTE

$26,666,666.67 Advance Date: December 16, 2013

FOR VALUE RECEIVED, AcelRx Pharmaceuticals, Inc., a Delaware corporation, for itself and each of its Subsidiaries (the "Borrower") hereby promises to pay to the order of Hercules Technology Growth Capital, Inc., a Maryland corporation or the holder of this Note (the "Lender") at 400 Hamilton Avenue, Suite 310, Palo Alto, CA 94301 or such other place of payment as the holder of this Secured Term Promissory Note (this "Promissory Note") may specify from time to time in writing, in lawful money of the United States of America, the principal amount of Twenty-Six Million Six Hundred Sixty-Six Thousand Six Hundred Sixty-Six and 67/100 Dollars ($26,666,666.67) or such other principal amount as Lender has advanced to Borrower, together with interest at a floating rate as set forth in that certain Loan and Security Agreement dated December 16, 2013, by and between Borrower and Lender (as the same may from time to time be amended, modified or supplemented in accordance with its terms, the "Loan Agreement").

This Promissory Note one of the Notes referred to in, and is executed and delivered in connection with, the Loan Agreement, and is entitled to the benefit and security of the Loan Agreement and the other Loan Documents (as defined in the Loan Agreement), to which reference is made for a statement of all of the terms and conditions thereof. All payments shall be made in accordance with the Loan Agreement, including the right of Borrower to pay a portion of the amounts due and owing under this Promissory Note in shares of Common Stock in accordance with, and subject to the limitations set forth in, Section 2.2(e) of the Loan Agreement (including the requirement that any shares of Common Stock issuable by Borrower upon conversion of this Note are subject to an effective resale registration statement or are eligible for resale to the public pursuant to Rule 144 without any limitation). All terms defined in the Loan Agreement shall have the same definitions when used herein, unless otherwise defined herein. An Event of Default under the Loan Agreement shall constitute a default under this Promissory Note.

Borrower waives presentment and demand for payment, notice of dishonor, protest and notice of protest under the UCC or any applicable law. Borrower agrees to make all payments under this Promissory Note without setoff, recoupment or deduction and regardless of any counterclaim or defense. This Promissory Note has been negotiated and delivered to Lender and is payable in the State of California. This Promissory Note shall be governed by and construed and enforced in accordance with, the laws of the State of California, excluding any conflicts of law rules or principles that would cause the application of the laws of any other jurisdiction.

BORROWER:

ACELRX PHARMACEUTICALS, INC.

By:
Title:

EXHIBIT C

NAME, LOCATIONS, AND OTHER INFORMATION FOR BORROWER

1. Borrower represents and warrants to Lender that Borrower's current name and organizational status as of the Closing Date is as follows:

Name:	AcelRx Pharmaceuticals, Inc.
Type of organization:	Corporation
State of organization:	Delaware
Organization file number:	3998627

2. Borrower represents and warrants to Lender that for five (5) years prior to the Closing Date, Borrower did not do business under any other name or organization or form except the following:

Name:
Used during dates of:
Type of Organization: Corporation
State of organization: Delaware
Organization file Number:
Borrower's fiscal year ends on December 31
Borrower's federal employer tax identification number is: 41-2193603

3. Borrower represents and warrants to Lender that its chief executive office is located at 351 Galveston Drive, Redwood City, CA 94063.

EXHIBIT D

BORROWER'S PATENTS, TRADEMARKS, COPYRIGHTS AND LICENSES

See attached chart of patents.

ACELRX, THE ACELRX LOGO, ARX, NANOTAB, ACCELERATE.INNOVATE.ALLEVIATE., ZALVISO AND ASSOCIATED LOGO ARE TRADEMARKS OF ACELRX PHARMACEUTICALS, INC.

EXHIBIT E

BORROWER'S DEPOSIT ACCOUNTS AND INVESTMENT ACCOUNTS

DEPOSIT ACCOUNTS

Depository Institution (name and address)	Account Type	Account Number	Account Holder
Wells Fargo Bank	Demand	4121466536	AcelRx Pharmaceuticals, Inc.

INVESTMENT ACCOUNTS

Securities Intermediary (name and address)	Account Type	Account Number	Account Holder
Morgan Stanley & Co.	Securities	14-78EW8	AcelRx Pharmaceuticals, Inc.

EXHIBIT F

COMPLIANCE CERTIFICATE

Hercules Technology II, L.P.
Hercules Technology Growth Capital, Inc.
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301

Reference is made to that certain Loan and Security Agreement dated December 16, 2013 and all ancillary documents entered into in connection with such Loan and Security Agreement all as may be amended from time to time, (hereinafter referred to collectively as the "Loan Agreement") between Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., each as a Lender, and AcelRx Pharmaceuticals, Inc. (the "Company") as Borrower. All capitalized terms not defined herein shall have the same meaning as defined in the Loan Agreement.

The undersigned is an officer of the Company, knowledgeable of all Company financial matters, and is authorized to provide certification of information regarding the Company; hereby certifies that in accordance with the terms and conditions of the Loan Agreement, the Company is in compliance for the period ending _____, 20__ of all covenants, conditions and terms and hereby reaffirms that all representations and warranties contained therein are true and correct on and as of the date of this Compliance Certificate with the same effect as though made on and as of such date, except to the extent such representations and warranties expressly relate to an earlier date, after giving effect in all cases to any standard(s) of materiality contained in the Loan Agreement as to such representations and warranties. Attached are the required documents supporting the above certification. The undersigned further certifies that these are prepared in accordance with GAAP (except for the absence of footnotes with respect to unaudited financial statement and subject to normal year end adjustments) and are consistent from one period to the next except as explained below.

REPORTING REQUIREMENT	REQUIRED	CHECK IF ATTACHED
Interim Financial Statements	Monthly within 30 days	☐
Interim Financial Statements	Within 45 days after each of the first 3 fiscal quarters of each fiscal year	☐
Audited Financial Statements	FYE within 90 days	☐

Very Truly Yours,

ACELRX PHARMACEUTICALS, INC.

By: _____

Name: _____

Its: _____

[Signature Page to Compliance Certificate]

EXHIBIT G

FORM OF JOINDER AGREEMENT

This Joinder Agreement (the "Joinder Agreement") is made and dated as of [ ], 20[ ], and is entered into by and between _____., a _____ corporation ("Subsidiary"), and HERCULES TECHNOLOGY II, L.P., a Delaware limited partnership, and HERCULES TECHNOLOGY GROWTH CAPITAL, INC., a Maryland corporation (collectively, "Lender").

RECITALS

A. Subsidiary's Affiliate, AcelRx Pharmaceuticals, Inc. ("Company") has entered into that certain Loan and Security Agreement dated December 16, 2013, with Lender, as such agreement may be amended (the "Loan Agreement"), together with the other agreements executed and delivered in connection therewith;

B. Subsidiary acknowledges and agrees that it will benefit both directly and indirectly from Company's execution of the Loan Agreement and the other agreements executed and delivered in connection therewith;

AGREEMENT

NOW THEREFORE, Subsidiary and Lender agree as follows:

1. The recitals set forth above are incorporated into and made part of this Joinder Agreement. Capitalized terms not defined herein shall have the meaning provided in the Loan Agreement.

2. By signing this Joinder Agreement, Subsidiary shall be bound by the terms and conditions of the Loan Agreement the same as if it were the Borrower (as defined in the Loan Agreement) under the Loan Agreement, mutatis mutandis, provided however, that Lender shall have no duties, responsibilities or obligations to Subsidiary arising under or related to the Loan Agreement or the other agreements executed and delivered in connection therewith. Rather, to the extent that Lender has any duties, responsibilities or obligations arising under or related to the Loan Agreement or the other agreements executed and delivered in connection therewith, those duties, responsibilities or obligations shall flow only to Company and not to Subsidiary or any other person or entity. By way of example (and not an exclusive list): (a) Lender's providing notice to Company in accordance with the Loan Agreement or as otherwise agreed between Company and Lender shall be deemed provided to Subsidiary; (b) a Lender's providing an Advance to Company shall be deemed an Advance to Subsidiary; and (c) Subsidiary shall have no right to request an Advance or make any other demand on Lender.

[REMAINDER OF PAGE INTENTIONALLY LEFT BLANK]

SUBSIDIARY:

_____.

By:
Name:
Title:

Address:

Telephone: _____
Facsimile: _____

HERCULES TECHNOLOGY II, L.P.

By: Hercules Technology SBIC Management, LLC, its General Partner

By: Hercules Technology Growth Capital, Inc., its Manager

By: _____
Name: _____
Title: _____

Address:
400 Hamilton Ave., Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

By: _____
Name: _____
Title: _____

Address:
400 Hamilton Ave., Suite 310
Palo Alto, CA 94301
Facsimile: 650-473-9194
Telephone: 650-289-3060

EXHIBIT H

[RESERVED]

EXHIBIT I

ACH DEBIT AUTHORIZATION AGREEMENT

Hercules Technology II, L.P.
Hercules Technology Growth Capital, Inc.
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301

Re: Loan and Security Agreement dated December 16, 2013 between AcelRx Pharmaceuticals, Inc. ("Borrower") and Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc. (collectively, "Company") (the "Agreement")

In connection with the above referenced Agreement, the Borrower hereby authorizes the Company to initiate debit entries for the periodic payments due under the Agreement to the Borrower's account indicated below. The Borrower authorizes the depository institution named below to debit to such account.

DEPOSITORY NAME	BRANCH
CITY	STATE AND ZIP CODE
TRANSIT/ABA NUMBER	ACCOUNT NUMBER

This authority will remain in full force and effect so long as any amounts are due under the Agreement.

ACELRX PHARMACEUTICALS, INC.

By: _____

Date: _____

EXHIBIT J

REPAYMENT ELECTION NOTICE

[INSERT DATE]

Hercules Technology II, L.P.
Hercules Technology Growth Capital, Inc.
400 Hamilton Avenue, Suite 310
Palo Alto, CA 94301

Reference is made to that certain Loan and Security Agreement dated December 16, 2013 and all ancillary documents entered into in connection with such Loan and Security Agreement all as may be amended from time to time, (hereinafter referred to collectively as the "Loan Agreement") between Hercules Technology II, L.P. and Hercules Technology Growth Capital, Inc., each as a Lender, and AcelRx Pharmaceuticals, Inc. (the "Company") as Borrower. All capitalized terms not defined herein shall have the same meaning as defined in the Loan Agreement.

Borrower hereby irrevocably elects to make **[**the Principal Installment Payment in the amount of $ _____ due on [_____] (the "Delivery Date") in shares of Common Stock in accordance with Section 2.2(e) of the Loan Agreement **][**an Optional Prepayment in the amount of $ _____ on [_____] (the "Delivery Date") in shares of Common Stock in accordance with Section 2.2(e) of the Loan Agreement **]**.[1] The number of shares of Common Stock to be delivered to Lender, on or prior to the Delivery Date, is [_____], which amount was determined in accordance with Section 2.2(e) of the Loan Agreement. The stock certificates shall be delivered free and clear of any restrictive legends.

The Borrower hereby represents, warrants and certifies to Lender that, as of the date hereof, all of the Stock Payment Conditions have been satisfied. The Borrower acknowledges and agrees that its right to pay the **[**Principal Installment Payment**][**Optional Prepayment**]** in Common Stock in accordance with this Repayment Election Notice is subject to the satisfaction of all of the Stock Payment Conditions on the Delivery Date and, to the extent any of the Stock Payment Conditions are not satisfied on the Delivery Date, Borrower shall pay the **[**Principal Installment Payment**][**Optional Prepayment**]** in cash.

Sincerely,

---

[1] *Note*: In accordance with Section 2.2(e) of the Loan Agreement, the Delivery Date must be at least 10 days following the date of delivery of this Repayment Election Notice.

ACELRX PHARMACEUTICALS, INC.

By: _____

Name: _____

Its: _____

SCHEDULE 1.1

COMMITMENTS

LENDER	TERM COMMITMENT	TERM COMMITMENT PERCENTAGE
Hercules Technology II, L.P.	$ 13,333,333.33	33.33%
Hercules Technology Growth Capital, Inc.	$ 26,666,666.67	66.67%
TOTAL COMMITMENTS	$ 40,000,000.00	100%

SCHEDULE 7.4

POST-CLOSING ITEMS

Borrower shall deliver or cause to be delivered to Lender:

1. On or before February 16, 2014, a Landlord's Waiver and Consent for 351 Galveston Drive, Redwood City, CA 94063 in form reasonably satisfactory to Lender.

2. On or before February 16, 2014, a Bailee Agreement approved by Patheon Inc. for Collateral located at 2110 East Galbraith Road, Cincinnati, OH 45237 in form reasonably satisfactory to Lender.

Exhibit 10.20

August 7, 2013

David Chung

Dear David:

On behalf of AceiRx Pharmaceuticals, Inc. (the "Company"), I am pleased to offer you the position of Chief Commercial Officer of the Company. Speaking for myself, as well as the other members of the Company's management team, we are all very impressed with your credentials and we look forward to your future success in this position.

The terms of your new position with the Company are as set forth below:

1. Position.

(a) You will become the Chief Commercial Officer of the Company, working out of the Company's headquarters office in Redwood City, California. You will report to Richard King, President & CEO.

(b) You agree to the best of your ability and experience that you will at all times loyally and conscientiously perform all of the duties and obligations required of and from you pursuant to the express and implicit terms hereof, and to the reasonable satisfaction of the Company. During the term of your employment, you further agree that you will devote at least 100% of your business time and attention to the business of the Company, the Company will be entitled to all of the benefits and profits arising from or incident to all such work services and advice, you will not render commercial or professional services of any nature to any person or organization, whether or not for compensation, without the prior written consent of the Company, such consent not to be unreasonably withheld, and you will not directly or indirectly engage or participate in any business that is competitive in any manner with the business of the Company. Nothing in this letter agreement will prevent you from accepting speaking or presentation engagements in exchange for honoraria or from serving on boards of charitable organizations, or from owning no more than one percent (1%) of the outstanding equity securities of a corporation whose stock is listed on a national stock exchange.

2. **Start Date.** Subject to fulfillment of any conditions imposed by this letter agreement, you will commence this new position with the Company on September 1, 2013 (the "Start Date").

3. **Proof of Right to Work.** For purposes of federal immigration law, you will be required to provide to the Company documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to us within three business days of your date of hire, or our employment relationship with you may be terminated.

AceiRx Pharmaceuticals, Inc.
351 Galveston Drive
Redwood City, CA 94063

4. Compensation. You will be paid a monthly salary of $27,500.00, which is equivalent to $330,000.00 on an annualized basis (the " Base Salary"). Your salary will be payable in two equal payments per month pursuant to the Company's regular payroll policy. The Base Salary will be reviewed annually as part of the Company's normal salary review process. In addition to your base salary, you will have the opportunity to earn a target annual bonus of up to 35% of your earned salary based on achievement of a series of personal and company objectives that the Board of Directors acting through the Compensation Committee will define annually. You will also receive a one-time sign on bonus in the amount of $16,500.00 to be paid alongside your first paycheck. The company will also provide a partial living cost for an apartment of $1,250.00 per month for a maximum of two years.

5. Stock Option Grant.

(a) Initial Grant. In connection with the commencement of your employment, the Company will recommend that the Board of Directors (the "Board") grant you an option to purchase 150,000 shares of the Company's Common Stock (" Option Shares") with an exercise price equal to the fair market value of the Common Stock on the date of the grant, as determined in good faith by the Board. The Option Shares will vest at the rate of 25% of the shares on the twelve (12) month anniversary of your Vesting Commencement Date (as defined in your Stock Option Agreement, which date will be your Start Date, as defined above) and the remaining Option Shares will vest monthly thereafter at the rate of 1/48 of the total number of the Option Shares per month, subject to the acceleration provisions set forth below. Vesting will, of course, depend on your continued employment with the Company. The option will be subject to the terms of the Company's 2006 Stock Plan (the "Plan") and the Stock Option Agreement between you and the Company.

(i) Effect of Termination Following a Change in Control. In the event that the Company undergoes a Change in Control (as such term is defined in the Plan) and within twelve (12) months following the closing of the Change in Control, the Company terminates your employment without Cause (as such term is defmed in the Plan) or you terminate your employment due to an Involuntary Termination (as such term is defined below), the vesting of the Option Shares shall accelerate in full such that 100% of the then unvested Option Shares will become vested and exercisable as of your termination date. For purposes of the Option Shares, an "Involuntary Termination" shall mean your voluntary termination of employment with the Company within thirty (30) days following the occurrence of any of the following events without your written consent and after providing the Company a reasonable opportunity to cure such event: (i) a material reduction or change in your job duties, reporting relationships, responsibilities and requirements inconsistent with your position with the Company and prior duties, reporting relationships, responsibilities and requirements prior to the Change in Control, provided that neither a mere change in title alone nor reassignment following a Change in Control to a position that is substantially similar to the position held prior to the Change in Control in terms of job duties, responsibilities or requirements shall constitute a material reduction in job responsibilities; (ii) a reduction in your then-current base salary by at least 20%, provided that an across-the-board reduction in the salary level of all other senior executives by the same percentage amount as part of a general salary level reduction shall not constitute such a salary reduction, or (iii) the relocation of your principal place for performance of your Company duties to a location more than thirty (30) miles from the Company's then current location at the time of the Change in Control.

6. **Benefits.**

(a) **Insurance Benefits.** The Company will provide you with the opportunity to participate in the standard benefits plans currently available to other Company employees, subject to any eligibility requirements imposed by such plans.

(b) **Vacation; Sick Leave.** You will be entitled to paid time off according to the Company's standard policies.

7. **Confidential Information and Invention Assignment Agreement .** Your acceptance of this offer and commencement of employment with the Company is contingent upon the execution, and delivery to an officer of the Company, of the Company's Confidential Information and Invention Assignment Agreement, a copy of which is enclosed for your review and execution (the " Confidentiality Agreement"), prior to or on your Start Date.

8. **At-Will Employment.** Your employment with the Company will be on an "at will" basis, meaning that either you or the Company may terminate your employment at any time for any reason or no reason, without further obligation or liability.

9. No **Conflicting Obligations.** You understand and agree that by accepting this offer of employment, you represent to the Company that your performance will not breach any other agreement to which you are a party and that you have not, and will not during the term of your employment with the Company, enter into any oral or written agreement in conflict with any of the provisions of this letter or the Company's policies. You are not to bring with you to the Company, or use or disclose to any person associated with the Company, any confidential or proprietary information belonging to any former employer or other person or entity with respect to which you owe an obligation of confidentiality under any agreement or otherwise. The Company does not need and will not use such information and we will assist you in any way possible to preserve and protect the confidentiality of proprietary information belonging to third pruties. Also, we expect you to abide by any obligations to refrain from soliciting any person employed by or otherwise associated with any former employer and suggest that you refrain from having any contact with such persons until such time as any non-solicitation obligation expires.

10. **Entire Agreement.** This letter, together with the Confidentiality Agreement, sets forth the entire agreement and understanding between you and the Company relating to your employment and supersedes all prior agreements and discussions between us. This letter may not be modified or amended except by a written agreement, signed by an officer of the Company, although the Company reserves the right to modify unilaterally your compensation, benefits, job title and duties, reporting relationships and other terms of your employment. This letter will be governed by the laws of the State of California without regard to is conflict of laws provision.

AceiRx Pharmaceuticals, Inc.
351 Galveston Drive
Redwood City, CA 94063

We are all delighted to be able to extend you this offer and look forward to working with you. To indicate your acceptance of the Company's offer, please sign and date this letter in the space provided below and return it to me, along with a signed and dated copy of the Confidentiality Agreement. This offer will terminate if not accepted by you on or before August 16, 2013.

Very truly yours,

ACELRX PHARMACEUTICALS, INC.

By:

Richard King
Chief Executive Officer

AceiRx Pharmaceuticals, Inc.
351 Galveston Drive
Redwood City. CA 94063

ACCEPTED AND AGREED:

DAVID CHUNG

Signature

Date: 8/7/13

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.28

CONFIDENTIAL
EXECUTION COPY

MANUFACTURE AND SUPPLY AGREEMENT

This **MANUFACTURE AND SUPPLY AGREEMENT** ("**Agreement**") is entered into as of December 16, 2013 (the "**Effective Date**") between **ACELRX PHARMACEUTICALS, INC.**, a company organized under the laws of the State of Delaware, United States (" **AcelRx**"), and having a principal place of business at 575 Chesapeake Drive, Redwood City, CA 94063, United States, and **GRÜNENTHAL GMBH**, a company organized under the laws of Germany ("**Grünenthal**"), having its registered office at Zieglerstrasse 6, 52078 Aachen, Germany. AcelRx and Grünenthal may be referred to herein from time to time individually as a "**Party**," and collectively as the "**Parties**".

WHEREAS, AcelRx is developing and owns or controls certain patents, know-how and other intellectual property relating to the Product (as defined hereinafter);

WHEREAS, AcelRx and Grünenthal are parties to a Collaboration and License Agreement of even date herewith (the " **License Agreement**"), pursuant to which AcelRx has granted Grünenthal certain Exclusive rights and licenses to manufacture, commercialize, use, sell, offer for sale and import the Product in the Field (as defined hereinafter) in the Territory (as defined hereinafter), and which provides that Grünenthal will procure its supply of the Product from AcelRx pursuant to the provisions of this Agreement; and

WHEREAS, AcelRx is willing to provide such supply of the Product to Grünenthal, on the terms and conditions set forth below.

NOW THEREFORE, in consideration of the mutual promises and agreements set forth herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows:

ARTICLE 1

DEFINITIONS

1.1 "**Accessories**" shall mean additional hardware accessories or components for use with the Product which are not included in the Reusables Kit or Dispenser Kit, e.g., a cartridge RFID label reader. For clarity, Accessories are optional purchase items and made available by AcelRx from time to time available on a purchase order basis and are identified as Accessories on Exhibit A.

1.2 "**AcelRx Technology**" shall mean AcelRx's proprietary technology and the intellectual property rights therein, for a sublingual patient-controlled analgesia (PCA) system.

1.3 "**Accounting Standards**" shall mean, with respect to AcelRx, US GAAP (United States generally accepted accounting principles as in effect from time to time), and with respect

to Grünenthal, the IFRS (International Financial Reporting Standards as in effect from time to time), in each case, as consistently applied throughout the period involved. Each Party shall promptly notify the other in the event that it changes the Accounting Standards pursuant to which its records are maintained, it being understood that each Party may only use internationally recognized accounting principles (e.g. IFRS, US GAAP, etc.).

1.4 "Affiliate" of a Party shall mean any Person that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such Party, as the case may be, but for only so long as such control exists. As used in this Section 1.2, "control" shall mean (a) direct or indirect beneficial ownership of at least 50% (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of the voting share capital or other equity interest in such Person or (b) the power to direct the management of such Person by contract or otherwise.

1.5 "Applicable Laws" shall mean the applicable provisions of any and all national, supranational, regional, state and local laws, treaties, statutes, rules, regulations, administrative codes, guidance, ordinances, judgments, decrees, directives, injunctions, orders, permits (including Marketing Approvals) of or from any court, arbitrator, Regulatory Authority or governmental agency or authority having jurisdiction over or related to the subject item.

1.6 "APQ" has the meaning set forth in Section 5.1(a).

1.7 "Auditor" shall have the meaning set forth in Section 3.4.

1.8 "Authorized Representative" shall mean Grünenthal who is designated by AcelRx for the Licensed Product to act and may be addressed by authorities and bodies in the EU instead of AcelRx according to the applicable EU directives and guidelines and based upon a written agreement between AcelRx and Grünenthal.

1.9 "Business Day" shall mean a day other than a Saturday or Sunday or any public holiday in the San Francisco, CA or Aachen, Germany, but excluding the nine (9) consecutive calendar days beginning December 24 in a Calendar Year and continuing through January 1 of the following year. For the avoidance of doubt, references in this Agreement to "days" shall mean calendar days.

1.10 "Calendar Year" shall mean a period of twelve consecutive months beginning on and including January 1 st.

1.11 "CE Mark" shall mean a marking obtained and maintained by AcelRx for the Licensed Product that identifies conformity with medical device conformity requirements for use, sale and importation in the EU.

1.12 "cGMP" shall mean the then-current good manufacturing practices required by the FDA, as set forth in the United States Federal Food, Drug and Cosmetic Act, as amended, and the regulations promulgated thereunder, for the Manufacture of APIs, intermediates, medical devices and combination products, and the then current good manufacturing practices required

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by the Regulatory Authorities in the EU and Australia , as may be updated from time to time and other Applicable Laws of the EU relating to the Manufacture of APIs, intermediates, medicinal product, medical devices and combination products.

1.13 "Confidential Information" has the meaning set forth in Section 8.1.

1.14 "**Confidentiality Agreement**" shall mean that certain Bilateral Secrecy Agreement between AcelRx and Grünenthal dated 18 January 2013, as amended by the 1st Amendment dated July 23, 1013.

1.15 "Device" shall mean any current or future device portion of the Product, or any part thereof.

1.1 "Dispenser Kit" shall mean a complete kit consisting of a dispenser, cap and thumbtag for use with or as part of the Device.

1.16 "**Distributor**" shall have the meaning set forth in the License Agreement

1.17 "Drug" shall mean the sufentanil drug cartridge for use with the Device.

1.14 "EU" or **"European Union"** shall mean the countries comprising the supra national community consisting of as of the Effective Date, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

1.18 "FDA" shall mean the U.S. Food and Drug Administration or similar federal, state or local Regulatory Authorities.

1.19 "FD&C Act" shall mean the United States Food, Drug and Cosmetic Act, as amended, and any regulations promulgated thereunder.

1.20 "**Field**" shall mean human use in treatment of pain for (a) use within or dispensed by a hospital; or (b) use within a hospice, nursing home or other medically supervised setting, **[*]**.

1.21 "**Firm Order**" has the meaning set forth in Section 2.3(c).

1.22 "**Force Majeure**" has the meaning set forth in Section 11.4.

1.23 "Fully Burdened Manufacturing Cost" shall mean the fully burdened Manufacturing cost of the Product (including packaging for shipment) calculated in conformity with Accounting Standards and expressed on a per unit Manufactured basis, including the cost of: **[*]**

For clarity, the calculation of the cost of Manufacturing set forth above shall be based upon all Product manufactured by AcelRx over a specified period of time and shall in any event not be

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based on a disproportionate allocation of those costs incurred in the manufacture of the Product to Grünenthal's units of Product relative to the costs allocated to units of Product for AcelRx and its other licensees. For further clarity, costs that are specific to the units of Product supplied to Grünenthal (e.g., subsection (d) costs) shall be limited to Product supplied to Grünenthal unless those costs apply to the other units of Product manufactured in any particular runs or campaigns and allocated accordingly.

1.24 "Governmental Authority" shall mean any court, agency, department, authority or other instrumentality of any national, supranational, state, county, city or other political subdivision.

1.25 "Harmonized Standards" shall mean technical specifications meeting the essential requirements of the European Commission Medical Device Directives, compliance with which will provide a presumption of conformity with the essential requirements for the Licensed Product.

1.26 "Initial Forecast" has the meaning set forth in Section 2.3(a).

1.27 "Initial Product" shall mean AcelRx Sufentanil NanoTab PCA System **[*]** which includes both Drug and Device.

1.28 "Manufacture" shall mean to manufacture, process, prepare, make, assemble, test, label, and/or package, store, release and deliver the Product (or any component thereof).

1.29 "Manufacturing Continuity Plan" shall mean a plan setting forth measures and implementation efforts reasonably designed to (a) identify and set forth plans to implement risk mitigation measures (e.g., identifying available alternative suppliers, plans for alternative Third Party manufacturers based on forecast orders and sales of Product worldwide, infrastructure and inventory management and security and protective measures) reasonably necessary to ensure minimal impact from a range of potential disruptive events on supply of Product, taking into consideration the obligations to supply under this Agreement, (b) anticipate an unplanned or unanticipated disruptive event in order to restore supply continuity, and (c) recover the capacity to Manufacture and deliver Product as promptly as reasonably practicable. The Manufacturing Continuity Plan shall identify key personnel, resources, services and actions which are reasonably anticipated to be required to manage the recovery process.

1.30 "Marketing Approval" and "MAA Approval" shall have the meaning set forth in the License Agreement.

1.31 "MEDDEV Guidelines" shall mean those guidelines published by the European Commission promoting a common approach by manufacturers and notified bodies involved in the conformity assessment procedures according to the relevant annexes of the directives, and by the competent authorities charged with safeguarding public health.

1.32 "Medical Device Directive" shall mean the directive 93/42/EEC published by the European Commission and any successors thereof.

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1.33 "Minimum Order Quantities" shall mean, minimum purchase order quantities submitted by Grünenthal to AcelRx during each period pursuant to this Agreement as follows: **[*]**.

1.34 "NDA" of a Product shall mean a New Drug Application as defined in Title 21 of the U.S. Code of Federal Regulations, §314.80 et seq., and all amendments and supplements thereto, which is filed with the FDA, or the equivalent application filed with Health Canada in Canada, including all documents, data, and other information concerning such Product thus filed that are necessary for gaining Marketing Approval for such Product.

1.35 "Person" shall mean any individual, corporation, partnership, limited liability company, trust, governmental entity, or other legal entity of any nature whatsoever.

1.36 "Pharmacovigilance Agreement" shall mean the Pharmacovigilance Agreement entered into between the Parties in accordance with the License Agreement.

1.37 "Planning Forecast" has the meaning set forth in Section 2.2.

1.38 "Primary Packaged Form" shall mean the bulk packaging of the Product in the form of primary labeled finished Product bearing the designation of AcelRx as the Manufacturer of the Product but requiring secondary labeling for the use, sale or distribution in the relevant country in the Territory.

1.39 "Product" shall mean the Initial Product and any improvement and/or modification thereto pursuant to the License Agreement, including additional dosage strengths, but solely to the extent such derivative, improvement or modification consists of a Device and Drug where the Drug (but not any other active ingredients) is delivered using the AcelRx Technology.

1.40 "Quality Agreement" has the meaning set forth in Section 3.2.

1.41 "Recalls" has the meaning set forth in Section 3.11(a).

1.42 "Regulatory Authority" shall mean any national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity (a) whose review and/or approval is necessary (i) for the Manufacture, packaging, use, storage, import, export, distribution, promotion, marketing, offer for sale and sale of the Product, and/or (ii) for reviewing regulatory filings for the Product (or a component thereof); and/or (b) having authority to review and enforce cGMP and/or other Applicable Laws relating to the Product or the Manufacture, development, commercialization, use or sale thereof. For clarity, Regulatory Authority shall, as applicable, include any notified body with respect to the Device.

1.43 "Regulatory Requirements" shall mean (a) all specifications, methods of Manufacture, and other information in one or more regulatory submissions related in any way to the Product, (b) all laws, rules, regulations, applicable regulatory guidance documents, and other requirements of any Regulatory Authority that govern the Product, including its Manufacture.

1.44 "Replacement Components" shall mean those items specified as Replacement Components on Exhibit A. For clarity, Replacement Components are optional purchase items

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and made available by AcelRx from time to time available on a purchase order basis and are identified as Replacement Components on Exhibit A.

1.45 "**Reusables Kit**" shall mean a complete kit consisting of a Controller, holster, and technician access badge.

1.46 "**Rolling Forecast**" has the meaning set forth in Section 2.3(a).

1.47 "**Small Quantity Cost**" has the meaning set forth in Section 2.6.

1.48 "Specifications" shall mean the specifications for the Product, as established by **[*]** and as required by a Regulatory Authority in the Territory for approval and such other specifications, such as specifications for packaging, storage conditions and labeling of the Product, as agreed by the Parties pursuant to this Agreement.

1.49 "**Sublicensee**" shall have the meaning set forth in the License Agreement.

1.50 "**Term**" has the meaning set forth in Section 10.1.

1.51 "**Territory**" shall mean the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia.

1.52 "Third Party" shall mean any Person other than AcelRx, Grünenthal and their respective Affiliates.

1.53 "**Transfer Price**" shall mean the Fully Burdened Manufacturing Cost of AcelRx; provided that **[*]** exclusive of any VAT, tax, surcharge or fee applied to the Product or any portion thereof in accordance with Applicable Laws, which tax, surcharge or fee shall be paid by Grünenthal. For clarity, the price per unit limitations shall apply to Drug cartridges, Dispenser Kits and Reusables Kits delivered in the applicable year, whether or not ordered in a prior year and in any event shall be subject to minimum purchase requirements set forth in this Agreement, including Minimum Order Quantities. For further clarity, pricing of Accessories and Replacement Components are not included in the Transfer Price.

1.54 "United States" or **"U.S."** shall mean the United States of America, including its territories and possessions and the District of Columbia.

ARTICLE 2

SUPPLY OF THE PRODUCT; ACCESSORIES AND REPLACEMENT COMPONENTS

2.1 Supply and Purchase of the Product. Subject to the terms of this Agreement, during the Term, AcelRx shall Manufacture and supply the Product for use in the Field for the Territory exclusively for Grünenthal (including its Sublicensees and Distributors), and subject to Section 5.3(d) and AcelRx's ability to timely deliver ordered quantities of Product meeting the requirements of this Agreement, Grünenthal shall purchase from AcelRx, during the first five (5) years after the Effective Date **[*]** of Grünenthal's and its Sublicensees' and Distributors'

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requirements of Product (and Devices for samples and demonstration only) for use in the Field for the Territory in such quantities as Grünenthal shall order pursuant to and in accordance with this Article 2. Unless and until Grünenthal undertakes the Manufacture and supply of Product for itself under the terms of this Agreement and the License Agreement, AcelRx shall be responsible for the Manufacture (including maintaining the supply chain) of Product for use in the Field for the Territory as provided in this Agreement. AcelRx shall keep Grünenthal promptly and fully informed of any material developments regarding its supply chain.

2.2 Rolling Forecast.

(a) Initial Forecast. Not less than **[*]** following the Effective Date, Grünenthal shall provide AcelRx a non-binding forecast (" **Preliminary Non-Binding Forecast**") of what Grünenthal expects to provide as its Initial Forecast, when that becomes due to be provided pursuant the following sentence. Not less than **[*]** prior to the first anticipated delivery of the Product to Grünenthal, Grünenthal shall provide AcelRx its initial **[*]** rolling forecast (**"Initial Forecast"**) and initial three (3) month purchase order, in each case, separated into quantities of Drug, Dispenser Kits and Reusables Kits. Except as may be expressly agreed by the Parties, the Initial Forecast shall be no more than **[*]**, and no less than **[*]**, of the Preliminary Non-Binding Forecast.

(b) Limitation. In no event shall AcelRx be required to establish capacity to supply more than **[*]** Drug cartridges or Dispenser Kits per year without the mutual, written agreement of the Parties. To the extent that the forecast quantities are expected to exceed such **[*]** Drug cartridges or Dispenser Kits per year, the Parties shall meet and discuss in good faith the potential to add additional capacity prior to the date that the forecast quantities are expected to exceed such amount.

(c) Rolling Forecast. Following the Initial Forecast, Grünenthal shall provide AcelRx **[*]** with a written **[*]** rolling forecast (the "**Rolling Forecast**") of the quantities of Drug, Dispenser Kits and Reusables Kits required by Grünenthal and its Sublicensees and Distributors, and each subsequent monthly update to the Rolling Forecast shall be provided no later than **[*]** Business Days after the beginning of the next monthly period; provided, that (i) during **[*]**, the monthly forecast amount of the Drug, Dispenser Kits and Reusables Kits shall not be less than **[*]** of the previous monthly forecast amount of the respective previous monthly forecast amounts of the Drug, Dispenser Kits and Reusables Kits; provided, further, that the monthly forecast amounts of (x) the Drug, Dispenser Kits and Reusables Kits shall not be more than **[*]** of the respective previous monthly forecast amounts of Drug, Dispenser Kits and Reusables Kits in the applicable previous Rolling Forecast; (ii) for **[*]**, the monthly forecast amount of the Drug, Dispenser Kits and Reusables Kits shall not be less than **[*]** of the previous monthly forecast amount of the respective previous monthly forecast amounts of the Drug, Dispenser Kits and Reusables Kits; provided, further, that the monthly forecast amounts of (x) the Drug, Dispenser Kits and Reusables Kits shall not be more than **[*]** of the respective previous monthly forecast amounts of Drug, Dispenser Kits and Reusables Kits in the applicable previous Rolling Forecast and (iii) thereafter, the monthly forecast amount of the Drug, Dispenser Kits and Reusables Kits shall not be less than **[*]** of the previous monthly forecast amount of the respective previous monthly forecast amounts of the

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Drug, Dispenser Kits and Reusables Kits; provided, further, that the monthly forecast amounts of (x) the Drug, Dispenser Kits and Reusables Kits shall not be more than **[*]** of the respective previous monthly forecast amounts of Drug, Dispenser Kits and Reusables Kits in the applicable previous Rolling Forecast.

(d) [*] Binding Commitments. With respect to the Drug, the first **[*]** of the Initial Forecast and each Rolling Forecast shall constitute a mutually binding commitment, and with respect to the Dispenser Kits and Reusables Kits, the first **[*]** of each Initial Forecast and each Rolling Forecast shall constitute a mutually binding commitment, to order, have supplied and take delivery the total quantity of such Drug, Dispenser Kits and Reusables Kits forecast for such binding Forecast periods (each commitment, a " **Firm Order**"); provided, that if AcelRx notifies Grünenthal that it is unable to meet the Firm Order quantities **[*]**. Each Firm Order shall be represented by purchase order(s) delivered in accordance with Section 2.4. In no event shall Drug be delivered in excess of the Firm Order for Drug.

(e) Remaining Forecast. Projections (with respect to Drug) for **[*]** of each Rolling Forecast and projections (with respect to Device) for **[*]** of each Rolling Forecast shall be made in good faith and shall constitute Grünenthal's best estimates of future orders but shall not be binding on Grünenthal or AcelRx.

(f) Excess Quantities. If there is an order in any month for more than the applicable Firm Order, AcelRx shall use commercially reasonable efforts, subject to the total annual **[*]** Drug cartridges or Dispenser Kits limit set forth in Section 2.2, to Manufacture any quantity of Drug, Dispenser Kits and Reusables Kits ordered by Grünenthal in excess of such levels, but in any event, AcelRx's failure to Manufacture any such excess quantities shall not be a breach of this Agreement.

2.3 Safety Stock. AcelRx shall maintain a stock of components, containers, labels, packaging materials and related items (**"Materials"**), finished Product or work-in-progress, in any combination thereof, amounting to **[*]** supply of Product or Drug based on the quantities of Product of the most recent Firm Order commitment of Grünenthal. All such Materials, finished Product, Drug or work-in-progress shall be of suitable quality as required under the Specifications and taken collectively would allow AcelRx to Manufacture or have available for delivery at least **[*]** of Product. For clarity, the obligation to maintain safety stock is subject to reduction with respect to Drug in the event that APQ requirements limit the amount of controlled substance available to AcelRx in its efforts to meet the requirements of this Section 2.4.

2.4 Purchase Orders.

(a) Grünenthal shall submit to AcelRx firm purchase order(s) for Drug, Dispenser Kits and Reusables Kits, which firm purchase orders shall be in accordance with the applicable Minimum Order Quantities for each of Drug, Dispenser Kits and Reusables Kits and in accordance with the applicable binding commitment requirements as provided in Section 2.3(d) of the Rolling Forecast.

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(b) Each purchase order shall specify the quantity of each of Drug, Dispenser Kit or Reusables Kit ordered per month, the required delivery date (which shall not, with respect to the Drug, be less than **[*]** following the date of such purchase order and with respect to the Dispenser Kit or Reusables Kit, be less than **[*]** following the date of such purchase order), and any special instructions or invoicing information. For the avoidance of doubt, Grünenthal may submit separate purchase orders for Drug, Dispenser Kits and/or Reusables Kits, which may be offset in time so as to provide for delivery of Drug and Dispenser Kits and/or Reusables Kits at approximately the same time. All such purchase orders remain subject to the terms of this Section 2.4. In addition, the Parties may agree to a delivery schedule that is other than monthly so long as the aggregate amount of Drug, Dispenser Kits and Reusables Kits correspond to the Firm Order amounts for the period in question and the Minimum Order Quantities are satisfied.

(c) AcelRx acknowledges/accepts the order from Grünenthal made in accordance with and governed by this Agreement, and any terms or conditions of such purchase order which conflict or are inconsistent with the terms of the Agreement are void and hereby rejected.

2.5 Accessories and Replacement Components. During the Term, AcelRx agrees to make available Accessories and Replacement Components for sale on a purchase order basis based on then available quantities of such Accessories and Replacement Components at **[*]**. In the case of Replacement Components, such purchase orders shall be subject to the pricing terms set forth in this Section 2.5 for the portions of the purchase order which do not exceed the Minimum Order Quantities, except with respect to Replacement Components provided in connection with breaches of the warranty set forth in Section 6.3(a). If requested by Grünenthal, AcelRx will discuss in good faith the entry into a separate supply or purchase arrangement for such Accessories and Replacement Components based on the requirements of Grünenthal.

ARTICLE 3

MANUFACTURING

3.1 Manufacture of Product; Samples.

(a) AcelRx shall Manufacture or have Manufactured the Product to meet the Specifications and in accordance with applicable Regulatory Requirements in the U.S. (or in the country of such Product's Manufacture), as then in effect. AcelRx and Grünenthal shall promptly notify each other of any new instructions or specifications required by the applicable Regulatory Authorities in the Territory. Amendments to the Specifications will be handled in accordance with Section 3.8(a)-(d). Grünenthal acknowledges that Product supplied to Grünenthal hereunder may be Manufactured by or on behalf of AcelRx in accordance with any Third Party Manufacturing-related agreements entered into by AcelRx.

(b) AcelRx shall Manufacture and have Manufactured the Device in accordance with applicable Regulatory Requirements in the U.S. (or in the country of such Device's Manufacture), as then in effect for use by Grünenthal (and its Affiliates, distributors or licensees) if the Device is used without Drug for demonstration purposes.

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3.2 Quality Agreement. Not later than **[*]**, AcelRx and Grünenthal shall enter into a quality agreement (**"Quality Agreement"**) setting forth in detail the quality assurance arrangements and procedures with respect to the Manufacture of the Product, reporting customer complaints, device incident handling, and conducting timely investigations with respect to the Product in the Territory.

3.3 CE Mark; Authorized Representative. AcelRx shall be responsible for obtaining and maintaining the CE mark in the European Union for the Device and for affixing the CE mark on the Device portion of the Product and to undertake all steps reasonably and, according to the Medical Device Directive, legally necessary to allow Grünenthal to act as the Authorized Representative of AcelRx as CE mark holder. The Parties shall enter into an Authorized Representative agreement not later than **[*]**, which agreement shall set forth the specific details, functions and regulatory duties pursuant to which the Parties will share incident assessment and reporting to authorities, conduct and maintenance of the conformity assessment procedure including implementation of a quality management system, requirements for labeling and instructions for use of the Product in the Territory and all details concerning the provision of and access to documentation. The Authorized Representative agreement shall include provisions specifying **[*]**.

3.4 Regulatory Inspections; cGMP and QA Audits. AcelRx shall cooperate with any inspection of its facilities by the FDA and, if applicable, by any Regulatory Authority or respective notified bodies overseeing the Manufacture of Product for the Territory. Subject to the terms and conditions of any Third Party Manufacturing-related agreements entered into by AcelRx, upon written request to AcelRx not less than **[*]** prior to the requested visit date, Grünenthal shall have the right to have its representatives visit AcelRx's Manufacturing facilities as well as all relevant Manufacturing sites of Third Party contract manufacturers and suppliers during normal business hours to assess AcelRx's compliance with cGMP and quality assurance standards and to discuss any related issues with its Manufacturing. Grünenthal may exercise such right no more than **[*]** which may occur upon reasonable prior written notice during normal business hours on Business Days. AcelRx shall use commercially reasonable efforts to cause its sub-contractors to reasonably cooperate with any such audit by such representatives of Grünenthal and/or its Affiliates. For purposes of clarity, any information obtained by Grünenthal during such visits shall be treated as Confidential Information of AcelRx in accordance with Article 8 of this Agreement. For purposes of this Sections 3.4, **[*]**.

3.5 Compliance with Laws. AcelRx and Grünenthal shall comply with all applicable Regulatory Requirements and laws of any Regulatory Authority in the Territory.

3.6 Form of Products. AcelRx shall deliver Product to Grünenthal in accordance with the Specifications in **[*]** form **[*]**. Grünenthal shall be responsible for ensuring that such final packaging, labeling and shipment of the Product are in compliance with Regulatory Requirements in the Territory and in any event consistent with the label for the Product approved by the Regulatory Authorities in the Territory. Upon written request by Grünenthal, AcelRx agrees to cooperate in good faith and use commercially reasonable efforts to enable Grünenthal's access to AcelRx's Third Party vendors for the Manufacture of the Product that may be useful in support of Grünenthal's responsibilities to export and package Product purchased by Grünenthal for use and sale in the Territory.

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3.7 Delivery and Acceptance.

(a) Delivery. Subject to the terms and conditions of this Agreement, AcelRx shall deliver all Product ordered by Grünenthal on the requested delivery date set forth on the applicable purchase order, provided that such delivery date is at least **[*]** after the date of the applicable purchase order and such order is consistent with Grünenthal's binding forecast quantities and is within **[*]** of the delivery date requested in the applicable purchase order. Deliveries shall be made EXW AcelRx's Manufacturing facility (INCOTERMS 2000) by common carrier selected by Grünenthal at Grünenthal's expense. The Party responsible for shipment of the Product out of the U.S. shall be responsible for obtaining all licenses or other authorizations (including controlled substances authorizations) for the exportation from the U.S. and importation of Product into the Territory, and shall contract, at its own expense, for shipment and control of the Product from AcelRx's facility. Title to, ownership of, and risk of loss of, the Product shall transfer at the shipping point. AcelRx will prepare appropriate shipping documentation for the Regulatory Authorities in the Territory. AcelRx and Grünenthal shall reasonably cooperate with and assist each other in all aspects of the shipment, importation and delivery process and AcelRx and Grünenthal shall coordinate and consult with one another with regard to any communications with any Regulatory Authority regarding any shipment of the Product.

(b) Certificate of Analysis; Certificate of Conformance. AcelRx shall perform or have performed on its behalf, on each batch of Product, all tests specified in the Specifications, the MAA and applicable Regulatory Requirements before delivery of any Product from that batch to Grünenthal. AcelRx shall deliver to Grünenthal by facsimile or by electronic mail on or before the date of shipment of any Product to Grünenthal a Certificate of Analysis or a Certificate of Conformance according to cGMP, as appropriate, for each batch of Product in that shipment of Product, certifying that Product conforms to the Specifications, along with the results of such analysis and any supporting data. If there is a disagreement in connection with a Certificate of Analysis or Certificate of Conformance, such dispute will be resolved with a submission to independent testing in a procedure substantially in the manner set forth in Section 3.7(c)(i).

(c) Acceptance upon Delivery. Grünenthal shall be under no obligation to accept any shipment of Product for which AcelRx has not provided a Certificate of Analysis or a Certificate of Conformance, as applicable. Grünenthal shall inspect all shipments of the Product promptly upon receipt, and Grünenthal may reject any shipment of the Product which is nonconforming. In order to reject delivery of a shipment of the Product, Grünenthal must give written notice to AcelRx of Grünenthal's rejection of any delivery **[*]** after receipt of such delivery or with regard to **[*]**. If no such notice of rejection is received, Grünenthal shall be deemed to have accepted such Product on the **[*]** after delivery, subject to later detection of hidden defects. For clarity, a **[*]**.

(i) After timely notice of rejection is received by AcelRx, Grünenthal shall cooperate with AcelRx in determining whether rejection is appropriate or justified. AcelRx

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will evaluate process issues and other reasons for any alleged nonconformity. AcelRx shall notify Grünenthal as promptly as reasonably possible whether it accepts Grünenthal's basis for any rejection, however not later than **[*]** after the respective notification. If AcelRx agrees with Grünenthal's determination that the rejected Product does not meet the Specifications, promptly on receipt of a notice of rejection of a shipment of Product and no later than **[*]** after receipt of such notice, AcelRx shall use commercially reasonable efforts to replace such rejected Product with conforming Product. If AcelRx disagrees with Grünenthal's determination that certain Product is nonconforming, (x) promptly on receipt of a notice of rejection of a shipment of Product and no later than **[*]** after receipt of such notice, at Grünenthal's request, AcelRx shall use commercially reasonable efforts at Grünenthal's request to replace such rejected Product and (y) the rejected Product shall be submitted to a mutually acceptable Third Party laboratory in the Territory, which shall determine whether such Product is nonconforming. The Parties agree that such Third Party laboratory's determination shall be final and binding on the Parties. The Party against whom the Third Party laboratory rules shall bear the reasonable costs of the Third Party testing. If the Third Party laboratory rules that the Product in question meets Specifications, Grünenthal shall purchase that batch at the agreed-upon price, irrespective of whether AcelRx has provided replacement Product, provided that in such event Grünenthal shall also pay for any replacement Product delivered if not previously paid. Otherwise the replacement delivery shall be at no charge to Grünenthal.

(ii) Grünenthal shall not destroy any rejected Product until it receives written notification from AcelRx that AcelRx does not dispute that the rejected Product fails to meet Specifications. At AcelRx's election and upon instruction from AcelRx, Grünenthal shall either (a) destroy the Product received in the rejected delivery promptly at AcelRx's cost and provide AcelRx with certification of such destruction, or (b) return such Product to AcelRx at AcelRx's cost

(d) Replacement Warranty for Failure in Use.

(i) AcelRx warrants that the Product shall have no material defect in workmanship for a period of **[*]**; provided, that (A) the Product has been properly stored and maintained by Grünenthal under industry standard conditions and in accordance with any Specifications, (B) such Product is delivered to end user customers with user manuals or the "Instructions for Use" of the Product in accordance with Grünenthal's then standard operating practices, and (C) the Product is used prior to the expiration of the shelf life of the Product.

(ii) AcelRx warrants the Accessories and Replacement Components against defects in materials and workmanship for **[*]** from the date of shipment to Grünenthal. If AcelRx receives notice of such defects during the warranty period, AcelRx shall, at its option, either repair or replace the Accessories or Replacement Components which prove to be defective. If AcelRx is unable, within a reasonable time, to repair or replace any Accessories and Replacement Components to a condition as warranted, Grünenthal shall be entitled to a refund of the purchase price upon return of the Accessories or Replacement Component to AcelRx The foregoing warranty shall not apply to defects resulting from: **[*]**.

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(iii) In the event of a breach of the warranty pursuant to this Section 3.7(d), AcelRx shall bear all costs, including transportation costs, in connection with the replacement of any non-conforming Product. AcelRx shall have the right to inspect defective Product to determine the validity of warranty claims under Section 3.7(d) and in compliance with all Regulatory Requirements, **[*]**. The remedy set forth in Section 3.7(d) shall be the sole remedy and recourse of Grünenthal with respect to replacement of a defective Product, Accessories and Replacement Components delivered to Grünenthal by AcelRx hereunder that fail in use by the end user customer, **[*]**.

3.8 Change in Specifications; Other Modifications.

(a) Changes in Specifications. Each Party shall promptly notify the other Party of (i) any change of the Specifications as well as any analytical methods that is required by any Regulatory Authority or in order to comply with any Regulatory Requirement, and/or (ii) any other material modifications to the Manufacturing process, applicable to the Product for use in the Field in the Territory, and the Parties shall discuss such change of Specifications, analytical methods and/or other material modification to the Manufacturing process prior to its implementation.

(i) Prior to the receipt of the first Marketing Approval of the Product for the Territory, **[*]**.

(ii) After the receipt of the first Marketing Approval of the Product for the Territory, such regulatory required Specification changes that are not conditions to the receipt of the first Marketing Approval of the Product for the Territory shall, **[*]** and the Parties shall coordinate and collaborate in making all necessary Regulatory Filings with the application Regulatory Authority in the Territory to effect such change. Grünenthal shall be responsible for making such Regulatory Filing in the Territory and paying filing fees required for such Regulatory Filing.

(b) Other Modifications. If any changes to the Product by AcelRx do not change the Specifications and do not require approval by any relevant Regulatory Authority in the Territory nor by the FDA, **[*]**.

(c) Grünenthal Requested Non-Regulatory Changes. If Grünenthal seeks any change to the Specifications or any other modifications to the Manufacturing process and such change or modification is not required by any Regulatory Authority or Regulatory Requirement, it shall notify AcelRx of such proposed change in reasonable detail **[*]**.

(d) Contradictory Modifications. If a Regulatory Authority requires any change of the Specifications in order to comply with any Regulatory Requirement applicable to the Product for use in the Field in the Territory, which change would materially impact the cost or regulatory or commercial status of the Product outside of the Field or Territory, **[*]**

(e) Records. AcelRx shall keep complete, accurate and authentic accounts, notes, data and records pertaining to the Manufacture and supply of each batch of the Product, for the minimum period provided in 21 CFR Part 211, or longer if required by Regulatory

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Requirements in the Territory or country of Manufacture, and upon Grünenthal's reasonable request and at its expense, shall make available to Grünenthal copies of or access to such records. Notwithstanding the foregoing, AcelRx shall at all times maintain such records and systems for the Parties to investigate causes of a Recall of the Product and conduct a Recall of the Product in compliance with all Applicable Laws.

3.9 Complaints Handling and Reporting. The Parties shall agree upon a procedure for handling complaints and device malfunction reports in the Quality Agreement.

3.10 Stability Samples; Retained Samples. AcelRx shall, during the Term, take such quantities of quality control stability samples, from batches of Product intended for delivery to Grünenthal, as are required by cGMP and applicable Regulatory Requirements and establish appropriate stability studies, in each case to support the claimed expiration dating for the Product delivered to Grünenthal. In addition, AcelRx shall retain sufficient number of representative units of the Product from each batch for the period required by the applicable Regulatory Requirements for record keeping, testing and regulatory purposes or as specified in the Quality Agreement.

3.11 Recalls.

(a) Recalls. AcelRx and Grünenthal each agree to notify the other within **[*]** if either Party discovers any issue that it reasonably believes could lead to a Product recall, product withdrawal, field correction or other related action (collectively, " **Recalls**"). If practicable, the Parties shall promptly following notification discuss the plans for a Recall, provided that Grünenthal and AcelRx shall have joint responsibility for determining whether a Recall in the Territory is necessary, and whether to cease shipping the Product. If the Parties decide, that a Product Recall is necessary, the Parties shall work together to develop and implement a Recall plan. Grünenthal shall have the final decision whether to initiate a recall for the Territory, the plans for any Recall for the Territory, and for determining the nature and urgency of any Product Recall for the Territory. In any event, AcelRx shall have the sole responsibility for any and all communications with FDA and other Regulatory Authorities outside of the Territory related to any Recall.

(b) AcelRx's Right to Request A Recall. Subject to 3.11(a), in case that AcelRx reasonably believes that the commercialization of the Licensed Product constitutes a serious health risk, AcelRx shall have the right to request Grünenthal to initiate a Recall of Product that arises solely from any Manufacturing defect in the Product or defect of the Drug or other components of the Product supplied to Grünenthal by AcelRx by written notice to Grünenthal. In the event a Recall is initiated by Grünenthal pursuant to an AcelRx request, the Parties shall work together to develop and implement a Recall plan and effectuate the Recall.

(c) Recall Costs and Expenses. All costs and expenses associated with implementing a Recall of a Product in the Territory shall be allocated between AcelRx and Grünenthal as follows: **[*]**

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3.12 Records. AcelRx shall keep complete, accurate and authentic accounts, notes, data and records pertaining to the Manufacture and supply of each batch of the Product, for a period of at least one (1) year after the expiration date (as provided in 21 CFR 211.180 (a) (b), 211.198 (b)), or longer if required by Regulatory Requirements, and upon Grünenthal's reasonable request, shall make available to Grünenthal copies of such records. After such time period, AcelRx shall notify Grünenthal prior to the destruction of any records retained under this Section 3.12 and, at Grünenthal's request, shall provide copies of such records to Grünenthal.

3.13 Legal Changes. Each Party shall immediately advise the other if it becomes aware of any legislation or Applicable Laws (including, all health and safety, custom, trade, tariff or other import laws, approvals process or vigilance reporting requirements) which is in effect or which may come into effect after this Agreement becomes effective and which affects the importation of the Product, Device, Drug, Accessory or Replacement Component into, or the distribution, sale, or use of the Product, Device, Drug, Accessory or Replacement Component in the Territory, and the Parties shall use commercially reasonable efforts to remain informed of all such legislation or Applicable Laws.

3.14 Manufacturing Continuity Plan. AcelRx shall develop and maintain the Manufacturing Continuity Plan. AcelRx agrees that not less than **[*]** prior to the anticipated date of first commercial sale of the Product in the Territory by Grünenthal, AcelRx shall deliver a Manufacturing Continuity Plan to Grünenthal for review and discussion. Thereafter, AcelRx shall not less than **[*]** review and update the Manufacturing Continuity Plan and, upon Grünenthal's request, AcelRx will make the Manufacturing Continuity Plan available to Grünenthal or its designated representatives for review.

ARTICLE 4

PAYMENT

4.1 Purchase Price for Supply.

(a) AcelRx shall Manufacture and supply the Product and Devices under this Agreement at a price equal to the Transfer Price.

(b) The Parties agree that they will renegotiate in good faith **[*]** In any event, if there is a net increase in the Manufacturing costs incurred by AcelRx in connection with the Manufacture and supply of the Products hereunder, the Parties shall in good faith negotiate a new Transfer Price for the Products to prevent AcelRx having to Manufacture and sell Product and Devices to Grünenthal at a loss under this Agreement. For clarity, in the event of a reduction in the Fully Burdened Manufacturing Cost, the then current Transfer Price shall be reduced to reflect such reduced Fully Burdened Manufacturing Cost.

(c) The prices of Accessories and Replacement Components will be fixed on **[*]** during the term of this Agreement.

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4.2 Payment Terms for Purchases.

(a) Invoice and Payment. AcelRx shall invoice Grünenthal upon delivery of ordered Product pursuant to Section 3.7(a). All payments for Product will be due and payable to AcelRx **[*]** after Grünenthal's receipt of such invoice, unless such shipment is rejected under Section 3.7(c), in which event no payment shall be due for such rejected Product and Grünenthal shall make payment to AcelRx: (a) for any replacement Product within **[*]** after Grünenthal accepts the replacement Product; and/or (b) for such original shipment within **[*]** after a Third Party laboratory, pursuant to Section 3.7(c)(i), confirms that the Product originally delivered complies with the Specifications and not subject to rejection.

(b) Currency. All references to "**Dollars**" or "**$**" shall mean the legal currency of the United States. All payments to be made under this Agreement shall be made in Dollars, unless expressly specified to the contrary herein.

(c) Late Payments. Any amounts not paid within thirty (30) days after the date due under this Agreement shall be subject to interest from the foregoing date through and including the date upon which payment is received, calculated at the interest rate equal to three percentage points (3%) over the rate of interest according to the average six-month rate(s) of the London Inter-Bank Offering Rate (**"LIBOR"**) for U.S. dollars, as quoted on the British Banker's Association's website currently located at www.bba.org.uk (or such other source as may be mutually agreed by the Parties) from time to time, effective for the applicable days of the period of default, on the last business day of the applicable Calendar Quarter prior to the date on which such payment is due, calculated daily on the basis of a 365-day year, or, if lower, the highest rate permitted under Applicable Law.

4.3 Audit of Transfer Price. In order to verify the Fully Burdened Manufacturing Cost comprising the Transfer Price, AcelRx shall provide to Grünenthal a written report of the calculation of the Fully Burdened Manufacturing Cost on a quarterly basis for the most recently completed calendar quarter. Grünenthal shall have the right to cause an independent, certified public accounting firm reasonably acceptable to AcelRx to audit AcelRx's records relating to the Fully Burdened Manufacturing Cost to confirm the amount of the costs and expenses reflected in such report. The accounting firm shall be obligated to keep in strict confidence his findings also vis-à-vis Grünenthal and will inform Grünenthal and AcelRx only about whether or not the calculation of the Transfer Price has been correct and the amount, if any, of the deviation from the charged Transfer Price. Grünenthal shall bear the full cost of such audit unless such audit discloses an over-charging by AcelRx of **[*]**, in which event AcelRx shall bear the costs of such audit.

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ARTICLE 5

SECURITY OF SUPPLY

5.1 Shortage of Products.

(a) Grünenthal understands and acknowledges that AcelRx is solely responsible for managing and maintaining its relationships with Third Party suppliers that it uses to obtain components necessary to Manufacture the Product, and that any disruption in the Manufacture of the Product or a component thereof that is due to any such Third Party supplier shall be AcelRx's responsibility, including with regard to any impact on the timely deliver to Grünenthal of Product ordered under this Agreement. In addition, Grünenthal understands and acknowledges that the Drug is a Schedule II controlled drug substance and that the quantities of Drug that may be Manufactured pursuant to this Agreement depend upon the annual Aggregate Production Quota (" **APQ**") assigned to AcelRx by the U.S. Drug Enforcement Administration. AcelRx shall apply for an APQ in quantities reasonably determined by AcelRx based upon Firm Orders and the forecasts of Grünenthal and AcelRx shall use commercially reasonable efforts to obtain such APQ in order to meet its supply obligations under this Agreement. AcelRx shall consult with Grünenthal as reasonably required during the APQ process and shall take into good faith consideration Grünenthal's suggestions and comments regarding the APQ process. **[*]**

(b) If AcelRx experiences a shortage of Product due to Force Majeure, failure to supply by a Device component supplier or insufficient APQ and is unable to supply the full quantity of Product ordered pursuant to this Agreement, Grünenthal shall be entitled to receive that quantity of Product which bears the same proportion to the total quantity of available Product as **[*]**. AcelRx shall use its commercially reasonable efforts to work with Grünenthal to meet Grünenthal's additional supply needs for Product during the period that any Product shortage conditions exist. Grünenthal shall **[*]** If the shortage of Product described in this Section 5.1(b) affects Drug or Device portions of the product unequally, or affects only the Drug or only the Device, then the proportional allocation of Product described herein shall instead be a separate, proportional allocation of each of the Drug and/or Device portions of the Product, based on the total quantity of each available and the total quantity of each sold by Grünenthal in the **[*]** preceding the supply shortage.

5.2 Cooperation. In the event AcelRx determines that shortage conditions will occur, or in the event of a force majeure, supplier delay or insufficient APQ that gives rise to shortage conditions, AcelRx will promptly notify Grünenthal of such conditions, and the Parties shall discuss in good faith appropriate mechanisms to address such shortage conditions.

5.3 Measures to Prevent Shortfall. The Parties desire to minimize the risk of discontinuity in such Manufacture and/or supply and AcelRx shall take such measuresas follows:

(a) Back-up Manufacturer. If AcelRx fails **[*]** (a "**Failure Event**"), such Failure Event shall constitute a material breach of this Agreement and AcelRx shall grant a Third Party Manufacturer reasonably acceptable to Grünenthal the right to make and have made the Product for Grünenthal's commercial sale in the Territory and promptly thereafter enable (at

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AcelRx's cost and expense) such Third Party Manufacturer with technology transfer to make such Product according to the then current Specifications. To the extent that Grünenthal has requested such Third Party Manufacturer be qualified in advance pursuant to Section 5.3(b) or otherwise pursuant to Section 2.4 of the License Agreement, such Third Party Manufacturer shall be qualified in advance. Following a Failure Event, Grünenthal shall no longer have an obligation to purchase and AcelRx shall no longer have an obligation to supply pursuant to this Agreement once such Third Party Manufacturer is qualified by Regulatory Approval to supply the Product for Grünenthal's commercial sale in the Territory.

(b) Request for Back-up Manufacturer. At such time as Grünenthal **[*]** upon the written request of Grünenthal, AcelRx agrees to reasonably consider and qualify (i.e., prepare for Regulatory Approval) a second site for Manufacture of the Product at a different facility that is capable of supplying Product in the Field for the Territory.

(c) Restrictions. The back-up license set forth in Section 5.3(a) shall not include the right for any Third Party Manufacturer to modify or make improvements to the Product. Such back-up license shall expire upon the expiration of the Term or early termination of this Agreement.

(d) Stand-By Contracts. Beginning not later than **[*]** AcelRx shall use commercially reasonable efforts to enter into Stand-By Contracts with each Third Party providing significant manufacturing and/or supply services to AcelRx in connection with the Manufacturing of the Device or other components of the Product for the Territory such that through these Stand-By Contracts Grünenthal will have access to such Third Party supplier if Grünenthal exercises its rights under such Stand-By Contracts. Each "**Stand-By Contract**" with such a Third Party manufacturing and supply service provider shall be a letter agreement in the form of **Exhibit B** providing that upon receipt notice from Grünenthal, **[*]**. Grünenthal covenants it shall not provide such a notice under a Stand-By Contract unless and until any of the following has occurred: (i) there has been a Failure Event, (ii) AcelRx has terminated this Agreement or the License Agreement other than as permitted thereunder due to a material breach by Grünenthal, (iii) upon the bankruptcy or insolvency of, or the filing of an action to commence insolvency proceedings against AcelRx, or the making or seeking to make or arrange an assignment for the benefit of creditors of AcelRx, or the initiation of proceedings in voluntary or involuntary bankruptcy, or the appointment of a receiver or trustee of AcelRx's property, in each case that is not discharged within one hundred twenty (120) days, or (d) this Agreement or the License Agreement are rejected in any proceeding for the bankruptcy or insolvency of AcelRx. To the extent AcelRx owns tooling, molds, equipment or other tangible materials that are held by or installed at a Third Party Manufacturing and supplier of AcelRx and which are used or useful in the Manufacture of Licensed Products or components thereof, the Stand-By Contract with such Third Party manufacturing and supplier **[*]**.

ARTICLE 6

REPRESENTATIONS AND WARRANTIES

6.1 Mutual Representations and Warranties. Each Party hereby represents and warrants to the other Party as of the Effective Date as follows:

(a) The execution, delivery, and performance of this Agreement have been duly authorized by all necessary corporate actions;

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(b) This Agreement constitutes a valid obligation of such Party and is binding and enforceable against such Party in accordance with the terms hereof; and

(c) Such Party has the corporate power and authority and the legal right to enter into this Agreement and to perform its obligations hereunder, and there is no contractual restriction or obligation binding on such Party which would be materially contravened by execution and delivery of this Agreement or by the performance or observance of its terms.

6.2 Product Warranties. AcelRx represents and warrants that the Product supplied to Grünenthal:

(a) comply with the Specifications;

(b) have been Manufactured and stored in compliance with Regulatory Requirements;

(c) shall have, upon delivery to Grünenthal a remaining shelf life of the Drug of (i) at least **[*]**.

(d) are not unfit for commerce under any Regulatory Requirements in any countries in the Territory where the Product is approved for sale (including, but not limited to, not being adulterated or misbranded as defined under the FD&C Act or an article that may not, under the FD&C Act, be introduced into interstate commerce); and

(e) assuming payment in full by Grünenthal, are free and clear of all security interests, liens and other encumbrances of any kind or character.

6.3 Limitation of Liability. TO THE MAXIMUM EXTENT PERMITTED BY APPLICABLE LAW, NEITHER PARTY NOR ANY OF THEIR RESPECTIVE AFFILIATES, DIRECTORS, OFFICERS, EMPLOYEES, OR AGENTS SHALL HAVE ANY LIABILITY OF ANY TYPE (INCLUDING, BUT NOT LIMITED TO, CLAIMS IN CONTRACT, NEGLIGENCE AND TORT LIABILITY) FOR ANY SPECIAL, INCIDENTAL, INDIRECT, PUNITIVE OR CONSEQUENTIAL DAMAGES, INCLUDING, BUT NOT LIMITED TO, THE LOSS OF OPPORTUNITY, LOSS OF USE OR LOSS OF REVENUE OR PROFIT IN CONNECTION WITH OR ARISING OUT OF THIS AGREEMENT OR THE DEVELOPMENT ACTIVITIES PERFORMED HEREUNDER, EVEN IF SUCH DAMAGES MAY HAVE BEEN FORESEEABLE. THE FOREGOING SHALL NOT LIMIT EITHER PARTY'S INDEMNIFICATION OBLIGATIONS NOR SHALL IT APPLY TO DAMAGES ARISING FROM EITHER PARTY'S BREACH OF ITS OBLIGATIONS UNDER ARTICLE 8. NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THIS AGREEMENT, THE TOTAL LIABILITY OF ACELRX UNDER THIS AGREEMENT OTHER THAN FOR

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CLAIMS OF PRODUCTS LIABILITY RESULTING FROM A HIDDEN DEFECT (AS DEFINED IN SECTION 3.7(C)) SHALL NOT EXCEED THE AMOUNT OF ALL PAYMENTS RECEIVED BY ACELRX FROM GRÜNENTHAL UNDER THIS AGREEMENT.

6.4 Insurance. Each Party, at its own expense, shall maintain product liability and other appropriate insurance with an insurance carrier in an amount consistent with industry standards, for a company in a similar position to such Party, during the Term, which shall include, but not be limited to, (i) product liability insurance which may include a self-insured retention and (ii) general liability insurance in the minimum amount of $2 million in the aggregate and $10 million umbrella coverage, which may include a self-insured retention. Each Party shall provide a certificate of insurance or other reasonably satisfactory documentation evidencing such coverage to the other Party upon request. It is understood that such insurance shall not be construed to create a limit of either Party's liability with respect to its indemnification obligations under Article 9.

6.5 Warranty Limitations or Disclaimers. SUBJECT TO 5.3, THE WARRANTIES, LIMITATIONS AND DISCLAIMERS DESCRIBED IN THIS ARTICLE 6 AND ARTICLE 3 ARE EXCLUSIVE AND SUPERSEDE ANY OTHER WARRANTY LIMITATIONS AND DISCLAIMERS GIVEN BY EITHER PARTY, WHETHER WRITTEN OR ORAL. EXCEPT FOR THE EXPRESS WARRANTIES IN SECTIONS 3.7 and 6.2, ACELRX MAKES NO WARRANTIES OF ANY KIND WITH RESPECT TO THE PRODUCT, ACCESSORIES OR REPLACEMENT COMPONENTS OR ANY COMPONENT OR PART THEREOF, WHETHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OF FITNESS FOR A PARTICULAR PURPOSE, OR ANY IMPLIED WARRANTIES ARISING FROM COURSE OF PERFORMANCE, COURSE OF DEALING, OR USAGE OF TRADE. GRÜNENTHAL SHALL NOT MAKE ANY REPRESENTATION OR WARRANTY ON BEHALF OF ACELRX THAT EXCEEDS THE EXPRESS WARRANTIES IN SECTIONS 3.7 AND 6.2.

ARTICLE 7

INTELLECTUAL PROPERTY

7.1 Existing Intellectual Property. Each Party shall retain all rights in all intellectual property rights owned or controlled by such Party prior to the Effective Date or developed or acquired by such Party during the term of this Agreement.

7.2 New Intellectual Property. All inventions made under this Agreement shall be deemed made under the License Agreement and subject to the provisions of ownership and licenses set forth under the License Agreement.

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ARTICLE 8

CONFIDENTIALITY

8.1 Confidentiality. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that any confidential or proprietary information and materials, patentable or otherwise, in any form (written, oral, photographic, electronic, visual or otherwise) which is disclosed by one Party (the "**Disclosing Party**") to the other Party (the "**Receiving Party**") (collectively, "**Confidential Information**") shall also be considered "Confidential Information" as defined in the License Agreement and shall be governed by the confidentiality terms set forth in the License Agreement; provided, that the Receiving Party may disclose the Disclosing Party's Confidential Information (a) to the Receiving Party's employees, consultants, Affiliates, agents, contractors, potential or actual investors, or sublicensees who are bound by obligations relating to confidentiality at least as restrictive of those contained in the License Agreement and who have a need to know such information in connection with the Receiving Party's performance of its obligations or practice of its rights under this Agreement, (b) to exercise its rights or perform its obligations under this Agreement, or (c) as contemplated by Section 9.5 of the License Agreement and as permitted under Section 9.3 of the License Agreement.

8.2 Confidentiality of this Agreement and its Terms. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, each Party agrees not to disclose to any Third Party the existence of this Agreement or the terms of this Agreement without the prior written consent of the other Party hereto, except that each Party may disclose the terms of this Agreement that are not otherwise made public as contemplated by Section 9.5 of the License Agreement and as permitted under Section 9.3 of the License Agreement.

8.3 Injunctive Relief. For the avoidance of doubt, either Party shall be entitled to seek injunctive relief to enforce the terms of this Article 8.

8.4 Use of Names. Neither Party shall make use of the name of the other Party or any of its Affiliates in any advertising or promotional material, or otherwise, without the prior written consent of such other Party.

ARTICLE 9

INDEMNIFICATION

[*]

ARTICLE 10

TERM

10.1 Term. This Agreement shall become effective upon the Effective Date and shall remain in full force and effect on a country-by-country basis through the later of (i) expiration of the Royalty Term (as defined in the License Agreement), (ii) expiration of Grünenthal's obligation to pay the Trademark and Supply Fee to AcelRx as set forth in Section 7.4 of the License Agreement or (iii) any applicable transition period thereafter as provided under Section

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14.5 of the License Agreement, unless earlier terminated pursuant to Section 10.2 below (the " **Term**"). The Parties may extend the term of this Agreement by mutual written agreement.

10.2 Termination. Each Party shall have the right to terminate this Agreement before the end of the Term:

(a) upon early termination of the License Agreement by Grünenthal under Section 13.3 (voluntary termination) thereof or termination of the License Agreement by AcelRx under Section 13.2(b) (uncured material breach) thereof, Grünenthal may terminate this Agreement, effective upon the effective date of the termination of the License Agreement; provided, that if AcelRx terminates the License Agreement under Section 13.2(b) (uncured material breach), then the right of Grünenthal to terminate this Agreement pursuant to this Section 10.2(a) shall be limited to the country/countries affected by the termination of AcelRx

(b) in its entirety or on a country-by-country basis by mutual written agreement of the Parties;

(c) with regard to the country or countries concerned upon written notice by either Party if the other Party is in material breach of this Agreement and has not cured such breach within ninety (90) days (thirty (30) days with respect to any payment breach) after notice from the terminating Party requesting cure of the breach. Any such termination shall become effective at the end of such ninety (90) day (thirty (30) days with respect to any payment breach) period unless the breaching Party has cured any such breach or default prior to the end of such period; or

(d) in its entirety upon the bankruptcy or insolvency of, or the filing of an action to commence insolvency proceedings against the other Party, or the making or seeking to make or arrange an assignment for the benefit of creditors of the other Party, or the initiation of proceedings in voluntary or involuntary bankruptcy, or the appointment of a receiver or trustee of such Party's property, in each case that is not discharged within one hundred twenty (120) days.

10.3 Effects upon Expiration or Termination.

(a) Continued Effectiveness. This Agreement shall remain in effect through the later of: (i) the Term (as defined in the License Agreement), subject to the payment of the Trademark and Supply Fee pursuant to Section 7.4 of the License Agreement and (ii) to the extent requested by Grünenthal, the applicable period set forth in Section 14.5 of the License Agreement.

(b) For clarity, in case of termination with regard to any country pursuant to Sections 2.8, 13.2(a) or 13.2(b) of the License Agreement, this Supply Agreement shall terminate automatically upon effective date of such termination with regard to the country or countries concerned and Section 5.2, second sentence of the License Agreement shall apply accordingly during the Term.

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(c) Cumulative Remedies. Except as expressly stated otherwise herein, remedies hereunder are cumulative, and nothing in this Agreement shall prevent either Party, in the case of a breach, from not terminating this Agreement and seeking to enforce its rights hereunder.

(d) Accrued Obligations. Except as set forth herein, any termination or expiration of this Agreement shall not relieve either Party of any obligation which has accrued prior to the effective date of such termination or expiration (including (X) the costs of any Product or Materials maintained for the Product ordered by Grünenthal hereunder, which are unique to the manufacture of Product in the Field in the Territory, and (Y) any remedy of Grünenthal under Article 3 with respect to Product Manufactured and supplied prior to the effective date of termination), which obligations shall remain in full force and effect for the period provided therein.

(e) Survival. The terms of Sections 6.1, 6.2, 6.3, 6.4, 6.5 and Articles 7, 8, 9, 10 (with the exception of 10.3(b)) and 11 shall survive any termination or expiration of this Agreement.

(f) No Waiver. The termination or expiration of this Agreement, as the case may be, shall not act as a waiver of any breach of this Agreement and shall not act as a release of either Party from any liability or obligation incurred under this Agreement through the date of such termination or expiration, including payments due to AcelRx pursuant to this Agreement.

ARTICLE 11

MISCELLANEOUS

11.1 Notices. Any notice, request, demand, waiver, consent, approval or other communication which is required or permitted to be given to any Party shall be in writing and shall be deemed given only if delivered to the Party personally or sent to the Party by registered mail, return receipt requested, postage prepaid, sent by a nationally recognized courier service guaranteeing next-day or second-day delivery, charges prepaid, addressed to the Party at its address set forth below, or sent by facsimile transmission to the number set forth below, or at such other address or fax number as such Party may from time to time specify by notice given in the manner provided herein to the Party entitled to receive notice hereunder:

For AcelRx:
AcelRx Pharmaceuticals, Inc.
575 Chesapeake Drive
Redwood City, CA 94063
Attention: Chief Executive Officer
FAX: +1-650-216-6500

With a copy to:
Cooley LLP
3175 Hanover St.
Palo Alto, CA 94306
Telephone: +1-650-843-5000
Facsimile: +1-650-843-4000
Attention: Glen Y. Sato

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For Grünenthal: Grünenthal GmbH
D-52099 Aachen

Attention: Chief Executive Officer

With a copy to: Grünenthal GmbH
D-52099 Aachen

Attention: Global Legal
FAX: 241-569-3547

11.2 Entire Agreement and Inconsistency. This Agreement (including any Exhibits or other attachments hereto), together with the License Agreement, the Quality Agreement and the Pharmacovigilance Agreement, constitutes the entire agreement between the Parties with respect to the subject matter hereof, and no oral or written statement may be used to interpret or vary the meaning of the terms and conditions hereof. In the event of a conflict or inconsistency between the provisions of this Agreement and the provisions of the License Agreement, the provisions of the License Agreement will prevail to the extent of the conflict or inconsistency. In the event of a conflict or inconsistency between the provisions of this Agreement and the provisions of the Quality Agreement or the Pharmacovigilance Agreement, this Agreement will prevail. In the event of a conflict or inconsistency between the provisions of this Agreement and any legal or regulatory requirements applicable for the Territory, amendments to this Agreement shall be considered promptly in good faith in order to meet such requirements.

11.3 Assignment. Neither Party may assign or otherwise transfer this Agreement without the prior written consent of the other Party; provided, however, that either Party may assign this Agreement without the consent of the other Party to any Affiliate or in connection with the acquisition of such Party or the sale of all or substantially all of the business or assets of the assigning Party relating to the subject matter of this Agreement, whether by merger, acquisition or otherwise. Subject to the foregoing, this Agreement shall inure to the benefit of each Party, its successors and permitted assigns. Any assignment of this Agreement in violation of this Section 11.3 shall be null and void.

11.4 Force Majeure. Failure of any Party to perform its obligations under this Agreement (other than of the obligations to make any payments or of confidentiality) shall not subject such Party to any liability or place them in breach of any term or condition of this Agreement to the other Party if, and solely to the extent, such failure is caused by Force Majeure. The corresponding obligations of the other Party will be suspended to the same extent. “Force Majeure” shall mean any unanticipated event, reason or cause beyond the reasonable control of a Party (including fire, flood, embargo, power shortage or failure, acts of war, insurrection, riot, terrorism, strike, lockout or other labor disturbance, epidemic, failure or default of public utilities

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or common carriers, destruction of production facilities or materials by fire, earthquake, or storm or like catastrophe, acts of God or any acts, omissions or delays in acting of the other Party); provided, however, that the Party affected shall promptly notify the other Party of the condition constituting Force Majeure as defined herein and shall exert commercially reasonable efforts to eliminate, cure and overcome any such causes and to resume performance of its obligations with all possible speed. If a condition constituting Force Majeure as defined herein prevents, or would likely prevent, a Party from performing its obligations under this Agreement for more than one hundred twenty (120) days, the Parties shall meet to negotiate a mutually satisfactory solution to the problem, if practicable, including the use of a Third Party to fulfill the obligations hereunder of the Party invoking the Force Majeure.

11.5 Headings. The descriptive headings contained in this Agreement are for convenience of reference only and shall not affect in any way the meaning or interpretation of the Agreement.

11.6 Independent Contractor. Each Party shall be acting as an independent contractor in performing under this Agreement and shall not be considered or deemed to be an agent, employee, joint venturer or partner of the other Party. Neither Party to this Agreement shall have any express or implied right or authority to assume or create any obligations on behalf of, or in the name of, the other Party, or to bind the other Party to any contract, agreement or undertaking with any Third Party.

11.7 Severability. In the event any provision of this Agreement should be held invalid, illegal or unenforceable in any jurisdiction, the Parties shall negotiate in good faith and enter into a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties. All other provisions of this Agreement shall remain in full force and effect in such jurisdiction. Such invalidity, illegality or unenforceability shall not affect the validity, legality or enforceability of such provision in any other jurisdiction.

11.8 No Third Party Beneficiaries. Nothing in this Agreement, either express or implied, is intended to or shall confer upon any Third Party any legal or equitable right, benefit or remedy of any nature whatsoever under or by reason of this Agreement.

11.9 Amendment. This Agreement may not be amended or modified except by an instrument in writing signed by authorized representatives of Grünenthal and AcelRx.

11.10 Governing Law. This Agreement and all questions regarding the existence, validity, interpretation, breach or performance of this Agreement, shall be governed by, and construed and enforced in accordance with, the laws of **[*]**, without reference to its conflicts of law principles.

11.11 Dispute Resolution. In the event of any dispute between the Parties that relates to interpretation of a Party's rights and/or obligations hereunder or any alleged breach of this Agreement, such dispute shall be resolved in accordance with the dispute resolution procedures set forth in Article 15 of the License Agreement.

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11.12 No Waiver. The failure of either Party to enforce at any time for any period the provisions of or any rights deriving from this Agreement shall not be construed to be a waiver of such provisions or rights or the right of such Party thereafter to enforce such provisions.

11.13 Counterparts. This Agreement may be executed in one or more counterparts, and by the respective Parties in separate counterparts, each of which when executed shall be deemed to be an original but all of which taken together shall constitute one and the same Agreement.

[SIGNATURES APPEAR ON THE NEXT PAGE]

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IN WITNESS WHEREOF, each Party hereto has executed or caused this Agreement to be executed on its behalf as of the Effective Date.

ACELRX PHARMACEUTICALS, INC.

By: /s/ Richard King

Name: Richard King

Title: President & CEO

GRÜNENTHAL GMBH

By: /s/ Eric Paul Paques

Name: Prof. Dr. Eric Paul Paques

Title: Chairman of the Corporate Executive Board

By: /s/ Alberto Grua

Name: DoH. Alberto Grua

Title: Chief Commercial Officer EV, Australia and North America

[Signature Page to Manufacture and Supply Agreement]

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EXHIBIT A

Accessories

- **[*]**

Replacement Components

- **[*]**

For clarity, all orders of Accessories and Replacement Components are subject to Section 2.7 of the Agreement.

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Exhibit B

Form of Standby Letter Agreement

[AcelRx letterhead]

[date]

VIA EMAIL PDF

[name], [title]
[Third Party manufacturing partner of AcelRx]
[other party address]
(hereinafter "**Company**")

[name], [title]
GRÜNENTHAL GMBH
Zieglerstrasse 6
52078 Aachen, Germany

RE: Continuity of Supply

Dear [names]:

[*]

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Exhibit 10.29

CONFIDENTIAL
EXECUTION COPY

COLLABORATION AND LICENSE AGREEMENT

This **COLLABORATION AND LICENSE AGREEMENT** ("***Agreement***") is entered into as of 16 December 2013 (the "***Effective Date***") between **ACELRX PHARMACEUTICALS, INC**., a company organized under the laws of the State of Delaware, United States (" ***AcelRx***"), and having a principal place of business at 575 Chesapeake Drive, Redwood City, CA 94063, United States, and **GRÜNENTHAL GMBH**, a company organized under the laws of Germany ("***Grünenthal***"), having its registered office at Zieglerstrasse 6, 52078 Aachen, Germany.

RECITALS

A. **WHEREAS,** AcelRx is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain, and is developing Zalviso ™ (formerly known as ARX-01), the Sufentanil NanoTab PCA System, AcelRx's novel sublingual patient-controlled analgesia (PCA) system. AcelRx owns or controls certain patents, know-how and other intellectual property relating to the Zalviso™ product; and

B. **WHEREAS,** Grünenthal desires to obtain from AcelRx certain exclusive rights and licenses to commercialize, use, sell, offer for sale and import the Licensed Product (as defined hereinafter) in the Field (as defined hereinafter) in the Territory (as defined hereinafter), and AcelRx is willing to grant to Grünenthal such rights and licenses and to exclusively supply Grünenthal with the Licensed Product for the Territory, all on the terms and conditions set forth in this Agreement and the Supply Agreement (as defined hereinafter).

NOW, THEREFORE, in consideration of the foregoing premises and the mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, AcelRx and Grünenthal hereby agree as follows:

ARTICLE 1

DEFINITIONS

As used in this Agreement, the following terms shall have the meanings set out in this Article 1 unless the context clearly and unambiguously dictates otherwise.

1.1 *"**Accessories**"* shall mean additional hardware accessories or components for use with the Licensed Product set forth on ***Exhibit 1.1*** which are not included in the Reusables Kit or Dispenser Kit (for example, and not by way of limitation, an RFID reader).

1.2 "***Accounting Standards***" shall mean, with respect to AcelRx, US GAAP (United States generally accepted accounting principles as in effect from time to time), and with respect

to Grünenthal, the IFRS (International Financial Reporting Standards as in effect from time to time), in each case, as consistently applied throughout the period involved. Each Party shall promptly notify the other in the event that it changes the Accounting Standards pursuant to which its records are maintained, it being understood that each Party may only use internationally recognized accounting principles (e.g. IFRS, US GAAP, etc.).

1.3 "***Affiliate***" of a Party shall mean any Person that, directly or indirectly, through one or more intermediaries, controls, is controlled by, or is under common control with such Party, as the case may be, but for only so long as such control exists. As used in this Section 1.1, "control" shall mean (i) direct or indirect beneficial ownership of at least 50% (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of the voting share capital or other equity interest in such Person or (ii) the power to direct the management of such Person by contract or otherwise.

1.4 "***AcelRx Copyrights***" shall mean all copyrights (including registrations and applications therefor), copyrightable works which are necessary or reasonably useful for the commercialization, use, sale, offering for sale and import of the Licensed Product in the Field in the Territory, respectively.

1.5 "***AcelRx Indemnitees***" shall have the meaning set forth in Section 12.1.

1.6 "***AcelRx Know-How***" shall mean all Know-How that is necessary or reasonably useful for the research, development, registration, Manufacture, commercialization, use, sale, offering for sale and import of the Licensed Product in the Field in the Territory, which Know-How is Controlled by AcelRx or any of its Affiliates as of the Effective Date or during the Term. For the avoidance of doubt, AcelRx Know-How shall not include any Joint Know-How.

1.7 "***AcelRx Patents***" shall mean all Patents that are necessary or reasonably useful for the research, development, registration, Manufacture, commercialization, use, sale, offering for sale and import of the Licensed Product in the Field in the Territory, which Patents are Controlled by AcelRx or any of its Affiliates as of the Effective Date or during the Term. For the avoidance of doubt, AcelRx Patents shall not include any Joint Patents or Assigned Patents. A list of AcelRx Patents as of the Effective Date, which are owned by AcelRx is set forth on ***Exhibit 1.7***, which list shall be updated from time to time upon written agreement between the Parties.

1.8 "***AcelRx Technology***" shall mean all AcelRx Know-How, AcelRx Patents and AcelRx's interest in Joint Patents and Joint Know-How.

1.9 "***AcelRx Trademarks***" shall mean Trademarks of AcelRx related to the Licensed Product in the Territory as set forth on ***Exhibit 1.9*** and any Alternative AcelRx Trademark.

1.10 "***Alternative AcelRx Trademark***" shall have the meaning set forth in Section 10.7.

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1.11 "***Anti-Corruption Laws***" shall mean the U.S. Foreign Corrupt Practices Act, as amended, the UK Bribery Act 2010, as amended, and any other applicable anti-corruption laws and laws for the prevention of fraud, racketeering, money laundering or terrorism in the Territory.

1.12 "***API***" shall mean an active pharmaceutical ingredient.

1.13 "***Applicable Laws***" shall mean the applicable provisions of any and all national, supranational, regional, state and local laws, treaties, statutes, rules, regulations, administrative codes, guidance, ordinances, judgments, decrees, directives, injunctions, orders, permits (including Marketing Approvals) of or from any court, arbitrator, Regulatory Authority or governmental agency or authority having jurisdiction over or related to the subject item.

1.14 "***Assigned Patents***" shall mean **[*]** as set forth in ***Exhibit 1.14***, if and when assigned to Grünenthal pursuant to the terms of this Agreement.

1.15 "***Assigned Trademarks***" shall mean the AcelRx Trademarks that are approved by the EMA and by any other Regulatory Authority in the Territory for use with the Licensed Product upon the grant of the respective Marketing Approval in the Territory, if and when assigned to Grünenthal pursuant to the terms of this Agreement.

1.16 "***Auditor***" shall have the meaning set forth in Section 8.5.

1.17 ***"Authorized Representative"*** shall mean Grünenthal who shall be designated by AcelRx for the Licensed Product to act towards and may be addressed by authorities and bodies in the Territory instead of AcelRx according to the applicable EU directives and guidelines and based upon a written agreement between AcelRx and Grünenthal in accordance with Section 3.3 of the Supply Agreement.

1.18 "***Bankruptcy Laws***" shall have the meaning set forth in Section 14.6.

1.19 "***Budget***" shall mean the budget included within the applicable Development Plan for conducting the clinical or non-clinical studies, regulatory activities (including making regulatory filings) and other activities under such Development Plan.

1.20 "***Business Day***" shall mean a day other than a Saturday or Sunday or any public holiday in San Francisco, California or Aachen, Germany, but excluding the nine (9) consecutive calendar days beginning on December 24 th and continuing through January 1 st of each calendar year during the Term. For the avoidance of doubt, references in this Agreement to "days" shall mean calendar days.

1.21 "***Calendar Quarter***" shall mean a period of three consecutive months during a Calendar Year beginning on and including January 1st, April 1st, July 1st or October 1st.

1.22 "***Calendar Year***" shall mean a period of twelve consecutive months beginning on and including January 1 st.

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1.23 "***Candidate EU Member***" shall have the meaning set forth in Section 2.5.

1.24 ***"CE Mark***" shall mean a marking obtained and maintained by AcelRx for the Licensed Product that identifies conformity with medical device conformity requirements for use, sale and importation in the EU.

1.25 "***Centralized Procedure***" shall mean the procedures of the EU for obtaining marketing authorisation for a medicinal product as set forth in Regulation (EC) No 726/2004 of 31 March 2004, as amended from time to time during the Term.

1.26 ***"Certificate of Analysis"*** or ***"COA"*** shall mean a document identified as such and provided by AcelRx to Grünenthal that states: (a) the results of analytical tests required by the specifications to be performed with respect to the Licensed Product, (b) the quantity of the Licensed Product, and (c) the batch from which such the Licensed Product was produced.

1.27 "***Change of Control***" shall mean, with respect to a party (a) the acquisition of beneficial ownership, directly or indirectly, by any Person of securities or other voting interest of such party representing 50% or more of the combined voting power of such party's then outstanding securities or other voting interests, (b) any merger, reorganization, consolidation or business combination involving such party that results in the holders of beneficial ownership of the voting securities or other voting interests of such party (or, if applicable, the ultimate parent of such party) immediately prior to such merger, reorganization, consolidation or business combination ceasing to hold beneficial ownership of 50% or more of the combined voting power of the surviving entity immediately after such merger, reorganization, consolidation or business combination, or (c) any sale, lease, exchange, contribution or other transfer (in one transaction or a series of related transactions) of all or substantially all of the assets of such party to which this Agreement relates. For clarity, Change of Control shall not include financing transactions, through public offering, private equity financing, debt financing or otherwise.

1.28 "***Clinical Price***" shall have the meaning set forth in Section 6.3.

1.29 "***CMC***" shall mean chemistry, manufacturing and controls.

1.30 "***cGMP***" shall mean the then-current good manufacturing practices required by the FDA, as set forth in the United States Federal Food, Drug and Cosmetic Act, as amended, and the regulations promulgated thereunder, for the Manufacture of APIs, intermediates, medical devices and combination products, and the then current good manufacturing practices required by the Regulatory Authorities in the EU, as may be updated from time to time and other Applicable Laws of the EU relating to the Manufacture of APIs, intermediates, medical devices and combination products.

1.31 "***Commercial Strategy***" shall have the meaning set forth in Section 5.1(a).

1.32 "***Commercially Reasonable Efforts***" shall mean that level of efforts and resources, with respect to a particular Party, at the relevant point in time, that is consistent with the usual practice followed by that Party, in the exercise of its reasonable scientific and business

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judgment relating to other prescription pharmaceutical products owned or licensed by it or to which it has exclusive rights, which have market potential and are at a stage of development or product life similar to the applicable Licensed Product, taking into account: **[*]**.

1.33 "***Commercial Milestone***" shall mean the applicable milestone set forth in Section 7.2(b).

1.34 "***Commercialization Plan***" shall have the meaning set forth in Section 5.1.

1.35 "***Contractors***" shall have the meaning set forth in Section 11.2(h).

1.36 "***Confidential Information***" shall have the meaning set forth in Section 9.1. "***Confidentiality Agreement***" shall mean that certain Bilateral Secrecy Agreement between AcelRx and Grünenthal dated 18 January 2013, as amended by the 1 st Amendment dated July 23, 2013.

1.37 "***Control***" (including any variations such as "***Controlled***" and "***Controlling***"), in the context of intellectual property rights, Know-How and Confidential Information, shall mean possession (whether by ownership or license, other than pursuant to this Agreement) by a Party of the ability to grant access to, or a license or sublicense of, such rights, Know-How and Confidential Information, without violating the terms of an agreement with a Third Party.

1.38 "***Development Plan***" shall mean the initial Development Plan as attached hereto as ***Exhibit 1.38*** and any subsequent amendments or updates to such Development Plan during the Term pursuant to Section 4.1.

1.39 "***Device***" shall mean any current or future device portion of the Licensed Product, or any part thereof.

1.40 ***"Device Failure"*** means a Licensed Product that is **[*]**.

1.41 "***Disclosing Party***" shall have the meaning set forth in Section 9.1.

1.42 "***Dispenser Kit***" shall mean a complete kit consisting of a dispenser tip, fastening cap and thumbtag for use with or as part of the Device.

1.43 "***Distributor***" shall mean a Third Party or an Affiliate of Grünenthal to whom Grünenthal or an Affiliate of Grünenthal has granted the right to market, promote, co-promote, advertise, detail, sell and/or distribute the Licensed Product in the Field in the Territory without the control of MAA Approval for the Licensed Product in the Field in the Territory.

1.44 "***Drug***" shall mean the sufentanil drug cartridge for use with the Device.

1.45 "***Effective Date***" shall have the meaning set forth in the opening paragraph of this Agreement.

1.46 "***EMA***" shall mean the European Medicines Agency.

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1.47 "***EU" or "European Union***" shall mean the supra national community consisting of as of the Effective Date, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

1.48 "***Expenses***" shall mean the costs and expenses paid to Third Parties (or payable to Third Parties and accrued in accordance with Accounting Standards) incurred by a Party or any of its Affiliates in conducting the clinical or non-clinical studies, regulatory activities (including making regulatory filings) and other activities in accordance with the applicable Development Plan.

1.49 "***FDA***" shall mean the U.S. Food and Drug Administration or similar federal, state or local Regulatory Authorities.

1.50 "***Field***" shall mean human use in treatment of pain for (a) use within or dispensed by a hospital; or (b) use within a hospice, nursing home or other medically supervised setting, **[*]**.

1.51 "***First Commercial Sale***" shall mean, on a country-by-country basis, the first *bona fide*, arm's length sale of the Licensed Product in a country following receipt of Marketing Approval of such the Licensed Product in such country for use of such the Licensed Product in such country. Sales of the Licensed Product for registration samples, compassionate use sales, named patient use, transfers to, by or among Grünenthal, its Affiliates and/or Sublicensees shall not constitute a First Commercial Sale.

1.52 "***Fully Burdened Manufacturing Cost***" shall mean the fully burdened Manufacturing cost of the Licensed Product (including packaging for shipment) calculated in conformity with Accounting Standards and expressed on a per unit Manufactured basis, including the cost of: **[*]**

For clarity, the calculation of the cost of Manufacturing set forth above shall be based upon all Licensed Product manufactured by AcelRx over a specified period of time and shall in any event not be based on a disproportionate allocation of those costs incurred in the manufacture of the Licensed Product to Grünenthal's units of Licensed Product relative to the costs allocated to units of Licensed Product for AcelRx and its other licensees. For further clarity, costs that are specific to the units of Licensed Product supplied to Grünenthal (including subsection (d) costs) shall be limited to Licensed Product supplied to Grünenthal unless those costs apply to the other units of Licensed Product manufactured in any particular runs or campaigns and allocated accordingly. For further clarity, costs that are specific to the units of Licensed Product supplied to Grünenthal (e.g., certain elements of subsection (a) and subsection (d) of Fully Burdened Manufacturing costs) shall be limited to Licensed Product supplied to Grünenthal unless those costs apply to the other units of Licensed Product manufactured in any particular runs or campaigns and allocated accordingly

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1.53 "***Further Development Studies***" shall mean clinical trials that are not Post Approval Commitments or Post Marketing Studies, including clinical trials for Label Expansion.

1.54 "***Generic Entry***" shall mean **[*]**.

1.55 "***Generic Product***" shall mean any pharmaceutical product **[*]**.

1.56 "***Good Clinical Practices***" or "***GCP***" shall mean the then-current standards, practices and procedures promulgated or endorsed by the EU as set forth in the guidelines entitled "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance," including related regulatory requirements imposed by the FDA and comparable regulatory standards, practices and procedures in jurisdictions outside the United States, as they may be updated from time to time.

1.57 "***Good Laboratory Practices***" or "***GLP***" shall mean the then-current good laboratory practice standards promulgated or endorsed by the EU, and comparable regulatory standards in jurisdictions outside the EU, as they may be updated from time to time.

1.58 "***Good Manufacturing Practices***" or "***GMP***" shall mean the then-current good manufacturing practices required by the EU for the manufacture and testing of pharmaceutical materials, and comparable laws or regulations applicable to the manufacture and testing of pharmaceutical materials in jurisdictions outside the EU, as they may be updated from time to time. Good Manufacturing Practices shall include applicable quality guidelines promulgated under the ICH.

1.59 "***Governmental Authority***" shall mean any court, agency, department, authority or other instrumentality of any national, supranational, state, county, city or other political subdivision.

1.60 "***Grünenthal Background IP****"* shall mean all Patents and Know-How Controlled by Grünenthal or its Affiliates prior to the Effective Date of this Agreement.

1.61 "***Grünenthal Indemnitees***" shall have the meaning set forth in Section 12.2.

1.62 "***Grünenthal Know-How***" shall mean all Know-How with respect to the Device or the Licensed Product that is generated by or on behalf of Grünenthal or any of its Affiliates during the Term pursuant to this Agreement in connection with the research, development, importation, use, manufacture, sale, having sold and offering for sale of the Licensed Product.

1.63 "***Grünenthal Patents***" shall mean all Patents that claim Inventions with respect to the Device or the Licensed Product generated by or on behalf of Grünenthal or any of its Affiliates during the Term pursuant to this Agreement in connection with the research, development, importation, use, manufacture, sale, having sold and offering for sale of the Licensed Product.

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1.64 "***Grünenthal Technology***" shall mean all Grünenthal Know-How and Grünenthal Patents, including Grünenthal's interest in Joint Patents and Joint Know-How. For clarity, Grünenthal Technology does not include Grünenthal Background IP.

1.65 "***Grünenthal Trademark***" shall have the meaning set forth in Section 10.7.

1.66 "***Harmonized Standards***" shall mean technical specifications meeting the essential requirements of the EU directives, compliance with which will provide a presumption of conformity with the essential requirements for the Licensed Product.

1.67 "***ICH***" shall mean the International Conference on Harmonization (of Technical Requirements for Registration of Pharmaceuticals for Human Use).

1.68 "***IND***" shall mean an Investigational New Drug Application (including any amendments thereto) filed with the FDA pursuant to 21 C.F.R. §312 before commencement of clinical trials of a pharmaceutical product, or any comparable filings with Health Canada in Canada, including clinical trial applications.

1.69 "***Initial Label****"* shall mean human use in moderate to severe post operative pain in adults, for use within a hospital.

1.70 "***Intervening Event***" shall have the meaning set forth in Section 16.1.

1.71 "***Inventions***" shall mean any and all inventions, discoveries, improvements, processes and techniques discovered, conceived or reduced to practice in the course of or as a result of activities under this Agreement, whether or not patentable or included in any claim of patents and patent applications, together with all intellectual property rights therein.

1.72 "***Joint Inventions***" shall mean any and all Inventions discovered, conceived or reduced to practice jointly by or on behalf Grünenthal or its Affiliates, on the one hand, and by or on behalf of AcelRx or its Affiliates, on the other hand during the Term pursuant to this Agreement.

1.73 "***Joint Know-How***" shall mean all Know-How included in Joint Inventions, other than any Joint Patent.

1.74 "***Joint Patents***" shall mean all Patents claiming any Joint Invention.

1.75 "***Joint Steering Committee***" or "***JSC***" shall have the meaning set forth in Section 3.1(a).

1.76 "***Know-How***" shall mean all tangible and intangible scientific, technical, clinical, regulatory, trade, marketing, commercial, financial or business information and materials, including compounds, solid state forms, compositions of matter, formulations, devices, techniques, processes, methods, trade secrets, formulae, procedures, tests, data, results, analyses, documentation, reports, information (including pharmacological, toxicological, non-clinical

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(including chemistry, manufacturing and control)), and clinical test design, methods, protocols, data, results, analyses, and conclusions, quality assurance and quality control information, regulatory documentation, information and submissions pertaining to, or made in association with, filings with any Regulatory Authority, knowledge, know-how, skill, and experience.

1.77 *"**Label Expansion**"* shall mean any expansion of the label beyond the Initial Label.

1.78 "***Licensed Product***" shall mean (a) AcelRx's ARX-01 (any and all components thereof, and the system, which as existing as of the Effective Date is described in ***Exhibit 1.78***), and (b) any and all improvements and/or modifications thereof.

1.79 "***Losses***" shall have the meaning set forth in Section 12.1.

1.80 "***MAA***" shall mean an application with the EMA or other competent Regulatory Authority in the Territory seeking Marketing Approval of the Licensed Product.

1.81 "***MAA Approval***" shall mean the approval of a MAA to sell the Licensed Product in a country or region in the Territory. " ***Manufacture***" shall mean to manufacture, generate, process, prepare, make, assemble, test, label, package, store, hold, handle, receive, release, transport, and deliver the Licensed Product (or any component thereof).

1.82 "***Marketing Approval***" of the Licensed Product shall mean all technical, medical and scientific approvals, licenses, registrations or authorizations from Regulatory Authorities in a country of the Territory necessary for the manufacture, commercialization, use, storage, promotion, marketing, sale, offering for sale and import of the Licensed Product in the Field in such country.

1.83 "***Material Agreements***" shall have the meaning set forth in Section 11.2(j). The Material Agreements existent on the Effective Date are listed in Exhibit 1.83

1.84 *"**MEDDEV Guidelines**"* shall mean those guidelines published by the European Commission promoting a common approach by manufacturers and notified bodies involved in the conformity assessment procedures according to the relevant annexes of the directives, and by the competent authorities charged with safeguarding public health.

1.85 *"**Medical Device Directive**"* shall mean the directive 93/42/EEC published by the European Commission and any successors thereof.

1.86 *"**Multi-Site Trials**"* means Post Marketing Studies that are conducted at multiple sites.

1.87 "***Non-Interventional Studies***" means studies in which results from the treatment of patients with pharmaceutical products are analysed with epidemiological methods.

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1.88 "***NDA***" of the Licensed Product shall mean a New Drug Application as defined in Title 21 of the U.S. Code of Federal Regulations, §314.80 et seq., and all amendments and supplements thereto, which is filed with the FDA including all documents, data, and other information concerning the Licensed Product thus filed that are necessary for gaining Marketing Approval for the Licensed Product.

1.89 "***Net Sales***" shall mean the gross amounts invoiced by or on behalf of Grünenthal, its Affiliates and/or Sublicensees (the " ***Selling Party***") for sales of the Licensed Product to Third Parties (other than Sublicensees), less deductions actually incurred, allowed, paid, accrued or otherwise specifically identified as related to, and specifically allocated to, the Licensed Product by Grünenthal, its Affiliates and/or Sublicensees using Accounting Standards applied on a consistent basis for:

(a) sales allowances actually paid, granted, allowed, accrued or taken, including trade, cash, quantity discounts, chargeback rebates, reimbursements, buying groups, health care insurance carriers or other institutions, adjustments arising from consumer discount programs or other similar programs;

(b) credits or allowances given or made for rejection of or return of previously sold the Licensed Product (whether as a result of recalls, market withdrawals, other corrective actions, damaged, defective goods or otherwise), for retroactive price reductions and billing errors, or other allowances specifically identifiable as relating to the Licensed Product, including allowances and credits related to inventory management;

(c) governmental and other rebates (or equivalents thereof) granted to managed health care organizations, pharmacy benefit managers (or equivalents thereof), national, state/provincial, local, and other governments, their agencies and purchasers, and reimbursers, or to trade customers;

(d) costs of freight, insurance, and other transportation charges directly related to the distribution of such the Licensed Product;

(e) customs or excise duties, sales tax, consumption tax, value added tax, and other taxes (except income taxes) or duties relating to sales, any payment in respect of sales to any Governmental Authority, or with respect to any government-subsidized program or managed care organization; and

(f) amounts previously included in Net Sales that are written-off by the Selling Party as uncollectible in accordance with the standard practices of such Selling Party for writing of uncollectible amounts, consistent applied; provided that if any such written-off amounts are subsequently collected, such collected amounts shall be included in Net Sales in the period in which they are subsequently collected.

In no event shall any particular amount identified above be deducted more than once in calculating Net Sales (i.e., no "double counting" of reductions). Sales of the Licensed Product between Grünenthal and its Affiliates or Sublicensees for resale shall be

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excluded from the computation of Net Sales, but the subsequent resale of such the Licensed Product by an Affiliate or Sublicensee, as applicable, to a Third Party shall be included within the computation of Net Sales. For clarity, for purposes of this Section 1.80, "the Licensed Product" shall include the Drug, Device, Reusables Kit, Dispenser Kit and Accessories, whether sold together or separately.

If the Licensed Product is sold as a Bundled Product (as hereafter defined) in a country in the Territory, then the Net Sales for the Licensed Product attributable to such Bundled Product shall be the average price of Licensed Product sold in such country in the Territory during the applicable period, provided that in any event any discount applied to such Bundled Product shall in any event be applied at the same discount across all products sold with the Bundled Product (i.e., no disproportionate discount shall apply to the Licensed Product). " ***Bundled Product***" means products in which either (a) a non-Licensed Product is sold or discounted together with a Licensed Product for purchase by or for resale to a customer, or (b) a non-Licensed Product is sold together with Licensed Product in a kit at a single price. In any event, Grünenthal, Sublicensees and their respective Affiliates shall conduct pricing and discounting activities in a good faith, consistent manner without disadvantaging the Licensed Product relative to the other products priced or sold as Bundled Product.

Notwithstanding anything to the contrary herein, sale, disposal or use of the Licensed Product for marketing, regulatory, development or charitable purposes, such as clinical trials, preclinical trials, compassionate use, named patient use, or indigent patient programs, without consideration, shall not be deemed a sale hereunder.

1.90 "***Party***" shall mean AcelRx or Grünenthal individually, and "***Parties***" shall mean AcelRx and Grünenthal collectively.

1.91 "***Patent(s)***" shall mean (a) all patents, certificates of invention, applications for certificates of invention, priority patent filings and patent applications, and (b) any renewal, division, continuation (in whole or in part), or request for continued examination of any of such patents, certificates of invention and patent applications, and any and all patents or certificates of invention issuing thereon, and any and all reissues, reexaminations, extensions, divisions, renewals, substitutions, confirmations, registrations, revalidations, revisions, and additions of or to any of the foregoing.

1.92 "***Patent Term Extension***" shall mean any term extensions, supplementary protection certificates and equivalents thereof offering patent protection beyond the initial term with respect to any issued Patents.

1.93 "***Person***" shall mean any individual, corporation, partnership, limited liability company, trust, governmental entity, or other legal entity of any nature whatsoever.

1.94 "***Pharmacovigilance Agreement***" shall having the meaning set forth in Section 4.5(c).

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1.95 "***Post Approval Commitments***" shall mean all clinical studies (including pediatric studies) conducted after receipt of a Marketing Approval for the Licensed Product that are requested by Regulatory Authorities or that are necessary to fulfill commitments made to the Regulatory Authority as a condition for the receipt and/or maintenance of such Marketing Approval in any country.

1.96 "***Post Marketing Studies***" shall mean all interventional studies of Licensed Product with the main objective to collect data to increase product knowledge or for marketing and market access purposes (e.g. post-marketing surveillance studies, patient outcome studies, patient preference studies) other than Non-Interventional Studies and Post Approval Commitments.

1.97 "***Price Approval***" shall mean, in any country where a Regulatory Authority authorizes reimbursement for, or approves or determines pricing for, pharmaceutical or medical device products, receipt (or, if required to make such authorization, approval or determination effective, publication) of such reimbursement authorization or pricing approval or determination (as the case may be).

1.98 "***R&D Milestone***" shall mean the applicable milestone set forth in Section 7.2(a).

1.99 "***Receiving Party***" shall have the meaning set forth in Section 9.1.

1.100 "***Regulatory Authority***" shall mean any national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity (a) whose review and/or approval is necessary (i) for the Manufacture, packaging, use, storage, import, export, distribution, promotion, marketing, offer for sale and sale of the Licensed Product, and/or (ii) for reviewing Regulatory Filings for the Licensed Product (or a component thereof); and/or (b) having authority to review and enforce cGMP and/or other Applicable Laws relating to the Licensed Product or the Manufacture, development, commercialization, use or sale thereof. For clarity, Regulatory Authority shall, as applicable, include any notified body with respect to the Device.

1.101 "***Regulatory Filings***" shall mean all applications, approvals, licenses, registrations, notifications, registrations, submissions and authorizations made to or received from a Regulatory Authority in a country necessary for the Manufacture, development, commercialization, use, storage, promotion, marketing, sale, offering for sale and import of the Licensed Product in such country, including any INDs, NDAs, the MAA Approval, any other Marketing Approvals, Price Approvals as well as the CE Mark.

1.102 *"**Reusables Kit**"* shall mean a complete kit consisting of **[*]**.

1.103 "***Royalty Term***" shall have the meaning set forth in Section 7.3.

1.104 "***SEC***" shall have the meaning set forth in Section 8.5(a).

1.105 "***Senior Executives***" shall have the meaning set forth in Section 15.1.

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1.106 "***sNDA***" shall mean a supplemental NDA.

1.107 "***Specifications***" shall mean the specifications for the Licensed Product, as established by inclusion in the Marketing Approval application filed for the Licensed Product and as required by a Regulatory Authority in the Territory for approval and such other specifications, such as specifications for packaging, storage conditions and labeling of the Licensed Product, as agreed by the Parties pursuant to the Supply Agreement.

1.108 "***Sublicensee***" shall mean a Third Party or an Affiliate of Grünenthal, other than a Distributor, to whom Grünenthal or an Affiliate of Grünenthal has granted a sublicense under the AcelRx Technology as permitted under Section 2.2(a) of this Agreement. For clarity, the term "Sublicensee" shall not include (i) any Distributors, wholesalers or importers that are not granted any sublicense under the AcelRx Technology under Section 2.2(a) or (ii) any contract manufacturers that are granted only the right to manufacture the Licensed Product in accordance with the terms and conditions of the Supply Agreement and herein for Grünenthal or its Affiliates or Sublicensees for commercialization in the Field in the Territory.

1.109 "***Supply Agreement***" shall have the meaning set forth in Section 6.1.

1.110 "***Term***" shall have the meaning set forth in Section 13.1.

1.111 "***Territory***" shall mean the European Union, Switzerland, Liechtenstein, Iceland, Norway and Australia.

1.112 "***Territory Specific Trials***" shall mean (a) all Post Approval Commitments that are requested only by the Regulatory Authorities in the Territory and (b) Post Marketing Studies that are conducted solely by Grünenthal for the Territory.

1.113 "***Third Party***" shall mean any Person other than AcelRx, Grünenthal and their respective Affiliates.

1.114 "***Third Party Claim***" shall have the meaning set forth in Section 12.1.

1.115 "***Trademarks***" shall mean trademarks, trade names, trade dresses, domain names, logos and brandings.

1.116 ***"United States***" or "***U.S.***" shall mean the United States of America, including its territories and possessions and the District of Columbia.

1.117 "***U.S. Specific Trials***" shall mean all trials necessary to support premarket approval(s) that may be issued by the FDA.

1.118 "***Valid Claim***" shall mean: (a) an unexpired claim of an issued AcelRx Patent, Assigned Patent or Joint Patent which has not been rejected or revoked or found to be unpatentable, invalid or unenforceable by a court or other authority in the subject country, from which decision no appeal is taken or which is unappealed within the time allowable for appeal,

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and that has not been explicitly disclaimed, or admitted to be invalid or unenforceable through reissue, disclaimer or otherwise; or (b) a bona fide claim of a pending patent application within the AcelRx Patents or Joint Patents, which claim has not been cancelled, abandoned, withdrawn or finally rejected or expired without the possibility of appeal or refiling and has been pending **[*]**.

ARTICLE 2

GRANT OF LICENSES

2.1 License Grants.

(a) **Technology and AcelRx Trademark Licenses to Grünenthal.** Subject to the terms and conditions of this Agreement, including the payment of royalties hereunder, AcelRx hereby grants and causes its Affiliates to grant to Grünenthal under the AcelRx Technology, the Assigned Patent(s) and the AcelRx Trademarks (i) an exclusive (even as to AcelRx, its Affiliates and Third Parties) license to develop (subject to Sections 2.1(c) and 2.3 hereunder), commercialize, import, sell, offer for sale the Licensed Product in the Field in the Territory, and (ii) a co-exclusive (with AcelRx or its Affiliates only) license to research, develop, Manufacture, have Manufactured, use and import the Licensed Product solely for use, commercialization, importation, sale or offer for sale in the Field in the Territory; *provided,* that the foregoing licenses to Grünenthal under the AcelRx Trademarks shall end upon assignment of the Assigned Trademark as provided under Section 10.1(c) and the foregoing licenses to Grünenthal under the Assigned Patents shall end upon assignment of the Assigned Patent as provided under Section 10.1(b) (subject to reinstatement in the case of Section 10.2(c)). For the avoidance of doubt, "Licensed Product" as used in this Section 2.1(a), and as applicable in other provisions of this Agreement, refers to and includes all the components of the Licensed Product (*e.g.* Device, Drug, Dispenser Kit, Reusables Kit and Accessories) as well as the system as a whole.

(b) **Copyright License to Grünenthal.** Subject to the terms and conditions of this Agreement, AcelRx hereby grants and causes its Affiliates to grant to Grünenthal a non-exclusive, royalty-free, fully-paid license under the AcelRx Copyrights solely to research, develop, commercialize, use, sell, offer for sale and import the Licensed Product in the Field in the Territory.

(c) **License to AcelRx.** Subject to the terms and conditions of this Agreement, including the licenses set forth in Sections 2.1(a) and 2.1(b), Grünenthal hereby grants and causes its Affiliates to grant to AcelRx (A) a royalty-free, fully-paid, exclusive license, with the right to grant sublicenses, under the Grünenthal Technology for AcelRx to Manufacture, have Manufactured, commercialize, use, sell, offer for sale and import the Licensed Product for any purpose outside the Territory and to perform AcelRx's obligations under this Agreement and the Supply Agreement, and (B) a royalty-free, fully-paid, non-exclusive license, with the right to grant sublicenses, under the Grünenthal Technology for AcelRx to conduct clinical and non-clinical development activities with respect to the Licensed

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Product worldwide and to perform AcelRx's obligations under this Agreement and the Supply Agreement but, during the Term, subject to the terms of Article 4 with respect to the Territory, including the limitations imposed by Section 4.3(d).

2.2 Sublicensees; Distributors.

(a) **Right to Sublicense and Sub-Contract.** Grünenthal shall have the right to sublicense any of its rights granted to it under this Agreement to its Affiliates as and when elected by Grünenthal. Grünenthal shall also have the right to sublicense its rights granted under this Agreement to any Third Parties (who may further sublicense to a Distributor), **[*]**. All such sublicense and sub-contract agreements with a Third Party or any Distributor shall be consistent with the terms and conditions of this Agreement and shall provide that further sublicensing or sub-contracting other than to a Distributor is prohibited. Grünenthal shall provide a copy of any such sublicense agreement with a Third Party Sublicensee promptly after execution, subject to prior redaction by Grünenthal with regard to provisions, according to Grünenthal's reasonable assessment, **[*]**. Grünenthal shall remain responsible for the performance of its Affiliates, Sublicensees and sub-contractors hereunder. For clarity, Affiliates of Grünenthal to which Grünenthal has sublicensed its rights hereunder may further sublicense consistent with this Section 2.2(a) the same as Grünenthal itself may grant sublicenses consistent with this Section 2.2(a).

(b) **Right to Engage Distributors.** Grünenthal and its Sublicensees shall have the right to engage Distributors under this Agreement, provided that Grünenthal shall remain responsible for the performance of its Distributors hereunder, including the restrictions on further sublicensing (including to sub-Distributors) and compliance of Applicable Laws by such Distributors in connection with the distribution of the Licensed Product hereunder. In the event of termination of this Agreement pursuant to Section 13.2(b) for breach by Grünenthal, upon Grünenthal's request, **[*]**.

2.3 Rights Reserved. Except for the rights and licenses expressly granted in this Agreement, AcelRx retains all rights under its intellectual property, including the AcelRx Technology, and Grünenthal retains all rights under its intellectual property, including Grünenthal Technology, and no rights shall be deemed granted by one Party to the other Party by implication, estoppel or otherwise. Further, notwithstanding the grants of exclusive rights in Section 2.1, AcelRx retains the rights, without limitation, to: (a) perform or have performed all of its obligations under this Agreement, whether within or outside the Territory, including, but not limited to, to conducting development activities as contemplated by Article 4 including the limitations imposed by Section 4.3(d) and manufacturing or having manufactured the Licensed Product for supply to Grünenthal as contemplated by Article 5, this Agreement and the Supply Agreement, and (b) to make, have made, manufacture and have manufactured the Licensed Product worldwide. For the avoidance of doubt, however subject to Section 2.7, the license granted to Grünenthal under Section 2.1 does not confer any rights to Grünenthal with respect to (x) any product other than the Licensed Product, (y) any product comprising any individual component(s) of the Licensed Product, or (z) any product comprising the Licensed Product or any individual component of the Licensed Product, in each case, together with one or more additional products, devices or APIs.

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2.4 Technology Transfer. Grünenthal shall have the right to **[*]** to facilitate the transfer of analytical methods for the market release of the Licensed Product and AcelRx Know-How including AcelRx manufacturing Know-How for use in Regulatory Filings or submissions to Regulatory Authorities or other similar purposes related to Regulatory Approval of the Licensed Product in the Territory. In that respect, as soon as reasonably practicable following **[*]**, AcelRx shall, subject to reimbursement by Grünenthal for reasonable out-of-pocket costs, make available to Grünenthal personnel of AcelRx who are appropriately knowledgeable or experienced in the Manufacture of the Licensed Product for use in the Field to facilitate the transfer of the analytical methods for the market release of the Licensed Products existing as of the time of such request with a goal to effect transfer as soon as practicable, but in any event **[*]**, subject to extension for any period in which the relevant personnel of Grünenthal are unavailable. In any event, Grünenthal shall cooperate with any such transfer and shall promptly undertake to complete the transfer. During the Term, AcelRx and Grünenthal shall agree upon a process to provide to Grünenthal, at Grünenthal's reasonable request, any updates required to complete the transfer of analytical methods for the market release of the Licensed Product and AcelRx Know-How including AcelRx manufacturing Know-How for use in Regulatory Filings or submissions to Regulatory Authorities or other similar purposes related to Regulatory Approval of the Licensed Product in the Territory. Further, during the Term, AcelRx and Grünenthal shall agree upon a process to provide to each other, at the other Party's reasonable request, any scientific product information or data reasonably required by such Party's medical affairs to complete any Licensed Product-related tasks within the responsibility of medical affairs.

2.5 EU Country Additions to the Territory. If during the Term any additional countries ("***Candidate EU Member***") apply to or become part of the European Union **[*]**.

2.6 Covenants of AcelRx. During the Term, AcelRx covenants that it and its Affiliates will not directly or indirectly, **[*]**.

2.7 [*]

2.8 Australia Termination Right. Either Party shall have the right to remove the country of Australia from the Territory upon prior written notice to the other Party if **[*]**. For clarity, effective upon such written notice from either Party, Australia shall no longer be included in the Territory either of this Agreement or the Supply Agreement, and such notice shall relieve both Parties of obligations with respect to one another relating to Australia.

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ARTICLE 3

GOVERNANCE

3.1 Joint Steering Committee.

(a) **Establishment.** Within **[*]** following the Effective Date, AcelRx and Grünenthal shall establish a committee (the " ***Joint Steering Committee***" or "***JSC***") to oversee, review and/or coordinate development, Manufacture, regulatory strategy and commercialization of the Licensed Product in the Field in the Territory.

(b) **Duties.** The Joint Steering Committee shall:

(i) review, coordinate, and approve the overall development and regulatory strategies for obtaining Marketing Approval of the Licensed Product in the Field in the Territory;

(ii) provide a forum for the Parties to present, discuss and approve the Development Plan and material changes to the Development Plan, including Budgets contained therein;

(iii) provide a forum for the Parties to present any proposals regarding material development, and regulatory and manufacturing matters pertaining to the Licensed Product in the Territory and seek input from the Parties on the foregoing matters;

(iv) provide a forum for the Parties to present and discuss the Commercialization Plan;

(v) exchange information with respect to prelaunch, launch and subsequent commercialization activities with respect to the Licensed Product in the Territory;

(vi) provide a forum for the Parties to exchange information and coordinate their respective activities with respect to development, regulatory and manufacturing matters pertaining to the Licensed Product in the Field in the Territory and outside the Field or Territory;

(vii) discuss and review any opportunities for global brand synergies;

(viii) discuss and provide a forum for the Parties to seek mutual agreement on the design of a second generation Device, it being understood that no such agreement shall be required for the development of a second generation Device by AcelRx; and

(ix) perform such other duties as are specifically assigned by the Parties to the Joint Steering Committee pursuant to this Agreement.

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(c) **Decision-Making.** Subject to Section 3.1(d), the JSC shall act by consensus. The representatives from each Party will have, collectively, one (1) vote on behalf of that Party. If the JSC cannot reach consensus on an issue that comes before the JSC and over which the JSC has oversight, then the dispute resolution provisions as provided under Article 15 shall apply.

(d) **Clarification to Decision-Making.** Notwithstanding Sections 3.1(b) or (c) or Section 3.2, the Parties shall maintain final decision making authority over specific areas related to the Licensed Product that are set forth in Articles 4, 5 and 6.

3.2 Subcommittees.

(a) **Establishment.** From time to time, the Joint Steering Committee may establish additional subcommittees to oversee particular projects or activities within the scope of authority of the Joint Steering Committee, as it deems necessary or advisable. Each subcommittee shall consist of such number of representatives of each Party as the Joint Steering Committee determines is appropriate from time to time and shall meet with such frequency as the Joint Steering Committee shall determine.

(b) **Development Subcommittee.** One such subcommittee the JSC may form may be the Development Subcommittee, which to the extent agreed by the JSC may have one or more of the following responsibilities:

(i) discuss regular reports regarding the development of the Product, and discuss, prepare and consider for approval annual and interim amendments to the Development Plan (and the development budget) for the Licensed Product;

(ii) discuss and manage the implementation of the Development Plan;

(iii) oversee the conduct of development;

(iv) create, implement and review the development strategy for development and Regulatory Approval in the Territory and the design of all clinical trials,;

(v) oversee any CMC related development activities, e.g. stability studies or packaging development, as well as other activities to prepare for supply of drug substance and finished form of the Licensed Product;

(vi) allocate budgeted resources and determine priorities for each clinical trial and under the Development Plan other than Territory Specific Trials;

(vii) review Third Party contractors proposed to conduct clinical trials of the Licensed Product;

(viii) facilitate the flow of information between the Parties with respect to the potential development of the Licensed Product outside of the Field and Territory;

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(ix) discuss whether to develop the Licensed Product for other indications in the Field in the Territory;

(x) allocate primary responsibility as between the Parties for tasks relating to development of the Licensed Product where not already specified in the Development Plan;

(xi) discuss the requirements for Regulatory Approval in the Territory and oversee and coordinate regulatory matters with respect to the Licensed Product in the Territory, including to review material regulatory filings prior to submission thereof;

(xii) establish a publication strategy for publications and presentations related to the Licensed Product in the Territory;

(xiii) facilitate the flow of Information between the Parties with respect to obtaining Regulatory Approval for the Licensed Product; and

(xiv) review global harmonization of the Product, including annual review of the Development Plan and the Commercialization Plan, identify opportunities for brand synergy, discuss, and agree areas for shared investment.

3.3 Alliance Managers. Each of AcelRx and Grünenthal shall appoint one appropriately qualified representative who possesses a general understanding of clinical, regulatory, manufacturing, quality assurance and marketing issues to act as its respective alliance manager for this relationship (each, an "**Alliance Manager**"). The Alliance Managers of each Party as of the Effective Date are named in Exhibit 3.3. Each party may appoint and replace its respective Alliance Manager at any time upon written notice to the other party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager. Each Alliance Manager shall be charged with creating and maintaining a collaborative work environment between the parties. Each Alliance Manager will also be responsible for:

(a) Coordinating the relevant functional representatives of the parties, in developing and executing strategies and plans for the Licensed Product;

(b) Providing a single point of communication for seeking consensus both internally within the respective party's organizations and together regarding key strategy and plan issues, including where all questions coming up will be channeled, where joint timelines, budget and capacity requirement are aligned; and

(c) Planning and coordinating: (i) cooperative efforts, (ii) helping to establish new work streams proactively at each party; and (iii) internal and external communications.

The Alliance Managers shall be entitled to attend meetings of the JSC and of any subcommittee, but shall not have, or be deemed to have, any rights or responsibilities of a member of the JSC or subcommittee unless formally appointed to such committees. Each

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Alliance Manager may bring any matter to the attention of the JSC or subcommittee when such Alliance Manager reasonably believes that such matter requires such attention.

3.4 Joint Steering Committee Membership. The Joint Steering Committee shall consist of individuals appropriately qualified and of appropriate seniority to discuss the development, manufacturing, regulatory and commercialization activities of the Parties and shall be responsible for coordinating communications, managing the roles, responsibilities and timelines for such activities based on the Development Plan. The Joint Steering Committee shall be composed of four members, two of whom shall be nominated by AcelRx and two of whom shall be nominated by Grünenthal . Any member of the Joint Steering Committee may designate an appropriately qualified substitute to attend and perform the functions of that member at any meeting of the Joint Steering Committee. Each Party may, with the consent of the other Party, such consent not to be unreasonably withheld or delayed, invite non-member representatives of such Party to attend meetings of the Joint Steering Committee.

3.5 Meetings. All Joint Steering Committee meetings shall be held as often as the members may determine, but in any event Joint Steering Committee meetings shall occur not less than once per Calendar Quarter. Such meetings may be held in person, or by any means of telecommunications or video conference, as the members deem necessary or appropriate; provided, that at least one meeting of the Joint Steering Committee per Calendar Year shall be held in person.

3.6 Minutes. Minutes for each of the Joint Steering Committee meetings shall be prepared by a Grünenthal or an AcelRx member of the Joint Steering Committee on an alternating basis. The draft minutes shall be sent to all members of the Joint Steering Committee for comment promptly after each such meeting (but in no event more than 15 days after each such meeting). All actions noted in the minutes shall be reviewed and approved at subsequent meetings of the Joint Steering Committee; *provided*, that if the Parties cannot agree as to the content of the minutes by the time the Joint Steering Committee next meets, such minutes shall be finalized to reflect any areas of disagreement.

3.7 Expenses. Each Party shall bear its own costs, including expenses incurred by the members nominated by it in connection with their activities as members of the Joint Steering Committee.

3.8 Dispute Resolution. If any subcommittee is unable to resolve a dispute within such subcommittee within **[*]** after written notice of a dispute from one Party to another, then such dispute shall be referred to the Joint Steering Committee for resolution. If the Joint Steering Committee is unable to resolve any dispute within **[*]** after written notice of a dispute at the level of the Joint Steering Committee from one Party to another, then either Party may, by written notice to the other Party, have such dispute referred to the Senior Executives in accordance with Section 15.1, and such dispute shall thereafter be handled in accordance with Section 15.1.

3.9 Discontinuation of Participation. The Joint Steering Committee (and any subcommittee established under this Article 3) shall continue to exist until the first to occur of:

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(a) the Parties mutually agreeing to disband the committee; or (b) AcelRx providing to Grünenthal written notice of its intention to disband and no longer participate in such committee at any time during the Term however not to be issued by AcelRx earlier than **[*]**. Once AcelRx has provided such written notice, AcelRx shall have no further obligations under this Agreement with respect to any such committee or subcommittee, and (x) any matters that would previously have been addressed by a subcommittee will be handled by the JSC, and (y) any matters that would previously have been addressed by the JSC will be handled by the Parties in accordance with the terms of this Agreement; provided, that in such event the consent of AcelRx (when and where required) for further clinical development of the Licensed Product in Field in the Territory shall be promptly given and not unreasonably withheld.

ARTICLE 4

DEVELOPMENT AND REGULATORY ACTIVITIES

4.1 Development Plan. The Parties will negotiate in good faith and enter into a Development Plan (including a Budget contained therein) with respect to the Licensed Product, which sets forth a comprehensive development program to support Regulatory Filings for the Licensed Product in the Territory and will be attached hereto as Exhibit 1.38, provided that, AcelRx shall be the controlling Party with regard to clinical development of the Licensed Product unless provided for otherwise in this Agreement. Grünenthal shall be responsible for the costs and conduct of Regulatory Filings in the Territory, including MAA Approval, and/or other regulatory approvals at a country-specific level. The JSC shall be responsible for initial review and discussion of the Development Plan as well as reviewing and approving the Development Plan and any changes to the Development Plan on an ongoing basis, and in no event less frequently than once annually. Notwithstanding Section 3.6, in the event that the JSC cannot agree on content of or changes to the Development Plan with respect to clinical development, the representatives of AcelRx to the JSC shall have the deciding vote, provided however that (i) AcelRx shall not exercise such right if it may result in increased costs for Grünenthal unless AcelRx is willing to bear such costs, and (ii) Grünenthal shall have the deciding vote for certain decision as set forth in Section 4.2. below. All material changes to the Development Plan shall be agreed to by the Parties in writing. Both Parties shall exchange safety relevant information obtained from any kind of investigation for reporting purposes such as, for non-limiting example, periodic safety reports. Further details shall be stipulated in the Pharmacovigilance Agreement.

4.2 Development Responsibilities. The Development Plan shall provide that:

(a) **Post Approval Commitments.**

(i) Grünenthal shall use Commercially Reasonable Efforts to conduct (at its cost) development activities for Territory-specific Post Approval Commitments for the Licensed Product in the Field that are not also required by the FDA in the U.S. for the Licensed Product in the Field. Grünenthal shall not be required to obtain AcelRx's consent to conduct such development activities but shall provide, through the JSC, reasonable detail regarding these Post Approval Commitments.

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(ii) AcelRx shall use Commercially Reasonable Efforts to conduct development activities for all Post Approval Commitments in the U.S., including such Post Approval Commitments required by the FDA and any Regulatory Authorities in the Territory that overlap in whole or in parts. AcelRx shall bear all costs for Post Approval Commitments required by the FDA **[*]**. In the event that AcelRx is required to expand its development activities for Post Approval Commitments beyond FDA requirements and in order to meet additional requirements by Regulatory Authorities in the Territory, then Grünenthal shall bear any incremental costs beyond those costs for such FDA-required Post Approval Commitments, provided that the development activities applicable to the Territory and allocation of related costs shall be discussed and agreed by the JSC prior to their initiation.

(b) **Non-Interventional Studies and Post Marketing Studies.**

(i) Grünenthal shall be free to conduct (at its cost) Non-Interventional Studies for the Licensed Product in the Field in the Territory without AcelRx's consent.

(ii) The Parties may also mutually agree to jointly conduct Post Marketing Studies for the Licensed Product in the Territory. In such case, responsibilities for the conduct of such Post Marketing Studies for the Licensed Product and sharing of related costs shall be mutually agreed by the JSC.

(c) **Further Development Studies.** Should a Party desire to conduct Further Development Studies for the Licensed Product, the Parties shall discuss the possible conduct of such development activities, including any sharing of costs. Grünenthal shall be required to obtain AcelRx's consent before conducting such Further Development Studies for the Licensed Product, such consent not to be unreasonably withheld. In the event that Grünenthal shares in the cost of any such Further Development Study, **[*]**.

4.3 Conduct of Development Activities.

(a) **Compliance with Development Plan and Applicable Laws.** All development and regulatory activities in connection with the clinical development program to support Regulatory Filings for the Licensed Product shall be conducted by and on behalf of the Parties in accordance with the Development Plan and the other provisions of this Agreement. Each Party shall conduct the development activities for which it is the responsible Party under the Development Plan in accordance with the Development Plan (including the applicable Budgets contained therein) and this Agreement. Each Party shall conduct those activities for which it is the responsible Party under the Development Plan in compliance in all material respects with all Applicable Laws and in accordance with GLP and GCP (when applicable) under the Applicable Laws of the country in which such activities are conducted.

(b) **Diligence.** The responsible Party shall use Commercially Reasonable Efforts to conduct and complete the studies and activities assigned to it in the Development Plan in order to achieve the goals of the Development Plan in accordance with the timelines specified therein. Without limiting the foregoing, each Party shall use Commercially Reasonable Efforts to conduct the studies and activities for which it is the responsible Party under the Development

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Plan by using its good faith efforts to allocate sufficient time, effort, equipment and facilities to such development activities and to use personnel with sufficient skills and experience as are required to accomplish such studies and activities in accordance with the Development Plan and the terms of this Agreement.

(c) **Information Regarding Development Activities.** Each Party shall maintain records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, which shall fully and properly reflect all work done and results achieved by or on behalf of such Party in the performance of its development activities under this Agreement. Each Party shall keep the Joint Steering Committee appropriately informed of the status of the clinical development program and other activities with respect the Licensed Product in the Field conducted under the Development Plan and other development activities under or pursuant to Sections 4.2 and 4.3. Upon request by the Joint Steering Committee, without limiting the foregoing, each Party shall promptly provide the Joint Steering Committee with summaries of data and results and, if requested by the Joint Steering Committee, all supporting data and results generated or obtained in the course of such Party's performance of studies and activities under the Development Plan. Upon reasonable prior written notice, each Party shall have the right to inspect records and notebooks reflecting the work done and results achieved by or on behalf of the other Party or its Affiliates in the performance of its development activities with respect to the Licensed Product in the Field pursuant to the Development Plan.

(d) **AcelRx Development Activities within the Territory.** During the Term, **[*]** without obtaining the prior written consent of Grünenthal, such consent not to be unreasonably withheld or delayed.

4.4 Regulatory Responsibilities for the Licensed Product.

(a) **Responsibilities for Obtaining and Maintaining Drug Regulatory Approvals for the Licensed Product.** During the Term, Grünenthal shall have the exclusive (even as to AcelRx, its Affiliates and Third Parties) right and shall use Commercially Reasonable Efforts to obtain and maintain the MAA Approval and any other Drug-related Regulatory Filings for the Licensed Product in the Field in the Territory at its sole cost and expense, and AcelRx shall use Commercially Reasonable Efforts to obtain and maintain the CE Mark and any other Device-related Regulatory Filings at its sole cost and expense. At Grünenthal's request, AcelRx shall use Commercially Reasonable Efforts to assist Grünenthal at AcelRx cost, with the preparation and filing of such Regulatory Filings. AcelRx shall provide Grünenthal with an updated dossier according to EU requirements and in EU compliant eCTD format as soon as possible however not later than **[*]** of the MAA in the EU as agreed upon in the Development Plan. AcelRx shall transfer or shall cause its consultants or subcontractors to transfer all responsibilities and activities related to the MAA Approval and any other Drug-related Regulatory Filings to Grünenthal as soon as reasonably practicable after the Effective Date.

(b) **Responsibilities for Obtaining and Maintaining Device Regulatory Approvals for the Licensed Product.** AcelRx shall use Commercially Reasonable Efforts to obtain and maintain a CE Mark and any other device-related Regulatory Filings including

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compliance with all Harmonized Standards for the Licensed Product in the Territory at its sole cost and expense. Grünenthal shall use Commercially Reasonable Efforts to assist AcelRx with the preparation and filing of such Regulatory Filings. AcelRx shall designate Grünenthal as Authorized Representative for the Licensed Product in the Territory as provided in the Supply Agreement. In case AcelRx has previously designated another party as Authorized Representative for the Licensed Product in the Territory, AcelRx shall promptly take all necessary actions to transfer such responsibility from such party to Grünenthal in accordance with the Supply Agreement.

(c) **CMC Information.** AcelRx shall be, at its cost, solely responsible for preparing and providing Grünenthal with the necessary pre-clinical, clinical and chemistry, manufacturing and control ("***CMC***") data to support and maintain MAA Approval for the Licensed Product in the Field in the Territory. Such documentation shall be compliant with EU requirements for eCTD format.

4.5 Regulatory Activities.

(a) **Conduct of Regulatory Activities.** Before the Effective Date of this Agreement, AcelRx has obtained clearance from the EMA that the Licensed Product can (but need not) be submitted through a Centralized Procedure and has submitted a respective letter of intent to the EMA and has requested a corresponding pre-submission meeting with the EMA and Grünenthal has received a copy of such documentation. Furthermore, AcelRx has initiated the clearance procedure(s) regarding the AcelRx Trademarks to be used for the commercialization of the Licensed Product under the EMA in accordance with the Centralized Procedure. Each Party shall conduct all of those regulatory activities for which it is the responsible Party as set forth in Section 4.4 or Section 4.5 as the case may be, and shall fund all regulatory activities for obtaining Marketing Approval in the Territory in accordance with Section 4.4 above. Each Party shall conduct such regulatory activities for which it is the responsible Party in compliance with this Agreement and in accordance with the Development Plan (including the Budget set forth therein) and shall use Commercially Reasonable Efforts to obtain Marketing Approval in the Field in the Territory.

(b) **Regulatory Communications.** During the period that a Party is the responsible Party for certain regulatory activities under the Development Plan, such responsible Party shall timely inform the other Party of all of its scheduled meetings with the Regulatory Authorities, invite such other Party to attend in such meetings as observers, and, if such other Party elects not to attend such meetings, provide such other Party with summaries of its meeting with the Regulatory Authority promptly after each meeting. In addition, each Party shall promptly provide the other Party with copies of all written communications and summary of material oral discussions with the Regulatory Authority with respect to the Licensed Product in the Field in the Territory. In addition to the information required to be provided to the other Party in other provisions of this Agreement, Grünenthal shall timely provide AcelRx with summaries of any of its communications and correspondence with the Regulatory Authorities in the Territory with respect to safety and manufacturing issues with respect to the Licensed Product for use in the Field in the Territory and AcelRx shall timely provide Grünenthal with

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summaries of any of its communications and correspondence with the Regulatory Authorities with respect to safety and manufacturing issues with respect to the Licensed Product for use outside the Field in the Territory or for use outside the Territory. The Parties shall, upon the request of a Party, discuss in good faith whether a regulatory services agreement would be necessary to facilitate the disclosures and information sharing as well as to specify responsibilities of each Party as required pursuant to this Article 4.

(c) **Pharmacovigilance.** AcelRx shall be responsible for the maintenance of the global safety database for the Licensed Product, including being solely responsible for the costs for such maintenance. Grünenthal shall be responsible for the maintenance of its own safety database for the Licensed Product with respect to the Territory, including being solely responsible for the costs for such maintenance of its database; provided that Grünenthal shall in any event ensure that all safety database information is provided to AcelRx in a timely manner and in an electronic format requested by AcelRx in order to maintain the Grünenthal safety information as part of the global safety database. Both Parties shall in any event ensure that all safety information is exchanged in both directions in a timely manner. The Parties shall enter into a pharmacovigilance agreement (the ***"Pharmacovigilance Agreement"***) as soon as practicable with a goal of entering into such Pharmacovigilance Agreement **[*]**, setting forth the specific details and processes pursuant to which the Parties will share adverse event, device incidents and other safety data. The Pharmacovigilance Agreement will include those terms required by ICH guidelines, EU Medical Device Directive and applicable MEDDEV Guidelines, such as (i) providing detailed procedures regarding the maintenance of core safety information and the exchange of safety data relating to the Licensed Product worldwide within appropriate timeframes and in an appropriate format to enable each party to meet both expedited and periodic regulatory reporting requirements; and (ii) ensuring compliance with the reporting requirements of all applicable Regulatory Authorities on a worldwide basis for the reporting of safety data in accordance with standards stipulated in the ICH guidelines and the Medical Device Directive , and all applicable regulatory and legal requirements regarding the management of safety data.

4.6 Expenses Report and Audit Right. In order to demonstrate the share of the aggregate amount of costs and expenses for which it is responsible pursuant to Section 4.2, each Party shall provide to the other Party a written report of all costs and expenses which it has paid or committed to pay, together with documented supporting evidence. The other Party shall have the right to cause an independent, certified public accounting firm reasonably acceptable to the other Party to audit the other Party's records relating to the allocated costs and expenses to confirm the amount of the costs and expenses reflected in such report. The auditing Party shall bear the full cost of such audit unless such audit discloses an over-charging by the audited Party **[*]** of the total amount of costs and expenses invoiced, in which case, the audited Party shall bear the full cost of such audit.

4.7 Language Translation for Device. AcelRx shall be responsible for and shall complete, at its cost, the preparation of the Device (including any modifications of the Device that may be necessary or useful) to receive and utilize languages other than American English for its intended operation as part of the Licensed Product, including all necessary technical

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development and implementation of hardware and firmware. Grünenthal shall determine the languages that are necessary for the Device to be implemented in for the Territory. AcelRx shall, consulting with Grünenthal, competitively bid subcontracts with Third Parties providing for the implementation of the software for the Device in the languages specified by Grünenthal for review and approval by the JSC, provided that any subcontracts and the costs for the implementation of the software for the Device in the languages specified by Grünenthal thereunder must be approved in advance by Grünenthal prior to AcelRx entering into such agreements. Grünenthal shall be responsible for the costs of software development, verification, validation and implementation that are necessary to enable specifically the translation and presentation into languages selected by Grünenthal pursuant to contracts approved by Grünenthal. For clarity, Grünenthal shall not be responsible for any Device modification or preparation costs such as those described in the first sentence of this Section 4.7.

4.8 Second Generation Device. The JSC shall review market or other research that is presented to it by a Party regarding potential modifications that could be made to the Device to improve or add to its functionality in desirable ways to become a second generation Device for the Territory. The JSC shall seek to agree upon a joint, mutually agreed recommendation for such a second generation Device. Neither Party shall have final decision-making control regarding the selection of such a second generation Device for the Territory, but in any event AcelRx shall not be limited in proceeding with a second generation Device with the understanding that Grünenthal may determine (through the JSC) that such Device will not be used in the Territory.

ARTICLE 5

COMMERCIALIZATION AND MARKETING

5.1 Commercialization of the Licensed Product.

(a) **Grünenthal's Commercialization Rights.** Pursuant to the license rights granted to Grünenthal under Sections 2.1 and 2.2, Grünenthal through its own efforts and that of its sublicensed Affiliates and permitted Third Party sublicensees, and its and their respective Distributors, shall have the exclusive (even as to AcelRx, its Affiliates and Third Parties) right to sell and otherwise commercialize any and all Licensed Products in the Field in the Territory, including the components thereof (*e.g.* Device, Drug, Dispenser Kit, Reusables Kit and Accessories) and the system as a whole. Grünenthal shall use Commercially Reasonable Efforts to: (i) establish the strategy for the commercialization of the Licensed Product in the Field in the Territory (the "***Commercial Strategy***") and (ii) commercialize the Licensed Product in the Field in the Territory. It is anticipated that Grünenthal may enter into distribution and alternative supply agreement(s) with its Affiliate(s) or Third Party(ies) for the commercialization of the Licensed Product in the Field in the Territory in accordance with this Agreement.

(b) **Commercialization Coordination**. No later than **[*]** before the first anticipated launch of the Licensed Product in the Territory Grünenthal shall prepare and submit to the Joint Steering Committee for review and discussion a commercialization plan setting forth

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the goals, Commercialization Strategies and plans for Grünenthal's prelaunch activities, launch and subsequent commercialization of the Licensed Product in the Field in the Territory and the level of anticipated sales force and promotion efforts dedicated to the Licensed Product, together with the budget in connection therewith (the "**Commercialization Plan**"). Grünenthal shall use Commercially Reasonable Efforts to conduct the commercialization activities in accordance with such Commercialization Plan; provided, that for purposes of this Section 5.1(b), Commercially Reasonable Efforts means that Grünenthal shall have **[*]**. Grünenthal shall consult with and provide regular updates to AcelRx through the Joint Steering Committee regarding the Commercial Strategy and shall discuss coordination of commercial activities in the Field in the Territory with activities in the rest of the world. In the event that the JSC cannot agree as to the content of the Commercialization Plan, Grünenthal shall have the decisive vote with respect to the commercialization activities concerned. Nothing contained in this Section or Agreement shall be construed to interfere with Grünenthal's right to set any resale prices.

(c) **Prompt Assertion of Claims**. If either Party is or becomes aware of facts that would constitute a reasonable basis to allege that the other Party is in material breach of this Agreement pursuant to Section 13.2(b), then the Party becoming aware of such facts will promptly notify the other Party in writing of the facts constituting such potential material breach. Promptly upon a Party's receipt of any notice from the other Party of a such potential breach by such Party receiving such notice (a "***Receiving Party***") pursuant to this Section 5.1(c), the Parties will discuss the specific nature of such potential breach and seek to identify an appropriate corrective course of action. If, no later than **[*]** after the Receiving Party's receipt of such a notice, (i) the Parties have not reached consensus regarding whether Receiving Party has failed to satisfy its obligations pursuant to this Agreement, and (ii) the Parties' have not agreed upon an appropriate corrective course of action for such failure, then such potential breach may be escalated by either Party and resolved pursuant to the provisions set forth in Article 15. If a Party fails to notify the other Party of a potential claim pursuant to this Section 5.1(c) within **[*]** after the date such first Party first becomes aware of sufficient facts that would reasonably constitute a material breach, then other Party will be deemed to have satisfied its obligations under this Agreement with respect to such potential material breach.

5.2 [*].

ARTICLE 6

CLINICAL SUPPLY

6.1 Clinical Supply and Purchase of the Licensed Product. Subject to the terms of this Agreement, during the Term and until AcelRx supplies Licensed Product under the Supply Agreement (as defined below), AcelRx shall Manufacture in accordance with cGMP and supply the Licensed Product for use by the Parties in connection with the research and development of the Licensed Product in the Field in the Territory in accordance with the Development Plan. All other supply, including commercial supply, of the Licensed Product shall be as set forth in a separate commercial supply agreement (the ***"Supply Agreement"***).

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6.2 Samples. AcelRx shall Manufacture and have Manufactured the Device or other samples of components of the Licensed Product (***"Samples"***) for use in training in accordance with applicable Regulatory Requirements in the Territory, as then in effect for use by Grünenthal (and its Affiliates, distributors or licensees) for sampling or demonstration purposes. For clarity, the Parties expressly contemplate that Samples shall consist of the Device and placebo cartridges Manufactured by AcelRx, and the Samples will be supplied to Grünenthal **[*]**. In any event, AcelRx will discuss the nature and quality of the Samples, planned quantities and cost with Grünenthal in advance of any Manufacture of Samples.

6.3 Price. All Licensed Product supplied under this Agreement to Grünenthal for research and development purposes shall be provided at AcelRx's Fully Burdened Manufacturing Cost for such items, as soon as practicable following written order from Grünenthal specifying the quantity and specifications for such Licensed Product.

6.4 Clinical Supply Terms. Grünenthal may submit purchase orders from time to time for clinical supply of Licensed Product and AcelRx shall use Commercially Reasonable Efforts to promptly fill such order. The provisions of Sections 3.1, 3.2, 3.7 and 4.2 of the Supply Agreement are hereby incorporated by reference with respect to such orders for clinical supplies.

ARTICLE 7

PAYMENTS

7.1 Initial Payment. In consideration for the licenses and rights granted to Grünenthal hereunder, Grünenthal shall pay to AcelRx a non-refundable, non-creditable payment in the amount of U.S. $30,000,000 (thirty million US dollars) by wire transfer of immediately available funds into an account designated by AcelRx no later than December 30, 2013.

7.2 Milestone Payments. In further consideration for the licenses and rights granted to Grünenthal hereunder, Grünenthal shall pay to AcelRx the following non-refundable, non-creditable milestone payments set out below following the first achievement of the corresponding milestone in the Territory during the Term. A Party shall notify the other Party in writing within **[*]** after the achievement of each milestone event with respect to the Licensed Product during the Term, and AcelRx shall invoice Grünenthal at the time of or following such notice for the applicable milestone payment. Grünenthal shall pay to AcelRx the amounts set forth below within **[*]** after its receipt of AcelRx's invoice.

(a) **R&D Milestones:**

R&D Milestones

	Milestone	**Milestone Payment Amount**
1.	Upon first MAA submission for a Licensed Product in the Territory during the Term.	$5,000,000 (five million US Dollars)
	[*]	[*]

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[*]

(b) **Commercial Milestones:**

Commercial Milestones	
Aggregate Annual Net Sales Level Achievement of the Licensed Product in the Territory ([*])	**Milestone Payment Amount**
[*]	[*]

Any milestone payment payable by Grünenthal pursuant to this Section 7.2 shall be made no more than once with respect to the achievement of each such milestone event.

7.3 Royalty Payments During Royalty Term.

(a) **Royalty Rate.** Subject to this Section 7.3 and the other terms and conditions of this Agreement, in further consideration for the licenses and rights granted to Grünenthal under this Agreement, Grünenthal shall pay to AcelRx royalties on a quarterly basis at the applicable royalty rate set forth below with the royalty based on aggregate annual Net Sales of such the Licensed Product in the Territory[*]:

Aggregate Annual Net Sales of the Licensed Product in the Territory	**Applicable Royalty Rate**
[*]	[*]

(b) **Third Party Licenses and Disputes.** If, during the Term,

(i) A license from any Third Party to any Patent(s) that **[*]** is required in order to research, develop, import, use, sell, have sold and offer for sale the Licensed Product sold by AcelRx to Grünenthal for use in the Field in the Territory, then AcelRx shall be solely responsible, including bearing all related costs, for either (A) obtaining a license for the Licensed Product for the importation, use, having sold or sale of the Licensed Product by Grünenthal, or (B) defending and indemnifying Grünenthal with respect to any action for such alleged infringement; and/or

(ii) Grünenthal is alleged to infringe any Third Party Patents or Third Party Trademarks with respect to the development, importation, use, having sold or sale of the Licensed Product as delivered and Manufactured by AcelRx for use in the Field in the Territory **[*]**, then Grünenthal shall promptly notify AcelRx of the notice of alleged infringement. AcelRx shall have the first right to obtain a license from such Third Party or to defend any action with respect to such alleged infringement. If AcelRx obtains any license in any jurisdiction for such Patent(s) or Trademarks, AcelRx shall also obtain the same rights with respect to the Territory for the benefit of Grünenthal. If AcelRx takes action in any jurisdiction against such

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Third Party Patent(s), AcelRx shall also discuss with Grünenthal whether to undertake any similar action with respect to the Licensed Product in the Territory. AcelRx shall keep Grünenthal reasonably and promptly informed with regard to such licenses or actions taken by AcelRx in relation to same. To the extent that AcelRx determines not to obtain a license from such Third Party (and does nothing more) or AcelRx determines to bring an action against such Patent or Trademark and does not obtain rights to enable Grünenthal's right to use, sell, have sold and offer for sale the Licensed Product as delivered by AcelRx in the Field in the Territory under such Patent or Trademark, then Grünenthal shall have the right to obtain a license from such Third Party directly **[*]** and any excess shall be applied towards future Calendar Quarters, as applicable. If AcelRx fails to undertake action against such alleged infringement following notification of alleged infringement of Third Party Patent(s) or Third Party Trademarks and Grünenthal thereafter takes action in any jurisdiction against such Third Party Patent(s) or Third Party Trademarks, then Grünenthal shall be allowed to deduct all reasonable out-of-pocket expenses as well as any damage payments incurred in such action from royalties and/or milestone payments otherwise due to AcelRx under this Agreement.

(c) **Generic Competition.** Upon Generic Entry in a country in the Territory, Grünenthal shall have the right upon thirty (30) days written notice to AcelRx, either (i) to terminate the Agreement with respect to such country, in which case the provisions of Section 14.5 shall apply; or (ii) to retain its licenses in such country, but reduce the royalties payable to AcelRx **[*]** until such time as the Generic Products are not being sold in such country, in which event the royalties on Net Sales shall be reinstated in the first Calendar Quarter following the removal of the Generic Products. For the avoidance of doubt, the **[*]** deduction set forth in this Section 7.3(c) shall apply only to the royalties on Net Sales for such country in the Territory in which **[*]** reduction in Net Sales has occurred. Calculation of the adjustments to royalties in any country in the Territory pursuant to this Section 7.3(c) shall be undertaken at the end of the Calendar Year based on the final then-applicable royalty rate on Net Sales in the Territory and Grünenthal shall include in the Royalty Report the Net Sales of Licensed Product in the country in the Territory with respect to which Generic Product reductions apply and the calculation of the applicable royalty in such country as a separate calculation from the unaffected countries in the Territory.

(d) **Device Failure Royalty Reduction.** In the event that (i) a Regulatory Authority in the Territory determines that as a result of a Device Failure the Licensed Product constitutes a potentially serious health risk and requests that a Recall of the Licensed Product should be initiated, or (ii) after the first anniversary of First Commercial Sale of the Licensed Product in the Territory, total Device Failures in any **[*]** then the royalty set forth in Section 7.3(a) shall be reduced **[*]** after the Calendar Quarter in which the Device Failure is finally determined.

For such purpose, Grünenthal shall, within **[*]** of return of a Licensed Product to Grünenthal from the end user customer, notify AcelRx in writing of any suspected Device Failure, including the details of use and return by the end user customer of Grünenthal, and AcelRx shall have **[*]** to review the documentation provided to dispute such claim of Device Failure. After timely notice of Device Failure is received by AcelRx, Grünenthal shall cooperate with AcelRx in

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determining whether return is appropriate or justified. If AcelRx disagrees with Grünenthal's determination that a certain Licensed Product is a Device Failure, the returned Licensed Product shall be submitted to a mutually acceptable Third Party laboratory, which shall determine whether such Licensed Product constitutes a Device Failure. The Parties agree that such Third Party laboratory's determination shall be final and binding on the Parties. The costs for such Third Party's laboratory's determination shall be borne by (i) AcelRx if a Device Failure is confirmed, and (ii) by Grünenthal if no Device Failure is determined. Each Party is responsible for its own internal costs related to such procedures.

(e) **Royalty Term.** On a country-by-country basis, Grünenthal's obligation to make royalty payments pursuant to this Section 7.3 will commence upon the First Commercial Sale of the Licensed Product in a country in the Territory and shall continue until the later of (i) expiration of the last-to-expire Valid Claim within the AcelRx Patents and/or Joint Patents that covers the making, use, sale, offer for sale or importation of the Licensed Product in the Field in such country, or (ii) **[*]** after the First Commercial Sale of the Licensed Product in such country (the " ***Royalty Term***"). Following the expiration of the Royalty Term, subject to the payment obligations set forth in Section 7.4, the license grants set forth in Section 2.1(a) and Section 2.1(c) will convert to royalty-free, fully-paid licenses.

7.4 Trademark and Supply Fee. In addition to the royalty payable pursuant to Section 7.3, in further consideration of the rights, licenses, commitments to supply after the Royalty Term as set forth in Section 10.3(c) of the Supply Agreement and assignment of the Assigned Trademark hereunder, on a country-by-country basis for so long as AcelRx continues to supply Licensed Product pursuant to the Supply Agreement, Grünenthal shall pay to AcelRx (i) beginning on a country-by-country basis on the **[*]** of the Net Sales of Licensed Product in such country, and (ii) **[*]** for such annual period ((a) and (b) collectively, the "***Trademark and Supply Fee***") until such time as, following Generic Entry in any country, the Net Sales of the Drug and Dispenser Kit in such country is reduced by **[*]**or more in the corresponding Calendar Quarter from the Net Sales in the preceding Calendar Year, in which event Grünenthal may elect within thirty (30) days to either (i) terminate the Trademark and Supply Fee in the Territory and AcelRx shall no longer have any obligation to supply under the Supply Agreement, or (ii) the Trademark and Supply Fee shall be reduced **[*]** in such country effective as of the end of the Calendar Quarter in which the Net Sales have been so reduced.

7.5 Royalty Reports; One Royalty. During the term of this Agreement following the First Commercial Sale of the Licensed Product, Grünenthal shall furnish to AcelRx a quarterly written report (**"*Royalty Report*"**) for the calendar quarter showing the gross amounts invoiced, permitted deductions and Net Sales of all the Licensed Product subject to royalty payments and the Trademark and Supply Fee sold by Grünenthal and its Affiliates, Sublicensees and Distributors on a country by country basis in the Territory during the reporting period and the amounts payable under this Agreement. Royalty Reports shall be due on the thirtieth (30th) day following the close of each calendar quarter. Royalties shown to have accrued by each Royalty Report shall be payable within three Business Days from the date such Royalty Report is

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due. Grünenthal shall keep complete and accurate records in sufficient detail to enable the amounts payable hereunder to be determined. Only one royalty and Trademark and Supply Fee, as applicable, shall be due by Grünenthal to AcelRx with respect to the sale of the same unit of the Licensed Product.

7.6 Obligations under Existing Third Party Agreements. AcelRx shall be solely responsible for any and all payments, fees or other costs payable under its agreements with Third Parties existing as of the Effective Date.

7.7 No Measure of Damages. Grünenthal and AcelRx acknowledge and agree that nothing in this Agreement (including milestone payment amounts set forth in Section 7.2) will be construed as representing any estimate or projection of the damages, if any, that may be payable if this Agreement or the Supply Agreement is terminated for any reason and that each Party acknowledges its right and burden to prove the amount of damages to which it may be entitled in any successful action brought for uncured material breach of this Agreement by the other Party. Neither Party makes any representation, warranty or covenant that is not expressly set forth in this Agreement or the Supply Agreement.

ARTICLE 8

PAYMENTS, BOOKS AND RECORDS

8.1 Payment Method. All payments to AcelRx under this Agreement shall be made by bank wire transfer in immediately available funds to an account in the name of AcelRx designated in writing by AcelRx. Payments hereunder shall be considered to be made as of the day on which they are dispatched by Grünenthal's designated bank.

8.2 Payment Currency; Currency Conversion.

(a) **United States Dollars.** Unless otherwise expressly stated in this Agreement, all amounts specified to be payable under this Agreement are in United States Dollars and shall be paid in United States Dollars.

(b) **Currency Conversion.** Net Sales invoiced in currency other than United States Dollars, shall be converted to United States Dollars using an average exchange rate for the calendar quarter with respect to which such royalty is accrued based on published in public sources, e.g., Bloomberg or Reuters.

8.3 Taxes.

(a) **Cooperation and Coordination.** The Parties acknowledge and agree that it is their mutual objective and intent to minimize, to the extent feasible, income and other taxes payable with respect to their collaborative efforts under this Agreement and that they shall use their reasonable efforts to cooperate and coordinate with each other to achieve such objective.

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(b) **Payment of Tax.** A Party receiving a payment shall pay any and all taxes levied on such payment. If the fiscal or taxing authorities of any relevant jurisdiction assert that amounts are required to be withheld from the payments due to a Party hereunder, or the tax laws in one or more jurisdictions have changed so as to explicitly require such treatment, the Party made aware of such assertion or change in law shall inform the other Party within thirty (30) days and shall consult with the other Party regarding the consequences of such assertion or change. If Applicable Laws require that taxes be deducted and withheld from a payment, the remitting Party shall (i) deduct those taxes from the payment, (ii) pay the taxes to the proper taxing authority, (iii) send evidence of the obligation together with proof of payment to the other Party within sixty (60) days following that payment and (iv) provide such assistance as the other Party may reasonably require in obtaining any refund of such amounts to which the other Party may be entitled, to the extent that such assistance does not cause the remitting Party to incur any liability in respect of the taxes asserted to be due. All payments made under this Agreement are net prices and shall be free and clear of any and all taxes (like sales- and use taxes , consumption taxes, goods- and sale taxes or value added taxes or comparable taxes), duties, levies, fees or other charges, except for required withholding taxes.

8.4 Records. Grünenthal shall keep, and require its Affiliates and Sublicensees to keep, complete, true and accurate books of accounts and records for the purpose of determining the amounts payable to AcelRx pursuant to this Agreement. Such books and records shall be kept for such period of time required by law, but no less than at least **[*]** following the end of the Calendar Quarter to which they pertain. Such records shall be subject to inspection in accordance with Section 8.5.

8.5 Audits. Upon not less than **[*]** prior written notice, Grünenthal shall permit an independent, certified public accountant selected by AcelRx and reasonably acceptable to Grünenthal, which acceptance will not be unreasonably withheld or delayed (for the purposes of this Section 8.5, the " ***Auditor***"), to audit or inspect those books or records of Grünenthal, its Affiliates and Sublicensees that relate to Net Sales and Royalty Reports for the sole purpose of verifying (a) the royalties payable hereunder in respect of Net Sales, (b) the withholding taxes, if any, required by Applicable Law to be deducted as a payment by Grünenthal in respect of such Net Sales and (c) the exchange rates used in determining the amount of United States dollars. The Auditor shall disclose to AcelRx only the amount and accuracy of payments reported and actually paid or otherwise payable under this Agreement. The Auditor shall send a copy of the report to Grünenthal at the same time it is sent to AcelRx. Such inspections may be made no more than once each Calendar Year and during normal business hours. Such records for any particular Calendar Quarter shall be subject to no more than one inspection. Inspections conducted under this Section 8.5 shall be at the expense of AcelRx, unless a variation or error producing an underpayment in amounts payable exceeding an amount equal to **[*]** for a period covered by the inspection is established, in which case all reasonable costs relating to the inspection for such period and any unpaid amounts that are discovered shall be paid by Grünenthal. AcelRx shall endeavor in such inspection not to disrupt the normal business activities of Grünenthal, or its Affiliates or Sublicensees. Promptly after receiving the audit report, Grünenthal shall submit to AcelRx any underpayment discovered in such audit, together with interest accrued in accordance with Section 8.7.

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8.6 Financial Reporting Cooperation. In the event that Grünenthal and/or any of its Affiliates determine, based on its analysis and subsequent discussions with their auditors, that Grünenthal or any one of its Affiliate is required to consolidate AcelRx under Grünenthal's Accounting Standards, AcelRx shall, for so long as Grünenthal or its Affiliate is required to so consolidate, collaborate in good faith with Grünenthal and its Affiliate to provide information as reasonably necessary under such consolidation requirement, provided that in no event shall any such other accommodation restrict AcelRx's ability to conduct its operations in the normal course of business and provided further that Grünenthal shall engage in good faith negotiations with its auditors to exempt and waive compliance with such requirement.

8.7 Late Payment. Any amounts not paid within **[*]** after the date due under this Agreement shall be subject to interest from the foregoing date through and including the date upon which payment is received, calculated at the interest rate equal to three percentage points (3%) over the rate of interest according to the average six-month rate(s) of the London Inter-Bank Offering Rate (**"LIBOR"**) for U.S. dollars, as quoted on the British Banker's Association's website currently located at www.bba.org.uk (or such other source as may be mutually agreed by the Parties) from time to time, effective for the applicable days of the period of default, on the last business day of the applicable Calendar Quarter prior to the date on which such payment is due, calculated daily on the basis of a 365-day year, or, if lower, the highest rate permitted under Applicable Law.

ARTICLE 9

CONFIDENTIALITY

9.1 Confidential Information. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that the receiving Party (the "***Receiving Party***") shall keep confidential and shall not publish or otherwise disclose or use for any purpose other than as provided for in this Agreement any confidential or proprietary information and materials, patentable or otherwise, in any form (written, oral, photographic, electronic, visual or otherwise) which is disclosed to it by the other Party (the " ***Disclosing Party***") including, but not limited to, all information concerning the Device and/or the Licensed Product, information disclosed by one Party to the other pursuant to the Confidentiality Agreement and any other technical or business information of whatever nature (collectively, "***Confidential Information***").

9.2 Exceptions. Notwithstanding Section 9.1 above, the obligations of confidentiality and non-use shall not apply to Confidential Information that, in each case as demonstrated by competent evidence:

(a) was already known to the Receiving Party or any of its Affiliates, other than under an obligation of confidentiality, at the time of disclosure;

(b) was generally available to the public or was otherwise part of the public domain at the time of its disclosure to the Receiving Party;

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(c) became generally available to the public or otherwise part of the public domain after its disclosure by the Disclosing Party and other than through any act or omission of the Receiving Party or any of its Affiliates in breach of this Agreement;

(d) was subsequently lawfully disclosed to the Receiving Party or any of its Affiliates by a Person other than the Disclosing Party, and who, to the best knowledge of the Receiving Party, did not directly or indirectly receive such information directly or indirectly from the Disclosing Party under an obligation of confidence; or

(e) was developed by the Receiving Party or its Affiliate without use of or reference to any proprietary information or materials disclosed by the Disclosing Party.

9.3 Permitted Disclosures. Notwithstanding the provisions of Section 9.1, each Party may disclose Confidential Information belonging to the other Party as expressly permitted by this Agreement or if and to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting Patents as permitted by this Agreement;

(b) prosecuting or defending litigation in the Territory as permitted by this Agreement;

(c) complying with applicable court orders or governmental regulations; and

(d) disclosure to Third Parties in connection with a potential license to, distribution agreement with or collaboration with such Third Party (including entry into any such agreement), or a potential merger or acquisition by such Third Party, and disclosure to potential Third Party investors in connection with a potential financing, provided, in each case, that any such Third Party agrees to be bound by similar terms of confidentiality and non-use at least as stringent as those set forth in this Article 9.

Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to Section 9.3(b) or (c), it shall, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use efforts to secure confidential treatment of such information at least as diligent as such Party would use to protect its own confidential information, but in no event less than reasonable efforts; *provided* that any Confidential Information so disclosed shall still be subject to the restrictions on use set forth in this Article 9. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information hereunder.

9.4 Confidentiality of this Agreement and its Terms. Except as otherwise provided in this Article 9, each Party agrees not to disclose to any Third Party the existence of this Agreement or the terms of this Agreement without the prior written consent of the other Party hereto, except that each Party may disclose the terms of this Agreement that are not otherwise made public as contemplated by Section 9.5 and as permitted under Section 9.3.

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9.5 Public Announcements.

(a) As soon as practicable following the Effective Date hereof, the Parties shall each issue a mutually agreed to press release announcing the existence of this Agreement substantially in the applicable form attached hereto as ***Exhibit* 9.5(a)** Except as required by law (including disclosure requirements of the U.S. Securities and Exchange Commission ("***SEC***"), the NASDAQ stock market or any other stock exchange on which securities issued by a Party or its Affiliates are traded), neither Party shall make any other public announcement concerning this Agreement or the subject matter hereof without the prior written consent of the other, which shall not be unreasonably withheld or delayed; *provided* that it shall not be unreasonable for a Party to withhold consent with respect to any public announcement containing any of such Party's Confidential Information. In the event of a required public announcement, to the extent practicable under the circumstances, the Party making such announcement shall provide the other Party with a copy of the proposed text of such announcement sufficiently in advance of the scheduled release to afford such other Party a reasonable opportunity to review and comment upon the proposed text.

(b) The Parties shall coordinate in advance with each other in connection with the filing of this Agreement (including redaction of certain provisions of this Agreement) with the SEC, the NASDAQ stock market or any other stock exchange or governmental agency on which securities issued by a Party or its Affiliate are traded, and each Party shall use reasonable efforts to seek confidential treatment for the terms proposed to be redacted; *provided* that each Party shall ultimately retain control over what information to disclose to the SEC, the NASDAQ stock exchange or any other stock exchange or governmental agency, as the case may be, and *provided further* that the Parties shall use their reasonable efforts to file redacted versions with any governing bodies which are consistent with redacted versions previously filed with any other governing bodies. Other than such obligation, neither Party (nor its Affiliates) shall be obligated to consult with or obtain approval from the other Party with respect to any filings to the SEC, the NASDAQ stock market or any other stock exchange or governmental agency.

9.6 Publication of the Licensed Product Information. Publication of any non-public scientific or technical information with respect to the Licensed Product shall be subject to prior review as follows: (a) at least thirty (30) days prior to submission of an original manuscript for publication, (b) at least seven (7) days prior to abstract submission for poster or podium presentation, or (c) at least seven (7) days prior to an oral or poster presentation, as the case may be, each Party shall provide to the other Party a draft copy thereof for such other Party's review (unless such Party is required by law to publish such information sooner, in which case such Party shall provide such draft copy to the other Party as much in advance of such publication as possible). The publishing Party shall consider in good faith any comments provided by the other Party during such time period. In addition, the publishing Party shall, at the other Party's reasonable request, remove therefrom any Confidential Information of such other Party.

9.7 Prior Non-Disclosure Agreements. As of the Effective Date, the terms of this Article 9 shall supersede any prior non-disclosure, secrecy or confidentiality agreement between the Parties (or their Affiliates) dealing with the subject of this Agreement, including the Confidentiality Agreement. Any information disclosed under such prior agreements shall be deemed disclosed under this Agreement.

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ARTICLE 10

PATENT PROSECUTION AND ENFORCEMENT

10.1 Ownership of Intellectual Property. Inventorship shall be determined in accordance with Applicable Law. Ownership of intellectual property shall be as follows:

(a) **Retained Rights.** Subject to Section 10.1(b), AcelRx has, and shall retain all right, title and interest in and to, the AcelRx Technology. Grünenthal has, and shall retain all right, title and interest in and to, the Grünenthal Background IP and Grünenthal Know-How.

(b) **Assignment of Assigned Patents.** Within thirty (30) days following the Effective Date, AcelRx shall execute such documents and perform such acts, at Grünenthal's expense, as may be reasonably necessary to effect an assignment of AcelRx's entire right, title, and interest in and to the Assigned Patents in the Territory to Grünenthal.

(c) **Assignment of Assigned Trademarks.** Within thirty (30) days following the payment of R&D Milestone [*] set forth in Section 7.2 (i.e., [*]) and within thirty (30) days following Marketing Approval for the Licensed Product in any other country of the Territory, AcelRx shall execute such documents and perform such acts, at Grünenthal's expense, as may be reasonably necessary to (i) in the case of the MAA Approval, effect an assignment to Grünenthal of AcelRx's entire right, title, and interest in and to the Assigned Trademarks in the EU and (ii) in the case of another Marketing Approval, effect an assignment to Grünenthal of AcelRx's entire right, title, and interest in and to the relevant Assigned Trademark, solely in such country in the Territory in which the Marketing Approval was obtained.

(d) **Disclosure of Inventions.** Grünenthal shall notify AcelRx in writing of any and all Inventions, generated by, resulting from or reduced to practice by or on behalf of Grünenthal, promptly after each such Invention is made or generated.

(e) **Joint Inventions.**

(i) **Joint Inventions in the Territory.** Subject to the license grants set forth in Section 2.1(a), Section 2.1(c) and Section 2.1(d), each Party can use, and grant licenses to use, any Joint Invention, Joint Patent or Joint Know-How in the Territory without the other Party's consent and has no duty to account to the other Party for such use or license, and each Party hereby waives any right it may have under the laws of any country to require any such consent or accounting .

(ii) **Joint Inventions outside the Territory.** Grünenthal hereby assigns to AcelRx its entire right, title and interest in and to any Joint Invention, Joint Patent or Joint Know-How developed during the Term for use outside the Territory.

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(f) **No Implied License.** It is agreed that neither Grünenthal nor AcelRx transfers to the other by operation of this Agreement any patent right, copyright, trademark right, or other proprietary right of any party, except as expressly set forth herein.

10.2 Patent Prosecution and Maintenance.

(a) **Initial Responsibility.** AcelRx shall be responsible for the preparation, filing, prosecution and maintenance of all AcelRx Patents and Joint Patents, at AcelRx's sole expense, using counsel of its choice which are reasonably acceptable to Grünenthal. Grünenthal shall be responsible for the preparation, filing, prosecution and maintenance of all Assigned Patents and Grünenthal Patents, at Grünenthal's sole expense, using counsel of its choice which are reasonably acceptable to AcelRx. Each Party shall keep the other Party fully and promptly informed of progress with regard to the preparation, filing, prosecution and maintenance of the each of the Patents for which it has responsibility as provided under this Section 10.2(a) AcelRx shall consider and adopt in good faith the requests and suggestions of Grünenthal with respect to strategies for filing and prosecuting AcelRx Patents in the Territory. Further, AcelRx shall notify Grünenthal without undue delay of any patent applications that are specific to the Licensed Product and the Parties shall discuss in good faith assignment of such patent applications to Grünenthal for the Territory. Upon assignment such patent applications shall become "Assigned Patents". Grünenthal shall consider and adopt in good faith the requests and suggestions of AcelRx with respect to strategies for filing and prosecuting Assigned Patents in the Territory.

(b) **Option of Grünenthal to Prosecute, Maintain and Enforce.** In the event that AcelRx desires to abandon or cease prosecution and maintenance of any AcelRx Patent or Joint Patent in the Territory, AcelRx shall provide reasonable prior written notice to Grünenthal of such intention to abandon (which notice shall, to the extent practicable, be given no later than 60 calendar days prior to the next deadline for any action that must be taken with respect to any such AcelRx Patent and Joint Patent in the relevant patent office). In such case, at Grünenthal's sole discretion, upon written notice from Grünenthal, Grünenthal may elect to continue prosecution and maintenance of any such AcelRx Patent or Joint Patent at its own expense **,** and AcelRx shall execute such documents and perform such acts, at Grünenthal's expense, as may be reasonably necessary to effect an assignment of AcelRx's entire right, title, and interest in and to such AcelRx Patents and/or Joint Patents in the Territory to Grünenthal. Any such assignment shall be completed in a timely manner to allow Grünenthal to continue prosecution and maintenance of any such AcelRx Patent and Joint Patent in the Territory. Any AcelRx Patents and Joint Patent with respect to which Grünenthal so elects to continue prosecution and maintenance of shall no longer be considered AcelRx Patents and Joint Patents under this Agreement with respect to which royalties are to be paid under this Agreement and shall be solely owned by Grünenthal without further obligation or accounting to AcelRx.

(c) **Option of AcelRx to Prosecute, Maintain and Enforce.** In the event that Grünenthal desires to abandon or cease prosecution and maintenance of any Assigned Patent, Grünenthal shall provide reasonable prior written notice to AcelRx of such intention to abandon (which notice shall, to the extent practicable, be given no later than 60 calendar days prior to the next deadline for any action that must be taken with respect to any such Assigned

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Patent in the relevant patent office). In such case, at AcelRx's sole discretion, upon written notice from AcelRx, AcelRx may elect to continue prosecution and maintenance of any such Assigned Patent at its own expense, and Grünenthal shall execute such documents and perform such acts, at AcelRx's expense, as may be reasonably necessary to effect an assignment of Grünenthal's entire right, title, and interest in and to such Assigned Patents in the Territory to AcelRx. Any such assignment shall be completed in a timely manner to allow AcelRx to continue prosecution and maintenance of any such Assigned Patent in the Territory. Any Assigned Patent with respect to which AcelRx so elects to continue prosecution and maintenance of shall no longer be considered Assigned Patents under this Agreement.

10.3 Infringement by Third Parties.

(a) **Notice.** In the event that either AcelRx or Grünenthal becomes aware of any infringement or threatened infringement by a Third Party of any AcelRx Patents, Joint Patents and/or Assigned Patents it will notify the other Party in writing to that effect. Any such notice shall include evidence to support an allegation of infringement or threatened infringement by such Third Party.

(b) **Defense of Patents.** Subject to this Section 10.3(b), AcelRx shall have the first right, as between AcelRx and Grünenthal, to bring and control any action or proceeding with respect to infringement of any AcelRx Patent and Joint Patent in the Territory, at its own expense and by counsel of its own choice and Grünenthal shall have the first right, as between AcelRx and Grünenthal, to bring and control any action or proceeding with respect to infringement of any Assigned Patent, at its own expense and by counsel of its own choice. The respective other Party shall have the right, at its own expense, to be represented in the Territory in any such action by counsel of its own choice, and the controlling Party and its counsel shall reasonably cooperate with the other Party and its counsel in strategizing, preparing and presenting any such action or proceeding in the Territory. If the Party having first right as set forth above fails to bring an action or proceeding with respect to infringement of any Patent in the Territory described in the preceding sentences within (i) ninety (90) days following the notice of alleged infringement or (ii) thirty (30) days before the time limit, if any, set forth in the appropriate laws and regulations for the filing of such actions, whichever comes first, the other Party shall have the right, but not the obligation (i.e., it has the right to indulge such infringement), to bring and control any such action in the Territory at its own expense and by counsel of its own choice. Upon the other Party's request, the Party having first right as set forth above shall timely join as party-plaintiff in any such litigation and to cooperate with the other Party in connection with such infringement action, including timely filing such action in the name of the Party having first right as set forth above if required. The requesting Party shall reimburse the other Party for its reasonable costs and expenses related to such explicitly requested activities. Except as otherwise agreed to by the Parties as part of a separate cost-sharing arrangement, any recovery or damages realized as a result of such action or proceeding shall be used first to reimburse the Parties' documented out-of-pocket legal expenses relating to the action or proceeding, and any remaining damages relating to the Licensed Product (including lost sales or lost profits with respect to the Licensed Product) shall be (a) shared 70%/30% for

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Grünenthal/AcelRx, respectively, in case AcelRx is the Party bringing suit; or (b) treated as Net Sales and subject to the payment obligations of Article 7, if Grünenthal is the Party bringing suit.

10.4 Infringement of Third Party Rights. Each Party shall promptly notify the other in writing of any allegation by a Third Party that the activity of either of the Parties pursuant to this Agreement infringes or may infringe the intellectual property rights of such Third Party in the Territory.

(a) AcelRx shall, at its own expense and by counsel of its own choice, have the sole right to control any defense of, and shall be solely responsible for, any and all such claims involving alleged infringement of Third Party rights in the Territory by any of (i) AcelRx's activities, (ii) the Manufacture of the Licensed Products by, on behalf of or under license from AcelRx, (iii) sale of Licensed Products by AcelRx to any licensee of AcelRx including Grünenthal, and/or (iv) the importation for, sale or offering for sale of such Licensed Products as supplied by AcelRx. Grünenthal shall have the right, at its own expense, to be represented in any such action by counsel of its own choice.

(b) To the extent not covered by Section 10.4(a), Grünenthal shall, at its own expense and by counsel of its own choice, have the sole right to control any defense of, and shall be solely responsible for, any and all such claims involving alleged infringement of Third Party rights in the Territory by Grünenthal's activities. AcelRx shall have the right, at its own expense, to be represented in any such action by counsel of its own choice.

10.5 Consent for Settlement. Neither Party shall enter into any settlement or compromise of any action or proceeding under this Article 10 which would materially alter, diminish, or be in derogation of the other Party's rights under this Agreement without the prior written consent of such other Party, which consent shall not be unreasonably withheld.

10.6 Patent Term Extensions. AcelRx shall have the right to file any Patent Term Extensions for AcelRx Patents and Joint Patents in the Territory, and AcelRx shall act with reasonable promptness in light of the development stage of the Licensed Product to apply for any such Patent Term Extensions, where it is agreed upon between the Parties. Grünenthal shall cooperate fully with AcelRx in making such filings or actions, for example and without limitation, making available all required regulatory data and information and executing any required authorizations to apply for such Patent Term Extension. Grünenthal shall have the right to file any Patent Term Extensions for Assigned Patents in the Territory. All expenses incurred in connection with activities of each Party pursuant to this Section 10.6 shall be entirely borne by such Party.

10.7 Trademarks: General. The Licensed Product shall be sold in each country of the Territory under the AcelRx Trademark "Zalviso" unless such AcelRx Trademark is determined to be unacceptable to the respective competent Regulatory Authority for the country/countries of the Territory concerned, in which event AcelRx and Grünenthal will agree on another AcelRx Trademark (the "***Alternative AcelRx Trademark***"). If all AcelRx Trademarks are determined to be unacceptable to the respective competent Regulatory Authority in the Territory, then Grünenthal shall have the right to select a trademark owned by Grünenthal

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(the "***Grünenthal Trademark***") for use with the Licensed Product in the Territory. Upon request of AcelRx, the Parties shall discuss whether Grünenthal may grant license rights under the Grünenthal Trademark to commercialize, sell, offer for sale the Licensed Product outside the Territory and under what terms. Grünenthal shall own the Assigned Trademark(s) in the relevant countries in the Territory, subject to prosecution and maintenance of such AcelRx Trademark with AcelRx's consent, which consent shall not be unreasonably withheld, and subject to Sections 14.2, 14.3, 14.4 and 14.5, as applicable. AcelRx shall provide all reasonable assistance required by Grünenthal in connection therewith. AcelRx will have the right to use the AcelRx Trademarks used with the Licensed Product in connection with the supply of Licensed Product to Grünenthal. Grünenthal shall not use the Assigned Trademark(s) or the Grünenthal Trademark in connection with (i) the using, promotion, marketing, importing, distributing, selling or offering for sale of any product other than the Licensed Product nor (ii) in connection with the using, promotion, marketing, importing, distributing, selling or offering for sale of any product outside the Territory. The Assigned Trademarks shall be used in accordance with the quality guidelines of AcelRx to ensure that the use of such Assigned Trademarks in the Territory are maintained in a manner consistent with the quality standards of AcelRx applicable outside of the Territory.

10.8 Trademark Enforcement. The Party that owns (the "**Trademark Owner**") the applicable Trademark (whether AcelRx Trademarks, Assigned Trademarks or Grünenthal Trademarks), shall have the right to take appropriate steps to protect its Trademark from all harmful or wrongful activities of Third Parties in the Territory. The steps the Trademark Owner may take include, but are not limited to, the filing and prosecution of: (a) litigation against infringement or unfair competition by Third Parties; (b) opposition proceedings against applications for trademark or service mark registration for marks that are confusingly similar to any one or more of such Trademarks; (c) cancellation proceedings against registration of marks that are confusingly similar to any one or more of such Trademarks; and (d) other appropriate administrative actions. The Trademark Owner shall have the right to include the other Party, at the Trademark Owner's cost, in such litigation, opposition, cancellation or other proceedings when necessary or appropriate. Such other Party shall cooperate with the Trademark Owner in any such proceeding by providing oral testimony and documentary and other relevant evidence at reasonable cost to the Trademark Owner. Any amounts obtained in connection with any such proceeding (whether awarded by a court, received in settlement or otherwise) shall be paid to the Trademark Owner. If the Trademark Owner and the other Party mutually agree to jointly participate in any litigation or other proceeding with respect to such any Trademark, their respective responsibilities, contributions to the costs and their participation in any recoveries will be agreed upon in writing before undertaking such action. If the other Party desires to file litigation or other proceeding against a Third Party, and the Trademark Owner declines to commence such litigation or proceeding, the other Party shall be entitled to commence and prosecute the litigation or proceeding at its own expense, and shall be entitled to all monetary damages and other benefits received as a result, and in such event, at the other Party's expense, the Trademark Owner shall cooperate with such other Party in the prosecution of such litigation or proceeding.

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10.9 Trademarks: Defense of Claims of Infringement. The Trademark Owner shall at its cost defend claims that the use of its Trademarks in the Territory infringes the rights of a Third Party, and indemnify and hold the other Party harmless with respect to any such claims (except to the extent that such claims are indemnified by such other Party under Article 12, or relate to a breach of representation or warranty made by such other Party under Article 11). Such other Party shall have the right to participate in such defense at its own expense to protect its rights under this Agreement relating to such Trademarks. If such other Party is named as a party to such a claim and the Trademark Owner is not so named, such other Party shall tender such defense to the Trademark Owner and the Trademark Owner shall defend such action at its expense.

10.10 Trademark Settlements. The Trademark Owner shall be authorized to enter into an agreement, consent order or other resolution of any claim by or against such a Third Party with respect to its Trademarks, provided however that with regard to the Assigned Trademark only after consulting with the other Party, such consent not to be unreasonably withheld. In no event shall such other Party be authorized to enter into any agreement, consent order or other resolution of any claim by or against such a Third Party with respect to such Assigned Trademarks without the other Party's prior written approval, which approval shall not be unreasonably withheld or delayed.

ARTICLE 11

REPRESENTATIONS, WARRANTIES AND COVENANTS

11.1 Mutual Representations, Warranties and Covenants. Each Party hereby represents and warrants to the other Party, as of the Effective Date, as follows:

(a) **Duly Organized.** Such Party is a corporation with restricted liability, duly organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification and failure to have such would prevent such Party from performing its obligations under this Agreement.

(b) **Due Authorization;** Binding Agreement. The execution, delivery and performance of this Agreement by such Party have been duly authorized by all necessary corporate or organizational action. This Agreement is a legal and valid obligation binding on such Party and enforceable in accordance with its terms and does not (i) to such Party's knowledge and belief, violate any law, rule, regulation, order, writ, judgment, decree, determination or award of any court, governmental body or administrative or other agency having jurisdiction over such Party or (ii) conflict with, or constitute a default under, any agreement, instrument or understanding, oral or written, to which such Party is a party or by which it is bound.

(c) **Consents.** Such Party has obtained, or is not required to obtain, the consent, approval, order or authorization of any Third Party, or has completed, or is not required

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to complete any registration, qualification, designation, declaration, or filing with, any Regulatory Authority or governmental authority, in connection with the execution and delivery of this Agreement and the performance by such Party of its obligations under this Agreement.

11.2 Representations, Warranties and Covenants of AcelRx. As used in this Section 11.2, "Best Knowledge" shall mean, as applied to AcelRx, that any of AcelRx's executive officers knows of a particular fact or other matter. AcelRx represents and warrants to Grünenthal that as of the Effective Date:

(a) **Right to Grant License.** (i) AcelRx owns all right, title and interest in and to, or has a license, sublicense or otherwise permission to use and license, all of the AcelRx Technology free and clear of all encumbrances; (ii) AcelRx has not previously assigned, transferred, conveyed or otherwise encumbered or granted, and will not during the Term assign, transfer, convey or otherwise encumber its right, title and interest in any of the AcelRx Technology or any rights granted to Grünenthal hereunder for the development or commercialization of the Licensed Product in the Field in the Territory; (iii) specifically, there are no existing agreements, options, commitments, or rights, with, of or to any person to acquire or obtain any rights to, any of the AcelRx Technology for the development or commercialization of the Licensed Product in the Field in the Territory and (iv) no royalties, license fees or other payments are required to be paid to any Third Party in connection with the execution, delivery and performance of this Agreement, or in connection with the research, development, importation, use, sale, and offer for sale of the Device or the Licensed Product.

(b) **Scope of License.** ***Exhibit 1.7*** and ***Exhibit 1.9*** set forth true and complete lists of all AcelRx Patents and Trademarks included in AcelRx Trademarks and AcelRx Copyrights Controlled by AcelRx or its Affiliates as of the Effective Date. ***Exhibit 1.7*** and ***Exhibit 1.9*** also indicate the current status, date and country of filing and issuance. The AcelRx Patents and AcelRx Know-How constitute all intellectual property Controlled by AcelRx and its Affiliates that is necessary or reasonably useful for the research, development, importation, use, sale and offer for sale of the Licensed Product(s) in the Field in the Territory and to the Best Knowledge of AcelRx there is not any other Patent necessary for such purposes that is not Controlled by AcelRx (including any intellectual property Controlled by any Third Party supplier of the Device, Drug or the Licensed Product). All official fees, maintenance fees and annuities for the AcelRx Patents, AcelRx Trademarks and AcelRx Copyrights have been paid through the Effective Date.

(c) **Patent Status and Trademark Status.** To AcelRx's Best Knowledge (i) all issued Patents listed on ***Exhibit 1.7*** are in full force and effect, valid, subsisting and enforceable, and inventorship of each Patent is properly identified on such Patents; (ii) none of the Patents listed on ***Exhibit 1.7*** is currently involved in any interference, reissue, reexamination, or opposition proceeding and (iii) neither AcelRx nor any of its Affiliates has received any written notice from any person, or has knowledge, of such actual or threatened proceeding and (bb) AcelRx has filed all trademark applications for the Trademark "Zalviso" and at least two alternative AcelRx Trademarks in all countries of the Territory. To AcelRx Best Knowledge none of the AcelRx Trademarks is subject to any opposition proceeding

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(d) **Non-Infringement by Third Parties.** to AcelRx's Best Knowledge, there are no activities by Third Parties that would constitute infringement of the AcelRx Patents or misappropriation of the AcelRx Know-How.

(e) **Non-Infringement of Third Party Rights.** the commercialization, Manufacture, use, sale or importation of the Device or the Licensed Product(s) in the Field in the Territory does not infringe or misappropriate any Patent or other intellectual property Controlled by a Third Party. Neither AcelRx nor any of its Affiliates has received any written notice from any Person, or has knowledge of, any actual or threatened claim or assertion that the use or practice of the AcelRx Patents or AcelRx Know-How infringes or misappropriates the intellectual property rights of a Third Party.

(f) **Non-Action or Claim.** to AcelRx's Best Knowledge, there are no actual, pending, alleged or threatened adverse actions, suits, claims, interferences or formal governmental investigations (i) involving the Device or the Licensed Product, including in connection with the conduct of any clinical trials or manufacturing activities, or (ii) questioning the validity of this Agreement or any action taken by AcelRx in connection with the execution of this Agreement, in each case, by or against AcelRx or any of its Affiliates in or before any court, Regulatory Authority or other governmental authority. There are no material unsatisfied judgments or outstanding orders, injunctions, decrees, stipulations or awards (whether rendered by a court, an administrative agency or an arbitrator) against AcelRx with respect to any AcelRx Technology, the Device or the Licensed Product.

(g) **Employee Agreements.** to AcelRx's Best Knowledge, all current and former employees and consultants of AcelRx and its Affiliates who are or have been substantively involved in the design, review, evaluation or development of the AcelRx Know-How or AcelRx Patents have executed written contracts or are otherwise obligated to protect the confidential status and value thereof and to vest in AcelRx or its Affiliates exclusive ownership of the AcelRx Know-How or AcelRx Patents.

(h) **Additional Legal Compliance.**

(i) to AcelRx's Best Knowledge, AcelRx and its Affiliates and any outsourcing company and contract research organization to which AcelRx or its Affiliates have subcontracted activities in connection with Device and the Licensed Product (the " ***Contractors***") have complied with all Applicable Laws, permits, governmental licenses, registrations, approvals, concessions, franchises, authorizations, orders, injunctions and decrees in the research, development, Manufacture and use of the Licensed Product and Device, and neither AcelRx nor any of its Affiliates or its Contractors has received any written notice from any governmental authority claiming that any such activities as conducted by them are not in such compliance.

(ii) no governmental authority (including the FDA) has commenced or, to AcelRx's Best Knowledge, threatened to initiate any action to enjoin production of the Device or the Licensed Product at any facility, nor has AcelRx or any of its Affiliates or, to the Best Knowledge of AcelRx, any of its Contractors, received any notice to such effect.

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(iii) all development activities conducted by AcelRx and its Affiliates and Contractors relating to the Licensed Product and/or Device have been conducted in compliance with all Applicable Laws, including all GCPs, GLPs and GMPs when applicable.

(iv) to AcelRx's Best Knowledge, no employee or agent of AcelRx or any of its Affiliates or Contractors has made an untrue statement of a material fact to any governmental authority with respect to the Licensed Product and/or Device (whether in any Regulatory Filings or otherwise), or failed to disclose a material fact to any governmental authority required to be disclosed with respect to the Licensed Product and/or Device.

(v) To AcelRx's Best Knowledge, AcelRx has disclosed or otherwise provided Grünenthal with all information that would have, or would be reasonably likely to have, a material effect on the ability of Grünenthal to develop or commercialize the Licensed Product in the Field in the Territory under the terms and conditions of this Agreement and that relates to (A) the AcelRx Technology, (B) any Third Party intellectual property rights or claims that relate to the commercialization or development of the Licensed Product in the Territory, and (C) the safety or efficacy of the Device or the Licensed Product.

(i) **Debarment.** AcelRx is not debarred under the United States Federal Food, Drug and Cosmetic Act and it does not, and will not during the Term, employ or use the services of any Person who is debarred, in connection with the development, Manufacture or commercialization of the Device or the Licensed Product(s). In the event that AcelRx becomes aware of the debarment or threatened debarment of any Person providing services to AcelRx, including the Party itself and its Affiliates, Contractors, licensees or Sublicensees, which directly or indirectly relate to activities under this Agreement, Grünenthal shall be immediately notified in writing.

(j) **Material Agreements.** To AcelRx's Best Knowledge, AcelRx is not in breach or default of any material agreement with a Third Party that is necessary or reasonably useful for the Manufacture, use, sale or importation of the Device and the Licensed Product(s) in the Field in the Territory (the "***Material Agreements***") and will use its Commercially Reasonable Efforts to keep such Material Agreements in full force for the Term of this Agreement and in accordance with Section 14.5. AcelRx has not waived or allowed to lapse or terminate any of its rights under such Material Agreements.

(k) **Disclaimer.** EXCEPT AS EXPRESSLY SET FORTH IN THIS AGREEMENT, OR ANY OTHER AGREEMENT CONTEMPLATED HEREUNDER, NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, AND EACH PARTY EXPRESSLY DISCLAIMS ALL IMPLIED WARRANTIES OF MERCHANTABILITY AND OF FITNESS FOR A PARTICULAR PURPOSE OR USE, NON-INFRINGEMENT, VALIDITY AND ENFORCEABILITY OF PATENTS, OR THE PROSPECTS OR LIKELIHOOD OF DEVELOPMENT OR COMMERCIAL SUCCESS OF THE PRODUCT.

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ARTICLE 12

INDEMNIFICATION

12.1 Indemnification of AcelRx. Grünenthal shall indemnify and hold harmless each of AcelRx and its Affiliates, and the directors, officers, shareholders and employees of such entities and the successors and assigns of any of the foregoing (the " ***AcelRx Indemnitees***"), from and against any and all losses, liabilities, damages, penalties, fines, costs and expenses (including reasonable attorneys' fees and other costs and expenses of litigation and settlements) ("***Losses***") from any claims, actions, suits or proceedings brought by a Third Party (a " ***Third Party Claim***") incurred by any AcelRx Indemnitee, arising from, or occurring as a result of (a) gross negligence or willful misconduct of Grünenthal, its Affiliates, Sublicensees, Distributors or other subcontractors; (b) the research, development and regulatory activities relating to the Licensed Product conducted by or on behalf of Grünenthal, its Affiliates or Sublicensees (other than AcelRx and its Affiliates and licensees); and (c) any material breach of any representations, warranties or covenants by Grünenthal under this Agreement or the Supply Agreement; except to the extent such Third Party Claims fall within the scope of the indemnification obligations of AcelRx set forth in Section 12.2.

12.2 Indemnification of Grünenthal. AcelRx shall indemnify and hold harmless each of Grünenthal and its Affiliates and the directors, officers, shareholders, employees and agents of such entities and the successors and assigns of any of the foregoing (the " ***Grünenthal Indemnitees***"), from and against any and all Losses from any Third Party Claims incurred by any Grünenthal Indemnitee, arising from, or occurring as a result of (a) gross negligence or willful misconduct of AcelRx, its Affiliates and or its subcontractors; (b) the research, development and regulatory activities, Manufacture, supply relating to the Licensed Product conducted by or on behalf of AcelRx, its Affiliates or Sublicensees (other than Grünenthal and its Affiliates and Sublicensees); and (c) any material breach of any representations, warranties or covenants by AcelRx under this Agreement or the Supply Agreement, except to the extent such Third Party Claims fall within the scope of the indemnification obligations of Grünenthal set forth in Section 12.1.

12.3 Procedure. A Party that intends to claim indemnification under this Article 12 or under Section 7.3(b)(i)(B) shall promptly notify the indemnifying Party in writing of any Third Party Claim, in respect of which the Indemnitee intends to claim such indemnification. The Indemnified Party shall provide the Indemnifying Party with reasonable assistance, at the Indemnifying Party's expense, in connection with the defense of the Third Party Claim for which indemnity is being sought. The Indemnitee may participate in and monitor such defense with counsel of its own choosing at its sole expense; provided, however, the Indemnitor shall have the right to assume and conduct the defense of the Third Party Claim with counsel of its choice. The Indemnitor shall not settle any Third Party Claim without the prior written consent of the Indemnified Party, not to be unreasonably withheld, unless the settlement involves only the payment of money. So long as the Indemnitor is actively defending the Claim in good faith, the Indemnitee shall not settle any such Third Party Claim without the prior written consent of the Indemnifying Party. If the Indemnitor does not assume and conduct the defense of the Third Party Claim as provided above, (a) the Indemnitee may defend against, and consent to the entry of any judgment or enter into any settlement with respect to the Third

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Party Claim in any manner the Indemnitee may deem reasonably appropriate (and the Indemnitee need not consult with, or obtain any consent from, the Indemnitor in connection therewith), and (b) the Indemnitor will remain responsible to indemnify the Indemnitee as provided in this Article 12. The failure to deliver written notice to the Indemnitor within a reasonable time after the commencement of any action with respect to a Third Party Claim shall only relieve the Indemnitor of its indemnification obligations under this Article 12 or under Section 7.3(b)(i)(B) if and to the extent the Indemnitor is actually prejudiced thereby.

12.4 Insurance. Each Party, at its own expense, shall maintain product liability and other appropriate insurance with an insurance carrier in an amount consistent with industry standards, for a company in a similar position to such Party, during the Term, which shall include, but not be limited to, (i) product liability insurance, which may include a self-insured retention, and (ii) general liability insurance in the minimum amount of $2 million in the aggregate and $10 million umbrella coverage, which may include a self-insured retention. Each Party shall provide a certificate of insurance or other reasonably satisfactory documentation evidencing such coverage to the other Party upon request. It is understood that such insurance shall not be construed to create a limit of either Party's liability with respect to its indemnification obligations under this Article 12 or under Section 7.3(b)(i)(B).

12.5 Set-Off. If and to the extent either Party is in material breach of this Agreement or the Supply Agreement for which notification has been provided and such Party fails to pay, reimburse, or credit the other Party for any amount owed when due under this Agreement or the Supply Agreement, whether under this Article 12 or under Section 7.3(b)(i)(B) or otherwise due under or in connection with this Agreement or the Supply Agreement, then the Party to whom such amount is owed may, at its election, without notice of its election and without demand, charge and setoff such amount against amounts otherwise due from it or its related entities to the other Party, including under this Agreement or the Supply Agreement, and the owing Party hereby authorizes all such charges and setoffs until such time as the material breach has been cured in accordance with the terms of this Agreement.

ARTICLE 13

Term and Termination

13.1 Term. This Agreement shall commence on the Effective Date, and unless terminated earlier as provided in this Article 13 or 2.8, shall continue in full force and effect on a country-by-country basis until the later of (i) expiration of the Royalty Term, and (ii) expiration of Grünenthal's obligation to pay the Trademark and Supply Fee to AcelRx as described in Section 7.4 (the "***Term***").

13.2 Early Termination. Each Party shall have the right to terminate this Agreement before the end of the Term:

(a) in its entirety or on a country-by-country basis by mutual written agreement of the Parties;

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(b) with regard to the country/countries concerned upon written notice by either Party if the other Party is in material breach of this Agreement and has not cured such breach within ninety (90) days (30 days with respect to any payment breach) after notice from the terminating Party requesting cure of the breach. Any such termination shall become effective at the end of such ninety (90) day (30 day with respect to any payment breach) period unless the breaching Party has cured any such breach or default prior to the end of such period;

(c) in its entirety upon the bankruptcy or insolvency of, or the filing of an action to commence insolvency proceedings against the other Party, or the making or seeking to make or arrange an assignment for the benefit of creditors of the other Party, or the initiation of proceedings in voluntary or involuntary bankruptcy, or the appointment of a receiver or trustee of such Party's property, in each case that is not discharged within one hundred twenty (120) days.

13.3 Additional Grünenthal Termination Right. Grünenthal shall have the right to terminate this Agreement in its entirety, for any or no reason upon one hundred eighty (180) days written notice.

ARTICLE 14

Effect of Expiration or Termination

14.1 Accrued Obligations. The expiration or termination of this Agreement, in whole or part, for any reason shall not release either Party from any liability which, at the time of such expiration or termination, has already accrued to such Party or which is attributable to a period prior to such expiration or termination, nor will any expiration or termination of this Agreement preclude either Party from pursuing all rights and remedies it may have under this Agreement, at law or in equity, with respect to breach of this Agreement. In particular, in the event this Agreement is terminated for any reason after the achievement of a particular milestone event, then Grünenthal shall have the obligation to make the milestone payment corresponding to such milestone event to AcelRx, regardless of whether the payment date of such accrued milestone payment occurs prior to, on or after the effective date of such termination.

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14.2 Effects of Expiration. Upon expiration of this Agreement in a country, Grünenthal shall continue to have under the Assigned Trademarks (i) an exclusive, royalty-free, fully-paid license to commercialize, sell, offer for sale the Licensed Product in the Field in the Territory, and (ii) a co-exclusive (with AcelRx only), royalty-free, fully-paid license to research, develop, register, make, have made, use and import the Licensed Product in the Field in the Territory; provided, that in consideration for the continuing licenses and rights granted in this Section 14.2, Grünenthal shall pay to AcelRx the Trademark and Supply Fee; provided, further, that Section 2.6 shall not apply to AcelRx in such expired country.

14.3 Effects of Termination for Cause by AcelRx or Termination by Grünenthal under Section 13.3 or on a Country-Specific Basis under Section 13.2(a), 13.2(b) or 13.4. Upon the early termination of this Agreement by Grünenthal under Section 13.3 or termination by AcelRx under Section 13.2(b) or 2.8 or termination by mutual agreement under Section 13.2(a), the following shall apply (and references to Territory shall be deemed references to the country or countries only that are terminated under Sections 13.2(a), 13.2(b) or 2.8, as applicable):

(a) **Winding Down of Development Activities.** In the event there are any on-going clinical trials of the Licensed Product in the Field in the Territory,

(i) The Parties shall work together in good faith to adopt, and AcelRx shall have the final decisional power with respect to, a plan to wind down the development activities in an orderly fashion, with due regard for patient safety and the rights of any subjects that are participants in any clinical trials of the Licensed Product and take any actions it deems reasonably necessary or appropriate to avoid any human health or safety problems and in compliance with all Applicable Laws, provided that AcelRx shall not use its decision power to increase Grünenthal's costs in winding down such development activities;

(ii) Each Party shall perform its outstanding non-cancellable obligations under the Development Plan that existed or accrued prior to the notice date of termination; and

(iii) All costs and expenses incurred from the effective date of the termination notice in winding down the development activities of Territory Specific Trials with respect to the applicable the Licensed Product(s) shall be borne solely by Grünenthal, of US-specific trials by AcelRx and for all other trials the costs shall be split equally between the Parties; *provided, however*, that in no case shall Grünenthal be obligated to pursue or support such activities for a period exceeding twelve (12) months after the date of notice of such termination.

(b) **Inventory.** To the extent ethical to do so given the then views of the Parties regarding the safety and efficacy of the Licensed Product, Grünenthal, its Affiliates, Distributors and Sublicensees shall continue, to the extent that Grünenthal, its Affiliates, Distributors and Sublicensees continue to have stocks of usable the Licensed Product, to fulfill orders received from customers for the Licensed Product in the Field in the Territory for more than six (6) months after the date of notice of termination. For the Licensed Product sold by

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Grünenthal after the effective date of a termination (i.e., after the expiration of the applicable termination notice period), Grünenthal shall continue to pay royalties on the amount of Net Sales of such the Licensed Product.

(c) **Assignment to AcelRx.** At AcelRx's option, which shall be exercised by written notice to Grünenthal, to the extent permitted under Applicable Laws, Grünenthal shall assign or cause to be assigned to AcelRx or its designee (or to the extent not so assignable, Grünenthal shall take all reasonable actions to make available to AcelRx or its designee the benefits of): (i) all Regulatory Filings (including INDs, NDAs and Marketing Approvals) for the Licensed Product in the Territory, including any such Regulatory Filings made or owned by its Affiliates or Sublicensees, (ii) the Assigned Patents, and (iii) the Assigned Trademarks. AcelRx shall notify Grünenthal before the effective date of termination, whether the foregoing should be assigned to AcelRx or its designee, and if the latter, identify the designee, and provide Grünenthal with all necessary details to enable Grünenthal to effect the assignment (or availability). If AcelRx fails to provide such notification prior to the effective date of termination, Grünenthal shall have no obligation to assign such subject matter to AcelRx and Grünenthal shall be free to utilize, abandon or transfer to Third Parties any such subject matter.

(d) **Grants by Grünenthal to AcelRx.** Grünenthal hereby grants AcelRx, effective upon the effective date of such termination, a fully paid, royalty free, non-exclusive license, with the right to grant sublicenses, under any and all Patents and Know-How Controlled by Grünenthal or its Affiliates and used or incorporated into the Licensed Product at the time of such termination for AcelRx to make, have made, use, sell, offer for sale and import the Licensed Product in the Field in the Territory. Upon termination of this Agreement in a country, Grünenthal shall assign or cause to be assigned to AcelRx or its designee the Assigned Trademarks in such country and Section 2.6 shall not apply to AcelRx in such terminated country.

(e) **Supply Agreement.** In addition, Grünenthal may terminate the Supply Agreement, effective upon the effective date of the termination of this Agreement. To the extent of any transfer of Manufacturing of the Licensed Product prior to such termination to Grünenthal or Third Parties under contract with Grünenthal, the Parties shall discuss and cooperate with the termination, unwinding and/or transfer of such Manufacturing of the Licensed Product back to AcelRx and/or Third Parties designated by it.

(f) **Transition.** Both Parties shall use Commercially Reasonable Efforts to cooperate with the other Party to effect a smooth and orderly transition in the development, sale and marketing, promotion and commercialization of the Licensed Product in the Territory during the notice and the wind-down periods. AcelRx may use, identify and finalize an agreement or other arrangement with a Third Party in relation to the Licensed Product and/or, to the extent AcelRx is able to take over such activities under Applicable Laws, take over, directly or through an Affiliate, all activities related to the Licensed Product, and in particular development activities on-going at the time of the effective date of the termination and the transfer of the Regulatory Filings (including INDs, MAAs and Marketing Approvals) into the name of AcelRx or AcelRx's designee so that the wind-down period will be as limited as possible; provided that in no event

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shall Grünenthal be obligated to assist or provided cooperation under this subsection (f) after one hundred eighty (180) days following any such termination of this Agreement.

(g) **Survival of Sublicense.** Upon Grünenthal's request, AcelRx shall allow Grünenthal's Sublicensees the continuation of their sublicense agreements directly with AcelRx if such Sublicensee is not in breach of its Grünenthal sublicense agreement, and Grünenthal shall either assign or cooperate in the transfer of such sublicense to AcelRx. For clarity, this Section 14.3(g) shall not apply to sublicensees that are Affiliates of Grünenthal.

14.4 Effects of Termination for Cause by Grünenthal. Upon the early termination of this Agreement by Grünenthal under Section 7.3(c), 13.2(b) or 13.2(c) the following shall apply (in addition to any other rights and obligations under this Agreement with respect to such termination):

(a) Winding Down of Development Activities. In the event there are any on-going clinical trials of the applicable Licensed Product(s) in the Field in the Territory,

(i) The Parties shall work together in good faith to adopt, and Grünenthal shall have the final decisional power with respect to, a plan to wind down the development activities in an orderly fashion, with due regard for patient safety and the rights of any subjects that are participants in any clinical trials of the Licensed Products and take any actions it deems reasonably necessary or appropriate to avoid any human health or safety problems and in compliance with all Applicable Laws;

(ii) Each Party shall perform its outstanding non-cancellable obligations under the Development Plan that existed or accrued prior to the notice date of termination; and

(iii) All costs and expenses incurred from the effective date of the termination notice in winding down the development activities with respect to the applicable Licensed Product shall be borne solely by AcelRx; *provided, however*, that in no case shall AcelRx be obligated to pursue or support such activities for a period exceeding twelve (12) months after the date of notice of such termination.

(b) License under AcelRx Technology. Grünenthal may elect to have all or any portion of the licenses granted to Grünenthal pursuant to Section 2.1 continue in effect, in which case Grünenthal's obligations to AcelRx under Article 7 of this Agreement and AcelRx's rights under Article 7 shall continue to the extent that Grünenthal has not terminated its rights in an applicable country(ies).

(c) Assignment of AcelRx Regulatory Filings (including Marketing Approvals). If Grünenthal elects to continue the license under Section 2.1, at Grünenthal's option, which shall be exercised by written notice to AcelRx, to the extent permitted under Applicable Laws, AcelRx shall assign or cause to be assigned to Grünenthal or its designee (or to the extent not so assignable, AcelRx shall take all reasonable actions to make available to Grünenthal or its designee the benefits of) all Regulatory Filings (including INDs, MAAs and

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Marketing Approvals) for the Licensed Product(s) in the applicable country(ies) in the Territory, including any such Regulatory Filings made or owned by its Affiliates and/or Distributors or licensees. Grünenthal shall notify AcelRx before the effective date of termination, whether the Regulatory Filings should be assigned to Grünenthal or its designee and, if the latter, identify the designee, and provide AcelRx with all necessary details to enable AcelRx to effect the assignment (or availability). If Grünenthal fails to provide such notification prior to the effective date of termination, AcelRx shall have no obligation to assign the Regulatory Filings to Grünenthal.

(d) Transition Assistance. AcelRx shall provide such assistance, at no cost to Grünenthal, as may be reasonably necessary or useful for Grünenthal to commence or continue developing or commercializing the applicable Licensed Products in the applicable countries of the Territory, to the extent AcelRx is then performing or having performed such activities, including without limitation transferring or amending as appropriate, upon request of Grünenthal, any agreements or arrangements with Third Party suppliers or vendors to supply or sell the Device and/or applicable Licensed Products.

(e) Grünenthal Regulatory Filings (including Marketing Approvals) In the event Grünenthal elects not to pursue the development or commercialization of the applicable Licensed Product(s) in the applicable country(ies), upon Grünenthal's request and to the extent permitted by Applicable Laws, AcelRx shall purchase all Regulatory Filings (including Marketing Approvals) that are owned by Grünenthal for the applicable Licensed Product for the applicable countries at an amount equal to the actual direct costs incurred by Grünenthal in obtaining, maintaining and transferring such Regulatory Filings.

(f) Grants by Grünenthal to AcelRx. Grünenthal hereby grants AcelRx, effective upon the effective date of such termination in the event Grünenthal elects not to continue the development and commercialization of the Licensed Product after such termination, a royalty free and exclusive license, with the right to grant sublicensees, under any and all Patents (to the extent not previously assigned) and Know-How Controlled by Grünenthal or its Affiliates and incorporated into the Licensed Product at the time of such termination for AcelRx to make, have made, use, sell, offer for sale and import Licensed Products in the Field in the Territory. Upon termination of this Agreement in a country, Grünenthal shall assign or cause to be assigned to AcelRx or its designee the Assigned Trademarks in such country. and Section 2.6 shall not apply to AcelRx in such terminated country.

14.5 Licensed Product Supply and Technology Transfer. At any time prior to the expiration of this Agreement or effective date of any termination or partial termination of this Agreement by Grünenthal under Section 13.2(b) or (c), upon request of Grünenthal, the Parties shall agree upon a transition plan of Manufacturing of the Licensed Product in the Territory to minimize any disruption to the research, development, importation, Manufacture, having Manufactured, use, sale, having sold and offering for sale of the Licensed Product in the Territory. The transition plan shall include a mutually agreed-upon schedule for transition activities, under which the transfer of manufacturing-related AcelRx Know-How shall occur at AcelRx's cost and expense. The Parties shall conduct transition activities pursuant to the

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transition plan. Grünenthal shall cooperate with AcelRx on such transfer, shall promptly undertake to complete the transfer and shall be responsible for additional costs that may be incurred for failure by Grünenthal to timely cooperate in accordance with the transition plan. In addition, upon Grünenthal's request, following the expiration of this Agreement or any termination or partial termination of this Agreement by Grünenthal under Section 13.2(b) or (c), AcelRx shall continue to supply Grünenthal and its Affiliates and Sublicensees with their requirements of the Licensed Product, pursuant to the Supply Agreement then in effect between the Parties **[*]**, which Supply Agreement shall remain in effect until the earlier of (i) the **[*]** of the effective date of expiration or termination, or (ii) such time as Grünenthal notifies AcelRx that Grünenthal or a Third Party manufacturer engaged by Grünenthal is capable of supplying the Licensed Product.

14.6 Rights Upon Bankruptcy. All rights and licenses granted under or pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code and other similar laws in any jurisdiction in the Territory or where a Party is situated (collectively, the ***"Bankruptcy Laws"***), licenses of rights to "intellectual property" as defined under the Bankruptcy Laws. If a case is commenced during the Term by or against a Party under Bankruptcy Laws then, unless and until this Agreement is rejected as provided in such Bankruptcy Laws, such Party (in any capacity, including debtor-in-possession) and its successors and assigns (including a trustee) shall perform all of the obligations provided in this Agreement to be performed by such Party. If a case is commenced during the Term by or against a Party under the Bankruptcy Laws, this Agreement is rejected as provided in the Bankruptcy Laws and the other Party elects to retain its rights hereunder as provided in the Bankruptcy Laws, then the Party subject to such case under the Bankruptcy Laws (in any capacity, including debtor-in-possession) and its successors and assigns (including a Title 11 trustee), shall provide to the other Party copies of all information necessary for such other Party to prosecute, maintain and enjoy its rights under the terms of this Agreement promptly upon such other Party's written request therefor. All rights, powers and remedies of the non-bankrupt Party as provided herein are in addition to and not in substitution for any and all other rights, powers and remedies now or hereafter existing at law or in equity (including the Bankruptcy Laws) in the event of the commencement of a case by or against a Party under the Bankruptcy Laws. In particular, it is the intention and understanding of the Parties to this Agreement that the rights granted to the Parties under this Section 14.6 are essential to the Parties' respective businesses and the Parties acknowledge that damages are not an adequate remedy.

14.7 Return of Confidential Information. Upon termination or expiration of this Agreement, except to the extent necessary or reasonably useful for a Party to exercise its rights under any license surviving such termination or expiration, each Party shall promptly return to the other Party, or delete or destroy, all relevant records and materials in such Party's possession or control containing Confidential Information of the other Party; provided that such Party may keep one copy of such materials for archival purposes only.

14.8 Survival. Expiration or termination of this Agreement shall not relieve the Parties of any rights or obligation accruing prior to such expiration or termination. In addition, upon expiration or termination of this Agreement, all rights and obligations of the Parties under

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this Agreement shall terminate, except those described in the following Articles and Sections: 7.3(b)(i)(B), 9, 12 (to the extent any Third Party Claims (X) arose prior to the effective date of termination, (Y) relate to Licensed Products sold to Third Parties prior to effective date of termination, or (Z) relate to Licensed Products Manufactured and supplied to Grünenthal prior to effective date of termination), 14, 15 and 16.

ARTICLE 15

DISPUTE RESOLUTION AND GOVERNING LAW

15.1 Dispute Resolution Process. The Parties recognize that disputes as to certain matters may from time to time arise during the Term that relate to interpretation of a Party's rights and/or obligations hereunder or any alleged breach of this Agreement. If the Parties cannot resolve any such dispute within thirty (30) days after written notice of a dispute from one Party to another, either Party may, by written notice to the other Party, have such dispute referred to the Chief Executive Officer of AcelRx and a Member of the Executive Board of Grünenthal (collectively, the "***Senior Executives***"). The Senior Executives shall negotiate in good faith to resolve the dispute within thirty (30) days. During such period of negotiations, any applicable time periods under this Agreement shall be tolled. If the Senior Executives are unable to resolve the dispute within such time period, either Party may pursue any remedy available to such Party at law or in equity, subject to the terms and conditions of this Agreement and the other agreements expressly contemplated hereunder. Notwithstanding anything in this Article 15 to the contrary, AcelRx and Grünenthal shall each have the right to apply to any court of competent jurisdiction for appropriate interim or provisional relief, as necessary to protect the rights or property of that Party.

15.2 Governing Law. This Agreement and all questions regarding the existence, validity, interpretation, breach or performance of this Agreement, shall be exclusively governed by, and construed and enforced in accordance with, the laws of [*], without reference to its conflicts of law principles.

15.3 Arbitration.

(a) Any disputes arising in connection with this Agreement shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce ("ICC") by three arbitrators appointed in accordance with the said Rules.

(b) Each of the Parties shall nominate an arbitrator and these two arbitrators shall endeavor to agree on the third arbitrator, who shall act as chairman of the arbitral tribunal, within 30 days from the date when both Parties have received from the ICC confirmation of the second arbitrator by the ICC Court. The place of arbitration shall be Geneva, Switzerland. The language of the arbitration proceedings shall be English. The decision and award of the arbitral tribunal shall be final and binding on the parties to the arbitration proceedings.

(c) Either Party also may, without waiving any remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect

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its rights hereunder. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages. Each Party shall bear its own costs and expenses and attorneys' fees and an equal share of the arbitrators' fees and any administrative fees of arbitration.

(d) The Parties agree that, in the event of a dispute over the nature or quality of performance under this Agreement, neither Party may terminate this Agreement until final resolution of the dispute through arbitration determination. The Parties further agree that any payments made pursuant to this Agreement pending resolution of the dispute shall be refunded if an arbitrator determines that such payments are not due.

ARTICLE 16

GENERAL PROVISIONS

16.1 Intervening Events. If the performance of any part of this Agreement by either Party is prevented, restricted, interfered with or delayed by any reason or cause beyond the reasonable control of such Party (including fire, flood, embargo, power shortage or failure, acts of war, insurrection, riot, terrorism, strike, lockout or other labor disturbance, shortage of raw materials, epidemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, or storm or like catastrophe, acts of God or any acts, omissions or delays in acting of the other Party) (an "***Intervening Event***"), the Party so affected shall, upon giving written notice to the other Party, be excused from such performance to the extent of such Intervening Event, provided that the affected Party shall use its substantial efforts to avoid or remove such causes of non-performance and shall continue performance with the utmost dispatch whenever such causes are removed.

(a) **Notification.** If either Party becomes aware that such an Intervening Event has occurred or is imminent or likely, it shall immediately notify the other.

(b) **Efforts to Overcome.** The Party which is subject to such Intervening Event shall exert all reasonable efforts to overcome it.

(c) **Keeping the Other Informed.** Such Party shall keep the other informed as to the progress of overcoming such Intervening Event.

16.2 Waiver of Breach. No delay or waiver by either Party of any condition or term in any one or more instances shall be construed as a further or continuing waiver of such condition or term or of another condition or term.

16.3 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to perform all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

16.4 Affiliates; Continuing Responsibility. Either Party shall have the right to assign, sublicense, subcontract or delegate this Agreement or any or all of its obligations or

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rights hereunder to an Affiliate upon written notice to the other Party; *provided, however*, the assigning, sublicensing, subcontracting or delegating Party hereby guarantees and shall remain fully and unconditionally obligated and responsible for the full and complete performance of this Agreement by such Affiliate and in no event shall such assignment, sublicensing, subcontracting or delegation be deemed to relieve such Party's liabilities or obligations to the other Party under this Agreement. The other Party shall, at the request of the assigning, sublicensing, subcontracting or delegating Party, enter into such supplemental agreements with the applicable Affiliates as may be necessary or advisable to permit such Affiliates to avail itself of any rights or perform any obligations of the assigning, sublicensing, subcontracting or delegating Party hereunder.

16.5 Modification. No amendment or modification of any provision of this Agreement shall be effective unless in a prior writing signed by both Parties hereto. No provision of this Agreement shall be varied, contradicted or explained by any oral agreement, course of dealing or performance or any other matter not set forth in an agreement in writing and signed by both Parties hereto.

16.6 Severability. In the event any provision of this Agreement should be held invalid, illegal or unenforceable in any jurisdiction, the Parties shall negotiate in good faith and enter into a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties. All other provisions of this Agreement shall remain in full force and effect in such jurisdiction. Such invalidity, illegality or unenforceability shall not affect the validity, legality or enforceability of such provision in any other jurisdiction.

16.7 Entire Agreement. This Agreement (including the Exhibits attached hereto and any letter delivering information referenced herein), the Supply Agreement, the Pharmacovigilance Agreement and the Quality Agreement constitute the entire agreement between the Parties relating to the subject matter hereof and supersede and cancel all previous express or implied agreements and understandings, negotiations, writings and commitments, either oral or written, in respect of the subject matter hereof. Each of the Parties acknowledges and agrees that in entering into this Agreement, and the documents referred to in it, it does not rely on, and shall have no remedy in respect of, any statement, representation, warranty or understanding (whether negligently or innocently made) of any person (whether party to this Agreement or not) other than as expressly set out in this Agreement and nothing in this clause shall, however, operate to limit or exclude any liability for fraud. In the event of a conflict or inconsistency between the provisions of this Agreement and the provisions of the Supply Agreementthis Agreement will prevail. In the event of a conflict or inconsistency between the provisions of this Agreement and any legal or regulatory requirements applicable for the Territory, Amendments to this Agreement shall be considered promptly in good faith in order to meet such requirements.

16.8 Language. The language of this Agreement and all activities to be pursued under this Agreement is English. Any and all documents proffered by one Party to the other in fulfillment of any provision of this Agreement shall only be in compliance if in English. Any translation of this Agreement in another language shall be deemed for convenience only and shall never prevail over the original English version. This Agreement is established in the English language.

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16.9 Notices. Any notice or communication required or permitted under this Agreement shall be in writing in the English language, delivered personally, sent by facsimile (and promptly confirmed by personal delivery, registered or certified mail or overnight courier), sent by internationally-recognized courier or sent by registered or certified mail, postage prepaid to the following addresses of the Parties (or such other address for a Party as may be at any time thereafter specified by like notice):

To AcelRx:

AcelRx Pharmaceuticals, Inc.
575 Chesapeake Drive,
Redwood City, CA 94063
Attention: Chief Executive Officer
Facsimile: +1-650-216-6500

To Grünenthal:

Grünenthal GmbH
D-52099 Aachen

Attention: Chief Executive Officer

with a copy to:

Cooley LLP
3175 Hanover St.
Palo Alto, CA 94306
Telephone: +1-650-843-5000
Facsimile: +1-650-843-4000
Attention: Glen Y. Sato

with a copy to:

Global Legal
Grünenthal GmbH
D-52099 Aachen
Facsimile: +49-241-5693547

Any such notice shall be deemed to have been given (a) when delivered if personally delivered; (b) on the next Business Day after dispatch if sent by confirmed facsimile or by internationally-recognized overnight courier; and/or (c) on the fifth (5 th) Business Day following the date of mailing if sent by mail or other internationally-recognized courier. Notices hereunder will not be deemed sufficient if provided only between or among each Party's representatives on the Joint Steering Committee.

16.10 Assignment; Change of Control of AcelRx.

(a) Subject to Section 16.4, this Agreement shall not be assignable or otherwise transferred, nor may any rights or obligations hereunder be assigned or transferred, by either Party to any Third Party without the prior written consent of the other Party; except that either Party may assign or otherwise transfer this Agreement without the consent of the other Party to an entity that acquires all or substantially all of the business or assets of the assigning Party relating to the subject matter of this Agreement, whether by merger, acquisition or otherwise. Subject to the foregoing, this Agreement shall inure to the benefit of each Party, its successors and permitted assigns. Any assignment of this Agreement in contravention of this Section 16.10 shall be null and void.

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(b) If AcelRx is subject to a Change of Control in which the party effecting the Change of Control of AcelRx is a competitor of Grünenthal, the following provisions shall apply:

(i) Grünenthal shall notify AcelRx of its belief that such party effecting the Change of Control of AcelRx is a competitor of Grünenthal and the Parties shall discuss such view and protective measures to ensure that Grünenthal Confidential Information is not accessible to such competitor. If the Parties are unable to agree upon a procedure within thirty (30) days of notification from Grünenthal, AcelRx will, and it will cause its Affiliates to, ensure that (A) no Grünenthal Confidential Information is disclosed to any Affiliate of AcelRx that becomes a AcelRx Affiliate as a result of such Change of Control or any representatives of such Affiliates, unless, in each case, such Affiliate or representatives, as applicable, have signed individual confidentiality agreements which include equivalent obligations to those set out in Article 9, and (B) no Grünenthal Confidential Information is disclosed whatsoever to any representatives of the acquiror or its Affiliates who are actively engaged in, or have direct supervisory responsibilities with respect to, the development or commercialization of any products for the treatment of pain.

(ii) If AcelRx is subject to a Change of Control, then, at Grünenthal's discretion, effective as of the date of such Change of Control, the JSC shall be deemed to be automatically terminated with no further duties, rights or obligations under this Agreement, and to the extent of any authority granted to the JSC hereunder.

(iii) If AcelRx disputes that the Change of Control involves a competitor, then the determination shall be subject to dispute resolution in accordance with Article 15.

16.11 No Partnership or Joint Venture. Nothing in this Agreement or any action which may be taken pursuant to its terms is intended, or shall be deemed, to establish a joint venture or partnership between Grünenthal and AcelRx. Neither Party to this Agreement shall have any express or implied right or authority to assume or create any obligations on behalf of, or in the name of, the other Party, or to bind the other Party to any contract, agreement or undertaking with any Third Party.

16.12 Interpretation. The captions to the several Articles and Sections of this Agreement are not a part of this Agreement but are included for convenience of reference and shall not affect its meaning or interpretation. In this Agreement (a) "include", "includes" and "including" are not limiting and shall be deemed to be followed by the phrase "without limitation" or like expression; (b) the singular shall include the plural and vice versa; (c) references to an agreement, statute or instrument mean such agreement, statute or instrument as from time to time amended, modified or supplemented; (d) references to a Person are also to its permitted successors and assigns; (e) the word "will" shall be construed to have the same meaning and effect as the word "shall"; and (f) the word "any" shall mean "any and all" unless otherwise indicated by context; and (g) masculine, feminine and neuter pronouns and expressions shall be interchangeable. Each accounting term used herein that is not specifically

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defined herein shall have the meaning given to it under Accounting Standards consistently applied, but only to the extent consistent with its usage and the other definitions in this Agreement.

16.13 Counterparts. This Agreement may be executed in any number of counterparts each of which shall be deemed an original, and all of which together shall constitute one and the same instrument.

16.14 Limitation of Liability. EXCEPT FOR LIABILITY FOR BREACH OF ARTICLE 9, NEITHER PARTY SHALL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, CONSEQUENTIAL OR PUNITIVE DAMAGES IN CONNECTION WITH THIS AGREEMENT OR ANY LICENSE GRANTED HEREUNDER; PROVIDED, HOWEVER, THAT THIS SECTION 16.14 SHALL NOT BE CONSTRUED TO LIMIT EITHER PARTY'S INDEMNIFICATION OBLIGATIONS UNDER SECTION 7.3(b)(i)(B) AND ARTICLE 12.

ARTICLE 17

COMPLIANCE WITH LAW

17.1 Export Laws. Notwithstanding anything to the contrary contained herein, all obligations of AcelRx and Grünenthal are subject to prior compliance with export and import regulations and such other laws and regulations in effect in such jurisdictions or any other relevant country as may be applicable, and to obtaining all necessary approvals required by the applicable agencies of the governments of any relevant countries. AcelRx and Grünenthal shall cooperate with each other and shall provide assistance to the other as reasonably necessary to obtain any required approvals.

17.2 Securities Laws. Each of the Parties acknowledges that it is aware that the securities laws of the United States and other countries prohibit any person who has material non-public information about a publicly listed company from purchasing or selling securities of such company or from communicating such information to any person under circumstances in which it is reasonably foreseeable that such person is likely to purchase or sell such securities. Each Party agrees to comply with such securities laws and make its Affiliates, licensees, Distributors, Sublicensees, employees, Contractors and agents aware of the existence of such securities laws and their need to comply with such laws.

17.3 Certain Payments. Each of the Parties acknowledges that it is aware that the United States and other countries have stringent laws which prohibit persons directly or indirectly from making unlawful payments to, and for the benefit of, government officials and related parties to secure approvals or permission for their activities. Each Party agrees that it will make no such prohibited payments, it will not indirectly make or have made such payments and it will make its Affiliates, employees and agents aware of the existence of such laws and their need to comply with such laws.

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17.4 Anti-Bribery and Anti-Corruption Compliance.

(a) Each Party agrees, on behalf of itself, its officers, directors and employees and shall cause its Affiliates, agents, representatives, consultants and subcontractors hired in connection with the subject matter of this Agreement (together with such Party, the " ***Representatives***") to agree that for the performance of its obligations hereunder:

(i) The Representatives shall not directly or indirectly pay, offer or promise to pay, authorize the payment of any money or give, offer or promise to give, or authorize the giving of anything else of value, to: (a) any government official in order to influence official action; (b) any individual or entity (whether or not a government official) (1) to influence such individual or entity to act in breach of a duty of good faith, impartiality or trust ("acting improperly"), (2) to reward such individual or entity for acting improperly or (3) where such individual or entity would be acting improperly by receiving the money or other thing of value; (c) any individual or entity (whether or not a government official) while knowing or having reason to know that all or any portion of the money or other thing of value will be paid, offered, promised or given to, or will otherwise benefit, a government official in order to influence official action for or against either Party in connection with the matters that are the subject of this Agreement; or (d) any individual or entity (whether or not a government official) to reward that individual or entity for acting improperly or to induce that individual or entity to act improperly.

(ii) The Representatives shall not, directly or indirectly, solicit, receive or agree to accept any payment of money or anything else of value in violation of the Anti-Corruption Laws.

(b) The Representatives shall comply with the Anti-Corruption Laws and shall not take any action that will, or would reasonably be expected to, cause either Party or its Affiliates to be in violation of any such laws or policies.

(c) Each Party, on behalf of itself and its other Representatives, represents and warrants to the other Party that to the best of such Party's and its Affiliates' knowledge, no Representative will participate or support its performance of its obligations hereunder has, directly or indirectly, (i) paid, offered or promised to pay or authorized the payment of any money, (ii) given, offered or promised to give or authorized the giving of anything else of value or (iii) solicited, received or agreed to accept any payment of money or anything else of value, in each case ((i), (ii) and (iii)), in violation of the Anti-Corruption Laws during the three (3) years preceding the date of this Agreement.

(d) Each Party shall promptly provide the other Party with written notice of the following events: (i) upon becoming aware of any breach or violation by such Party or its Representative of any representation, warranty or undertaking set forth in Sections 17.4(a)-(c); or (ii) upon receiving a formal notification that it is the target of a formal investigation by a governmental authority for a material Anti-Corruption Law violation or upon receipt of information from any of the Representatives connected with this Agreement that any of them is the target of a formal investigation by a governmental authority for a material Anti-Corruption Law violation.

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(e) Without prejudice to any auditing or inspection rights set forth elsewhere in this Agreement, each Party shall for the term of this Agreement and six (6) years thereafter, for the purpose of allowing the other Party to audit and monitor the performance of its compliance with this Agreement and particularly this Section 17.4 permit the other Party, its Affiliates, any auditors of any of them and any governmental authority to have reasonable access to any premises of such Party or other Representatives used in connection with this Agreement, together with a right to reasonably access personnel and records that relate to this Agreement. The results of any such audit shall constitute Confidential Information of the audited Party, in respect of which the other Party shall comply with the provisions contained in Article 9 (subject to the terms and exceptions set forth therein or in this Section 17.4).

(i) To the extent that any audit by a Party requires access and review of any commercially or strategically sensitive information of the other Party or any of its other Representatives relating to the business of such Party or any other Representatives (including information about prices and pricing policies, cost structures and business strategies), such activity shall be carried out by a Third Party professional advisor appointed by the other Party and such professional advisors shall only report back to the other Party such information as is directly relevant to informing the other Party on such Party's compliance with the particular provisions of the Agreement being Audited.

(ii) Each Party shall, and shall cause its Representatives to, provide all cooperation and assistance during normal working hours as reasonably requested by the other Party for the purposes of an Audit. Such other Party shall ensure that any Third Party auditor enters into a confidentiality agreement consistent with applicable requirements of Article 12 hereof in all material respects. Such other Party shall instruct any Third Party auditor or other Person given access in respect of an Audit to cause the minimum amount of disruption to the business of the audited Party and its Affiliates and to comply with relevant building and security regulations.

(iii) The costs and fees of any Audit shall be paid by the auditing Party, except that if an inspection or Audit reveals any breach or violation by the audited Party (including through its other Representatives) of any representation, warranty or undertaking set forth in Sections 17.4(a)-(c), the costs of such inspection or Audit shall be paid by the audited Party. The audited Party shall bear its own costs of rendering assistance to the Audit.

(f) On the occurrence of any of the following events: (A) A Party becomes aware of, whether or not through an Audit, that the other Party (or any other Representative) is in breach or violation of any representation, warranty or undertaking in Sections 17.4(a)-(c) or of the Anti-Corruption Laws; or (B) notification is received under Section 17.4(d) relating to any suspected or actual material Anti-Corruption Law violation by a Party or its Representative, in either case ((A) or (B)), the other Party shall have the right, in addition to any other rights or remedies under this Agreement or to which such other Party may be entitled in law or equity, to

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(x) take such steps as are reasonably necessary in order to avoid a potential violation or continuing violation by such other Party or any of its Affiliates of the Anti-Corruption Laws, including by requiring that the Party agrees to such additional measures, representations, warranties, undertakings and other provisions as such other Party believes in good faith are reasonably necessary and (y) terminate any or all of the activities conducted by the Party pursuant to this Agreement or this Agreement in its entirety, immediately in the event that a Party reasonably concludes that there is no Provision available that would enable such Party or its Affiliates to avoid a potential violation or continuing violation of applicable Anti-Corruption Laws.

(g) Any termination of this Agreement pursuant to Section 17.4(f) shall be treated as a termination for breach.

(h) Each Party shall be responsible for any breach of any representation, warranty or undertaking in this Section 17.4 or of the Anti-Corruption Laws by any of its Representatives.

(i) Each Party may disclose the terms of this Agreement or any action taken under this Section 17.4 to prevent a potential violation or continuing violation of applicable Anti-Corruption Laws, including the identity of the other Party and the payment terms, to any Governmental Authority if such Party determines, upon advice of counsel, that such disclosure is necessary.

(SIGNATURE PAGE FOLLOWS)

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IN WITNESS WHEREOF, each Party hereto has executed or caused this Agreement to be executed on its behalf as of the Effective Date.

ACELRX PHARMACEUTICALS, INC.

By: /s/ Richard King

Name: Richard King

Title: President & CEO

GRÜNENTHAL GMBH

By: /s/ Eric Paul Paques

Name: Prof. Dr. Eric Paul Paques

Title: Chairman of the Corporate Executive Board

By: /s/ Alberto Grua

Name: DoH. Alberto Grua

Title: Chief Commercial Officer EV, Australia and North America

[Signature Page to Collaboration and License Agreement]

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CONFIDENTIAL

Exhibit 1.1

Accessories

[*]

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Exhibit 1.7

AcelRx Patents

Docket No.	Patent App.No./Pub No/Patent No.	Location	Status/Validation
	DEVICE-SIDE PATENTS		
[*]	[*]	[*]	[*]
[*]	[*]	[*]	[*]
[*]			
[*]	[*]	[*]	[*]
[*]	[*]	[*]	[*]
[*]	[*]	[*]	[*]

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CONFIDENTIAL

Exhibit 1.9

AcelRx Trademarks

Zalviso™

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Exhibit 1.14

Assigned Patents

Docket No.	Patent App.No./Pub No/Patent No.	Location	Status/Validation
[*]	[*]	[*]	[*]

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Exhibit 1.38

Development Plan

[*]

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Exhibit 1.78

Licensed Product

The sufentanil sublingual microtablet system is comprised of the components shown below.

CONTROLLER

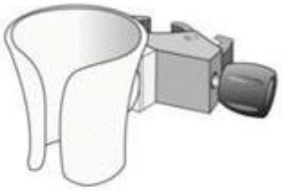
DISPENSER

CAP

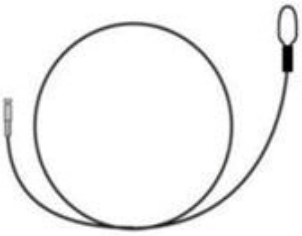
DRUG CARTRIDGE

PATIENT ID THUMB TAG

AUTHORIZED ACCESS CARD (AAC)



HOLSTER



SECURITY TETHER

CLEANING PLUG

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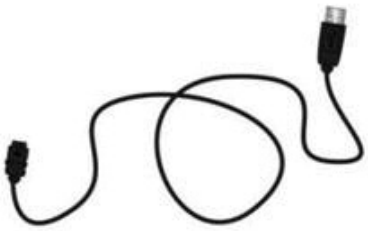
CHARGER



DATA CABLE

TECHNICIAN ACCESS BADGE (TAB)

CARTRIDGE LABEL RFID READER

[*]

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Exhibit 1.83

Material Agreements

[*]

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Exhibit 3.3

Alliance Managers

For Grünenthal:

[*] VP Portfolio Development

For AcelRx:

[*] VP Clinical Operations

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Exhibit 9.5(a)

Form of Press Release(s)

AcelRx Press Release

FOR IMMEDIATE RELEASE

AcelRx and Grünenthal Announce Collaboration for EU Commercialization of ZALVISO™

- FDA establishes the PDUFA action date of July 27, 2014 for Zalviso -

- Conference Call Scheduled Monday, December 16th 2013 for 8:30 a.m. Eastern Time –

Redwood City, California and Aachen, Germany – December 16, 2013 - AcelRx Pharmaceuticals, Inc. (Nasdaq: ACRX) and Grünenthal GmbH announced today that they have entered into a commercial collaboration, covering the territory of the European Union, certain other European countries and Australia for ZALVISO™ (previously known as ARX-01) for potential use in pain treatment within or dispensed by a hospital, hospice, nursing home or other medically supervised setting. ZALVISO, a drug-device combination product utilizing the opioid agonist sufentanil formulated in a proprietary sublingual tablet formulation and delivered through a pre-programmed, non-invasive proprietary delivery device is AcelRx's lead program. AcelRx retains all rights in remaining countries, including the U.S. and Asia.

Under the terms of the agreement, AcelRx will receive an upfront cash payment of $30 million. AcelRx is eligible to receive approximately $220 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements. Grünenthal will also make tiered royalty, supply and trademark fee payments in the mid-teens up to the mid-twenties percent range, on net sales of ZALVISO in the Grünenthal territory.

"As an established leader in providing pain management solutions to patients throughout Europe, Grünenthal is an excellent partner for AcelRx and for ZALVISO," said Richard King, President and CEO. "Grünenthal's commercial track record across Europe demonstrates their ability to achieve commercial success in this large market, and will, following regulatory approval, enable patients in Europe suffering with moderate-to-severe pain in a medically supervised setting to receive the benefits of our innovative, patient-centric product ZALVISO."

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

“We are extremely pleased to enter into this collaboration with AcelRx and its proven concept of a patient-controlled analgesia system to address a significant unmet medical need, thereby allowing hospitals to avoid the challenges of intravenous line-related infections, as well as freeing hospital personnel from the need to program intravenous infusion pump systems. With ZALVISO Grünenthal is building on its presence in the hospital market, an area that provides us with significant growth opportunities in the mid- and long-term,” said Prof. Eric-Paul Pâques, Grünenthal’s Chief Executive Officer.

Grünenthal will be responsible for all commercial activities for ZALVISO, including obtaining and maintaining pharmaceutical product regulatory approval in the Grünenthal territory. AcelRx will be responsible for maintaining device regulatory approval in the Grünenthal territory and manufacturing and supply of ZALVISO to Grünenthal for commercial sales and clinical trials.

ZALVISO PDUFA Date

In addition, AcelRx announced today that the U.S. Food and Drug Administration (FDA) has established a Prescription Drug User Fee Act (PDUFA) action date of July 27, 2014, for AcelRx’s New Drug Application (NDA) for Zalviso. AcelRx announced on December 2, 2013 that FDA accepted for filing the Zalviso NDA.

Conference Call at 8:30 a.m. Eastern time on Monday, December 16, 2013

AcelRx will conduct a conference call and webcast today, December 16, 2013 at 8:30 a.m. Eastern time (5:30 a.m. Pacific time) to discuss the Grünenthal partnership. To listen to the conference call, dial in approximately ten minutes before the scheduled call to (877) 870-4263 for domestic callers, (855) 669-9657 for Canadian callers, or (412) 317-0790 for international callers. Those interested in listening to the conference call live via the Internet may do so by visiting the Investors section of the company’s website at www.acelrx.com and selecting the webcast link for Grünenthal collaboration conference call. A webcast replay will be available on the AcelRx website for 90 days following the call by visiting the Investors section of the company’s website at www.acelrx.com

About ZALVISO

ZALVISO is an investigational pre-programmed, non-invasive, handheld system that allows hospital patients with moderate-to-severe acute pain to self-dose with sublingual sufentanil microtablets to manage their pain. ZALVISO is designed to address the limitations of IV PCA by offering:

- A high therapeutic index opioid – ZALVISO uses the high therapeutic index, highly lipophilic opioid sufentanil, enabling delivery via a non-intravenous route, and also supporting fast onset of effect.

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- A non-invasive route of delivery – The sublingual route of delivery used by ZALVISO eliminates the risk of IV-related analgesic gaps and IV complications, such as catheter-related infections in IV PCA treated patients. In addition, because ZALVISO patients do not require direct connection to an IV PCA infusion pump through IV tubing, ZALVISO allows for ease of patient mobility.
- A simple, pre-programmed PCA solution – ZALVISO is a pre-programmed PCA system designed to eliminate the risk of programming errors.

About AcelRx Pharmaceuticals, Inc.

AcelRx Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. AcelRx's lead product candidate, ZALVISO, is designed to solve the problems associated with post-operative intravenous patient-controlled analgesia which 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 complexity of infusion pumps. AcelRx has announced positive results from each of the three Phase 3 clinical trials for ZALVISO and has submitted an NDA to the FDA seeking its approval. AcelRx has also announced positive top-line results for a Phase 2 trial for ARX-04, a sufentanil formulation for the treatment of moderate-to-severe acute pain, funded through a grant from the U.S. Army Medical Research and Materiel Command. The company has two additional pain treatment product candidates, ARX-02 and ARX-03, which have completed Phase 2 clinical development. For additional information about AcelRx's clinical programs, please visit www.acelrx.com.

About Grünenthal

The Grünenthal Group is an independent, family-owned, international research-based pharmaceutical company headquartered in Aachen, Germany. Building on its unique position in pain treatment, its objective is to become the most patient-centric company and thus to be a leader in therapy innovation. Grünenthal is one of the last five remaining research-oriented pharmaceutical companies with headquarters in Germany which sustainably invests in research and development. Research and development costs amounted to about 26 percent of revenues in 2012. Grünenthal's research and development strategy concentrates on selected fields of therapy and state-of-the-art technologies. We are intensely focused on discovering new ways to treat pain better and more effectively, with fewer side-effects than current therapies. Altogether, the Grünenthal Group has affiliates in 26 countries worldwide. Grünenthal products are sold in more than 155 countries. Today, approx. 4,400 employees are working for the Grünenthal Group worldwide. In 2012, Grünenthal achieved revenues of USD 1,251 mn.

More information: www.grunenthal.com.

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Forward Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to potential approval of the NDA for Zalviso in the U.S. and the timing thereof, the potential of approval of the MAA for Zalviso in the EU and the timing thereof, the ability to successfully manufacture Zalviso to meet the requirements of Grünenthal and the therapeutic and commercial potential of Zalviso in the Grünenthal territory. These forward-looking statements are based on AcelRx's current expectations and inherently involve significant risks and uncertainties. AcelRx's actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to: AcelRx's ability to receive regulatory approval for Zalviso; any delays or inability to obtain and maintain regulatory approval of AcelRx's product candidates, including Zalviso, in the United States, Europe, Australia and other countries; the ability to attract additional funding partners or collaborators with development, regulatory and commercialization expertise; the ability to obtain sufficient financing to commercialize Zalviso; the market potential for AcelRx's other product candidates; the accuracy of AcelRx's estimates regarding expenses, capital requirements and needs for financing; and other risks detailed in the "Risk Factors" and elsewhere in AcelRx's U.S. Securities and Exchange Commission filings and reports, including its Quarterly Report on Form 10-Q filed with the SEC on November 5, 2013. AcelRx undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in its expectations

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GRÜNENTHAL GROUP
Press Release

Grünenthal and AcelRx enter into partnership for EU commercialization of ZALVISO®

Aachen, Germany / Redwood City (California), USA – December 16, 2013 – Grünenthal GmbH today announced that the company entered into a commercial partnership with AcelRx Pharmaceuticals, Inc. for ZALVISO, a patient-controlled analgesia device for self-administration of sufentanil nanotablets by patients following surgery. The agreement covers the countries of the European Union, EEA and Australia. AcelRx will supply Grünenthal with the product and retains all rights in remaining countries including the US and Asia. With this partnership Grünenthal, a family-owned company headquartered in Aachen, Germany, significantly strengthens its hospital franchise and underlines its strong market position as a pain specialist in the pharmaceutical market.

Strategic portfolio expansion for the benefit of more than 20 million patients

According to market research there are more than 20 million patients in Europe who could potentially benefit from this innovative alternative to current treatment options in acute post-operative pain management. Additionally, this device is an excellent expansion of Grünenthal's existing portfolio of innovative drugs for the treatment of moderate to severe chronic pain.

"We are extremely pleased to enter into this collaboration with AcelRx and its proven concept of a patient-controlled analgesia system to address a significant unmet medical need, thereby allowing hospitals to avoid the challenges of intravenous line-related infections, as well as freeing hospital personnel from the need to program intravenous infusion pump systems. With ZALVISO Grünenthal is building on its presence in the hospital market, an area that provides us with significant growth opportunities in the mid- and long-term," said Prof. Eric-Paul Pâques, Grünenthal's Chief Executive Officer.

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"As an established leader in providing pain management solutions to patients throughout Europe, Grünenthal is an excellent partner for AcelRx and for ZALVISO" said Richard King, President and CEO. "Grünenthal's commercial track record across Europe demonstrates their ability to achieve commercial success in this large market, and will enable patients in Europe suffering with moderate-to-severe pain in a medically supervised setting to receive the benefits of our highly innovative, patient-centric product ZALVISO."

Market launch of ZALVISO in Europe planned for 2015
An NDA for ZALVISO was submitted to the FDA on September 27 and accepted for filing by the FDA on December 02. An approval for the US-market could be expected in the third quarter of 2014. Grünenthal and AcelRx are planning to submit a MAA to EMA around mid-2014 with an anticipated approval and go to market in Europe by the end of 2015. Under the terms of the agreement, Grünenthal pays an upfront cash payment of $30 million to AcelRx and up to $220 million in additional milestone payments, based upon successful regulatory and product development efforts and net sales target achievements as well as royalty payments on net sales of ZALVISO in the Grünenthal territory.

About Grünenthal
The Grünenthal Group is an independent, family-owned, international research-based pharmaceutical company headquartered in Aachen, Germany. Building on its unique position in pain treatment, its objective is to become the most patient-centric company and thus to be a leader in therapy innovation. Grünenthal is one of the last five remaining research-oriented pharmaceutical companies with headquarters in Germany which sustainably invests in research and development. Research and development costs amounted to about 26 percent of revenues in 2012. Grünenthal's research and development strategy concentrates on selected fields of therapy and state-of-the-art technologies. We are intensely focused on discovering new ways to treat pain better and more effectively, with fewer side-effects than current therapies. Altogether, the Grünenthal Group has affiliates in 26 countries worldwide. Grünenthal products are sold in more than 155 countries. Today, approx. 4,400 employees are working for the Grünenthal Group worldwide. In 2012, Grünenthal achieved revenues of USD 1,251 mn.

More information: www.grunenthal.com.

About AcelRx Pharmaceuticals, Inc.
AcelRx Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of acute and breakthrough pain. AcelRx's lead product candidate, ZALVISO, is designed to solve the problems associated with post-operative intravenous patient-controlled analgesia which 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 complexity of infusion pumps. AcelRx has announced positive results from each of the three Phase 3 clinical trials for ZALVISO and has

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Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Form S-8 Nos. 333-187206, 333-180334, 333-172409; Form S-3 Nos. 333-190003, 333-183237, 333-182245) and in the related prospectuses of AcelRx Pharmaceuticals, Inc. of our reports dated March 17, 2014, with respect to the financial statements , and the effectiveness of internal control over financial reporting of AcelRx Pharmaceuticals, Inc. included in this Annual Report on Form 10-K for the year ended December 31, 2013.

/s/ Ernst & Young LLP

Redwood City, California
March 17, 2014

Exhibit 31.1

CERTIFICATIONS

I, Richard A. King, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2014

/s/ Richard A. King

Richard A. King
Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, James H. Welch, certify that:

1. I have reviewed this annual report on Form 10-K of AcelRx Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 17, 2014

/s/ James H. Welch
James H. Welch
Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Richard A. King, Chief Executive Officer of AcelRx Pharmaceuticals, Inc. (the "Company"), and James H. Welch, Chief Financial Officer of the Company, each hereby certifies that, to the best of his or her knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2013, to which this Certification is attached as Exhibit 32.1 (the "Annual Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 17th day of March, 2014.

/s/ Richard A. King	/s/ James H. Welch
Richard A. King	James H. Welch
Chief Executive Officer	Chief Financial Officer

"This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of AcelRx Pharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing."