ADVENTRX PHARMACEUTICALS INC
Form 10-K
March 10, 2011

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K

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

For the fiscal year ended December 31, 2010

or

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

For the transition period from _____ to _____

Commission File No. 001-32157

ADVENTRX Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**84-1318182**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No.)*
12390 El Camino Real, Ste 150, San Diego, CA	**92130**
(Address of principal executive offices)	*(Zip Code)*

(858) 552-0866

(Registrant s telephone number, including area code)

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

Title of each class:	Name of each exchange on which registered:
Common Stock, par value $0.001 per share	**NYSE Amex 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 o No þ

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

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

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 o No o

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting

company in Rule 12b-2 of the Exchange Act.

Large accelerated filer o	Accelerated filer o	Non-accelerated filer o	Smaller reporting company þ

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of June 30, 2010 was approximately $24.0 million based upon the closing price of the registrant s common stock on the NYSE Amex reported for such date. Shares of the registrant s common stock held by each officer and director of the registrant and by each person or entity who is known by the registrant to own beneficially 5% or more of the registrant s outstanding common stock have been excluded for purposes of the foregoing calculation on the basis that such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 1, 2011, the registrant had 23,664,858 shares of its common stock issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement to be filed subsequent to the date hereof with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant s 2011 annual meeting of stockholders are incorporated by reference into Part III of this report. Such definitive proxy statement will be filed with the Commission not later than 120 days after the end of the registrant s fiscal year ended December 31, 2010.

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Forward-Looking Statements

This Annual Report on Form 10-K, particularly in Item 1 Business, and Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations, and the information incorporated herein by reference, include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including, but not limited to, statements regarding our business strategy, expectations and plans, our objectives for future operations and our future financial position. When used in this report, the words believe, may, could, will, estimate, continue, anticipate, i indicate, seek, should or would and similar expressions are intended to identify forward-looking statements. Am the factors that could cause or contribute to material differences between our actual results and those indicated from the forward-looking statements are risks and uncertainties inherent in our business, including, but are not limited to: the extent to which we acquire new technologies, product candidates, products or businesses and our ability to integrate them successfully into our operations; our ability, or that of a future partner, to obtain regulatory approval for our product candidates and, if approved, to successfully commercialize them in the U.S. and/or elsewhere; our ability to obtain stockholder approval of the issuance of milestone-related shares in connection with our acquisition of SynthRx, Inc. on a timely basis, or at all; our ability to obtain stockholder approval to complete any other product pipeline expansion transaction, if necessary, on a timely basis, or at all; the potential that we may enter into a merger or other business combination whereby the stockholders who own the majority of our voting securities prior to the transaction own less than a majority after the transaction; our ability to obtain additional funding on a timely basis or on acceptable terms, or at all; the potential that we may enter into one or more commercial partnerships or other strategic transactions relating to Exelbine and/or ANX-514, and the terms of any such transactions; the extent to which we rebuild our workforce and our ability to attract and retain qualified personnel and manage growth; our ability to develop sales, marketing and distribution capabilities to launch Exelbine, should we obtain regulatory approval to market it, and any other current or future product candidate, should we obtain regulatory approval to market any of them and determine to commercialize any of them without a partner; delays in the commencement or completion of nonclinical testing, bioequivalence or clinical trials of or manufacturing, regulatory or launch activities related to our product candidates; the success of future bioequivalence or clinical trials; whether any of our product candidates for which we receive regulatory approval, if any, achieve broad market acceptance; competition in the marketplace for our products, if any are approved; our ability to maintain our relationships with the single source manufacturers and suppliers for certain of our product candidates and their component materials and the ability of such manufacturers and suppliers to successfully and consistently manufacture and supply, as applicable, our products and their component materials on a commercial scale, if we receive regulatory approval to commercialize our product candidates; the satisfactory performance of third parties on whom we rely significantly to conduct our nonclinical testing and bioequivalence and clinical studies and other aspects of our development programs; undesirable side effects that our product candidates may cause; our ability to protect our intellectual property rights with respect to our product candidates and proprietary technology; claims against us for infringing the proprietary rights of third parties; healthcare reform measures and reimbursement policies that, if not favorable to our products, could hinder or prevent our products commercial success; potential product liability exposure and, if successful claims are brought against us, liability for a product or product candidate; our ability to maintain compliance with NYSE Amex continued listing standards and maintain the listing of our common stock on the NYSE Amex or another national securities exchange; and and other risks and uncertainties described in Part I, Item 1A Risk Factors of this report.

We have based the forward-looking statements we make on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, short-term and long-term business operations and objectives, and financial needs. In light of these risks and uncertainties and our assumptions, the forward-looking events and circumstances discussed in this report and in the information incorporated herein by reference may not occur. We cannot guarantee future results, events, levels of activity, performance or achievement. Accordingly, you are cautioned not to place undue reliance on forward-looking statements. Except as required by law, we do not intend to update the forward-looking statements discussed in this report publicly or to update the reasons actual results could differ materially from those anticipated in these

forward-looking statements, even if new information becomes available in the future.

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PART I

Item 1. Business.

Overview

We are a specialty pharmaceutical company focused on acquiring, developing and commercializing proprietary product candidates. We have not yet marketed or sold any products or generated any significant revenue.

Our lead product candidates, Exelbine (vinorelbine injectable emulsion), or ANX-530, and ANX-514 (docetaxel emulsion for injection), are novel emulsion formulations of currently marketed chemotherapy drugs. We believe Exelbine and ANX-514 may improve the safety of the currently marketed reference products, Navelbine® (vinorelbine tartrate) Injection and Taxotere® (docetaxel) Injection Concentrate, respectively.

In November 2010, we submitted a new drug application, or NDA, for Exelbine to the U.S. Food and Drug Administration, or FDA, and in January 2011, we announced that the FDA accepted the Exelbine NDA for filing and established a Prescription Drug User Fee Act, or PDUFA, goal date of September 1, 2011 to finish its review of the Exelbine NDA.

In February 2011, we met with the FDA to discuss ANX-514 and the data package we presented to FDA to support approval of ANX-514 based on data from our bioequivalence study of ANX-514. The FDA indicated that a randomized safety study comparing ANX-514 and Taxotere would be required to support approval of ANX-514. The study would be primarily descriptive but with a sample size sufficient to demonstrate a comparable safety profile. The FDA recommended that the study also collect data on response rate and duration of response. We are developing a study protocol for submission to the FDA and intend to continue discussions with the FDA regarding the phase 3 clinical study and other requirements for approval of ANX-514.

In 2010, we additionally began to focus on expanding our product pipeline through one or more in-license, asset acquisition or merger transactions. In August 2010, we announced that we engaged the investment banking firm Canaccord Genuity Inc. to advise us in connection with expanding our product pipeline and that our board of directors formed a special committee to assist the board in evaluating potential opportunities in this regard. The special committee, the members of which are Drs. Michael Goldberg, Odysseas Kostas (chair) and Eric Rowinsky, met regularly during the year with management and Canaccord Genuity to identify and evaluate opportunities and determine whether to recommend them to the full board of directors.

Pending Acquisition of SynthRx, Inc.

In February 2011, we entered into an agreement and plan of merger to acquire SynthRx, Inc., a privately-held company developing a purified form of a rheologic and antithrombotic agent, poloxamer 188, or 188, in exchange for shares of our common stock. We expect to consummate the acquisition of SynthRx in the first half of 2011. 188 is a nonionic block copolymer surfactant that adheres to hydrophobic surfaces that develop when cells are damaged. It has been shown to restore hydration lattices and minimize the cascade of adhesive, inflammatory and coagulation responses that cause adhesion of cells, impaired blood flow and tissue ischemia. Improving blood flow in the microvasculature may benefit patients with sickle cell disease in acute crisis, which is associated with microvascular occlusion. As discussed in more detail below, we initially intend to develop purified 188 for the treatment of sickle cell crisis in a pediatric population and, if our acquisition of SynthRx closes and we are able to reach agreement with the FDA on a study protocol on a timely basis, we may initiate a phase 3 clinical trial of purified 188 for that indication in 2012.

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Business Strategy

Our goal is to be a successful specialty pharmaceutical company focused on acquiring, developing and commercializing proprietary product candidates. Currently, we are focused primarily on oncology and, assuming our acquisition of SynthRx closes, disorders and conditions resulting from microvascular-flow abnormalities. However, we may pursue other therapeutic areas. Our near-term goals include consummating our acquisition of SynthRx, preparing for the commercial launch of Exelbine and reaching agreement with the FDA regarding phase 3 clinical study protocols for ANX-514 and purified 188, should the SynthRx acquisition close, and initiating the phase 3 studies. Specifically, with respect to our business strategy, we intend to:

Acquire SynthRx and pursue development of purified 188. We expect to consummate our acquisition of SynthRx in the first half of 2011. We initially intend to develop SynthRx s lead product candidate, purified 188, for the treatment of sickle cell crisis in a pediatric population. If we consummate our acquisition of SynthRx and we are able to reach agreement with the FDA on a study protocol on a timely basis, we may initiate a phase 3 clinical trial of purified 188 for that indication in 2012.

Seek regulatory approval for Exelbine in the U.S. In November 2010, we submitted an NDA for Exelbine to the FDA, and in January 2011, we announced that the FDA accepted the Exelbine NDA for filing and established a PDUFA goal date of September 1, 2011 to finish its review of the Exelbine NDA. We plan to work with the FDA to the extent possible to move Exelbine toward approval.

Reach agreement with FDA regarding a phase 3 safety study for ANX-514. Based on our February 2011 meeting with the FDA to discuss ANX-514, we believe a single, additional, randomized, phase 3 safety study could support FDA approval of ANX-514. We are developing a study protocol for submission to the FDA and intend to continue discussions with the FDA regarding requirements for regulatory approval of ANX-514.

Establish sales and marketing capabilities in the U.S. The oncology marketplace in general, and the anticipated target audience for Exelbine in particular, is concentrated. We believe a meaningful portion of the potential U.S. market for Exelbine can be accessed through an experienced sales force that targets key constituents of the treatment/product-selection decision-making process. In addition, we will evaluate opportunities to leverage an existing sales force by adding complementary products with a similar target audience. We have undertaken and expect to continue to undertake activities to prepare for the commercial launch of Exelbine, including developing and/or acquiring certain internal sales, distribution and marketing and associated regulatory compliance capabilities and contracting with third parties to supplement and enhance our internal capabilities. However, we remain receptive to partnering Exelbine in the U.S. if presented with terms that we believe would increase its value for our stockholders.

Acquire, develop and commercialize additional product candidates, products and/or capabilities. We continue to evaluate opportunities to expand our product pipeline and believe that, due to a challenging capital raising environment, many drug development programs with substantial potential are available at attractive valuations. We may also seek to acquire currently-marketed products that could complement our portfolio and provide a sales and marketing platform for our existing or future product candidates.

Pursue additional indications and commercial opportunities for our product candidates independently and through collaborations. We may increase the value of our product candidates by seeking approval for label changes and pursuing other commercial opportunities. For example, beyond sickle cell disease, we believe purified 188 may have clinical benefits in other acute events related to microvascular-flow abnormalities, such as heart attack, stroke and hemorrhagic shock.

Opportunities in Cancer Therapy

Despite recent advances in the treatment of certain tumor types, cancer remains a serious disease. The Centers for Disease Control and Prevention consistently ranks cancer as the second most common cause of death in the U.S. The American Cancer Society estimates that, in the U.S. in 2009, almost 1.5 million people were diagnosed with and over 550,000 people died from cancer.

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Exelbine and ANX-514 are designed to improve treatments for cancer patients. Treatment selection for cancer patients depends on the histology, stage and progression of the disease, along with the number and types of prior therapies, if any. Treatment options include surgery, radiation, chemotherapy, hormone therapy and immunotherapy, both alone and in combination with each other. Treatment of cancer with chemicals is referred to as chemotherapy.

Cancer treatments, including chemotherapy, typically are associated with side effects, some of which can be severe and, in rare cases, fatal. Not all side effects are the result of an active ingredient. Many side effects are associated with the manner in which a particular drug s active ingredient is formulated that is, side effects can be associated with the non-active components required to administer a drug. We believe formulating drugs with less toxic components can reduce undesirable side effects and provide other advantages. Without compromising the efficacy of a particular drug s active ingredient, novel formulations may provide patients with superior treatment options.

Our Novel Emulsion Formulations

Background and Opportunity

Reformulating existing pharmaceutical products is an increasingly common product lifecycle-management strategy. Finding new markets for and ways to modify and enhance existing products is often an essential element of pharmaceutical companies efforts to innovate and improve treatment outcomes in the context of patent expirations and competitive pressures.

Navelbine and Taxotere are intravenously-injected chemotherapy drugs commonly used to treat solid tumors. We believe the current formulations of these drugs have limitations, such as phlebitis, erythema, hypersensitivity reactions and fluid retention, that present opportunities for improvement. We are developing novel ways to formulate the active ingredient underlying each of these drugs that we believe may improve their safety profiles without adversely affecting efficacy. In addition, we believe our formulations may provide benefits to patients and practitioners that do not manifest themselves in traditional measures of safety or efficacy, such as handling and administration advantages for healthcare practitioners and patients.

Commercialization

Currently, we intend to build a commercial capability in the U.S. focused on Exelbine, as well as other products that we may develop or acquire. We believe we can achieve our strategic goals through a targeted approach that combines contracting with oncology group purchasing organizations, or GPOs, to help create awareness of our products and deploying a specialized, experienced sales force to call on physicians and nurses at community oncology practices and other organizations with defined characteristics, such as high vinorelbine use.

In preparing for the potential commercial launch of Exelbine, we expect to develop or acquire certain internal marketing, distribution and sales capabilities and associated regulatory compliance capabilities, as well as contract with third parties to supplement and enhance our internal capabilities.

HCPCS Product Codes and Reimbursement

In the U.S. and elsewhere, healthcare providers, including hospitals, nursing homes and physician offices, typically purchase and administer to patients the drugs that patients are restricted from self-administering. Healthcare providers then seek reimbursement, primarily from third-party payors such as Medicare, Medicaid and private insurance companies. As a result, sales of physician-administered prescription pharmaceuticals are dependent in large part on the availability and rate of reimbursement to healthcare providers from third-party payors.

The Healthcare Common Procedure Coding System, or HCPCS, was established to identify and provide unique codes for healthcare goods and procedures, including codes for injectable oncology drugs such as Exelbine and ANX-514, should they be approved. Ultimately, the Centers for Medicare and Medicaid Services, or CMS, is responsible for reviewing and approving applications for new HCPCS codes for healthcare goods. Generic equivalents of drugs are assigned the same HCPCS product code as the original drug. Virtually all U.S. payors, including Medicare and private insurance plans, use the HCPCS, including the product codes assigned by CMS.

In determining a specific reimbursement rate for a drug, CMS publishes an average sales price for the drug based on manufacturer-reported sales data for all drugs within the same HCPCS product code, including applicable discounts and rebates, as well as a reimbursement rate, expressed as a percentage of the average sales price. Because generic equivalents of drugs are assigned the same HCPCS product code as the original drug, generic competition can be expected to decrease the level of reimbursement for all drugs with the same HCPCS product code (both the original

drug and its generic equivalents) until price equilibrium is reached. Most private payors use similar methods for determining reimbursement rates, sometimes based on average wholesale prices or CMS published average sales price.

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A key component to our commercial strategy in the U.S. for Exelbine is to obtain a unique HCPCS product code that is distinct from the HCPCS product code for Navelbine and its generic equivalents. If our products are provided unique HCPCS product codes, they will be reimbursed based on their own sales prices, without including sales prices of the applicable reference product or its generic competition. We believe this will allow for appropriate pricing for our products relative to competitive products.

Exelbine (vinorelbine injectable emulsion)

Background; Limitations of Current Vinorelbine Formulations

Exelbine is a novel emulsion formulation of the chemotherapy drug, vinorelbine. Navelbine, a branded formulation of vinorelbine, is approved in the U.S. to treat advanced non-small cell lung cancer as a single agent or in combination with cisplatin, and approved in the European Union, or EU, to treat non-small cell lung cancer and advanced or metastatic breast cancer. Generic equivalents of Navelbine have been available in the U.S. since February 2003.

Navelbine and its generic equivalents are vesicants and often associated with injection site reactions, including phlebitis, erythema and pain at the site of injection. As reported in the Navelbine label, injection site reactions occurred in approximately one-third of 365 patients treated in three clinical studies with Navelbine as a single agent, with 5% of these reactions categorized as severe.

Exelbine was designed to be a bioequivalent formulation of Navelbine that may reduce the incidence and severity of injection site reactions to Navelbine. Our formulation emulsifies vinorelbine into a homogeneous suspension of nanoparticles that is designed to reduce the interaction between vinorelbine and the venous endothelium during administration into a peripheral vein, thereby reducing irritation associated with administration of the drug.

Exelbine New Drug Application

We submitted our Exelbine NDA under Section 505(b)(2) of U.S. Federal Food, Drug and Cosmetic Act, or FDCA, which pathway is discussed below under Government Regulations Section 505(b)(2) New Drug Applications. As such, in seeking approval of Exelbine, we are relying in part on the FDA s findings of safety and effectiveness with respect to Navelbine. We are seeking approval of Exelbine for the same indications as Navelbine. Our November 2010 Exelbine NDA included data from one clinical bioequivalence study designed to assess the pharmacokinetic equivalence of Exelbine and Navelbine, the reference drug for Exelbine, as well as 12 months of site-specific stability data from our intended commercial manufacturer to support expiration dating, which fulfilled a request communicated to us by the FDA following our prior submission of the Exelbine NDA in December 2009. In its refusal-to-file letter relating to our December 2009 Exelbine NDA submission, the FDA identified only this one chemistry, manufacturing and controls, or CMC, reason for the refusal to file.

Our decision to continue to develop Exelbine was based in part on positive results from the bioequivalence study we conducted, which was an open-label, single-dose, cross-over comparison of Exelbine and Navelbine. The FDA had indicated to us that data from such a study of approximately 28 patients that demonstrated the bioequivalence of Exelbine to Navelbine would be sufficient to support an NDA. Pharmacokinetic equivalence, the primary endpoint of our bioequivalence study, was observed between Exelbine and Navelbine. Based on federal regulations and FDA guidance regarding bioequivalence studies, pharmacokinetic equivalence was demonstrated by a statistical comparison of both the areas under the curve (AUC) and maximum plasma concentrations (Cmax). In addition, in post hoc analyses, relative to Navelbine, Exelbine demonstrated a statistically significant reduction in injection site reactions. Notably, in our study, the incidence of injection site reactions attributed to Navelbine was consistent with its product label.

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If approved, the drug prescribing information, or label, for Exelbine generally will be the same as for Navelbine, but may reflect differences between Exelbine and Navelbine or data generated during our bioequivalence trial, including comparative adverse event information. Ultimately, because the label for Exelbine, if approved, will be based on discussions with the FDA, we cannot predict with accuracy its final label. After we obtain marketing approval, we may conduct clinical studies while marketing Exelbine to expand its label in ways that might increase its use. If any clinical study we conduct, in addition to our bioequivalence study, is essential to the FDA s approval of an application to use Exelbine to treat a new indication, or to support a label change in product use, Exelbine may be eligible for three years of marketing exclusivity for that indication or use. Marketing exclusivity means that the FDA will not approve an abbreviated NDA, or ANDA (an ANDA is for a generic drug product), or an NDA submitted under Section 505(b)(2) of the FDCA during the exclusivity period based on the conditions of approval of our product.

Market and Opportunity

Based on data from IMS Health, total vinorelbine sold in the U.S. in 2009 was approximately 9.4 million milligrams. We estimate that the current average sales price for generic, or multi-source, vinorelbine in the U.S. is between $1.40 and $1.50 per milligram. The dollar value of the U.S. vinorelbine market has varied since 2003, when generic equivalents first became available in the U.S., in part due to competition among manufacturers of Navelbine and its generic equivalents. For instance, in September 2009, a new manufacturer of generic Navelbine entered the U.S. market. According to industry data, the price for this new entrant s product was lower than alternatives, which induced a lower average sales price for all products sharing the same HCPCS product code. To remain price-competitive and, because practitioners are reimbursed by CMS based on a percentage of average sales price, to prevent practitioners from being reimbursed at a level that is less than the acquisition cost of their product, other manufacturers may further reduce the prices for their products. As a result, each new entrant s pricing strategy may erode the total dollar value of the entire U.S. vinorelbine market.

As more fully described above under HCPCS Product Codes and Reimbursement, if Exelbine is granted a HCPCS product code that is distinct from the HCPCS product code for Navelbine and its generic equivalents, Exelbine would not be impacted directly by pricing competition in the way that products sharing the same HCPCS product code may be impacted. This should provide us the flexibility to establish an appropriate price for Exelbine and one that is different than the prices of multi-source vinorelbine. While we have not determined a price for Exelbine if it were approved by the FDA, we expect decision makers to value its unique formulation as compared to Navelbine and its generic equivalents, and we anticipate pricing Exelbine in the U.S. between $5 and $10 per milligram. If Exelbine is approved, granted a unique HCPCS product code and priced at a premium to multi-source vinorelbine, the potential dollar value of the U.S. Exelbine market likely will be greater than the dollar value of the existing U.S. vinorelbine market, assuming the same volume of vinorelbine demand.

Our market research, conducted among practicing oncologists and oncology nurses, suggests that healthcare practitioners prefer and would use a formulation of vinorelbine that reduced or eliminated injection site reactions while providing comparable efficacy, provided the financial impact to the practitioner of using such a formulation, relative to alternative formulations, is neutral or positive. Furthermore, for a variety of reasons, including anticipated frequent intravenous drug delivery and to avoid injection site reactions and loss of venous access, Navelbine often is administered through a central line, a more invasive procedure in which a catheter is inserted into and left for a period of time in a large vein in the neck, chest or groin. We believe Exelbine ultimately may provide an alternative to placing a central line for those patients for whom central lines are used primarily to avoid injection site reactions.

FDA Acceptance of Brand Name Exelbine

In March 2010, we announced that the FDA accepted our proposed proprietary name, Exelbine, for our novel emulsion formulation of the chemotherapy drug vinorelbine. The FDA s acceptance of our Exelbine brand name is conditioned upon its review of our Exelbine NDA and its confirmation of the information in the NDA regarding the safety of interchanging Exelbine with other vinorelbine injectable products.

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ANX-514 (docetaxel emulsion for injection)

Background; Limitations of Taxotere

ANX-514 is a novel emulsion formulation of the chemotherapy drug, docetaxel. Taxotere, a branded formulation of docetaxel, is approved to treat breast, non-small cell lung, prostate, gastric and head and neck cancers. Based on data from IMS Health, sales of Taxotere in 2010 were $1.2 billion in the U.S. and $2.9 billion worldwide, making it one of the top-selling anti-cancer agents in the world. However, in the U.S., patents covering docetaxel expired in 2010 and generic equivalents of Taxotere are expected to enter the market in 2011.

Despite its demonstrated efficacy and commercial success, the Taxotere formulation has limitations; principally, toxicity associated with its excipient, polysorbate 80. Docetaxel, the active ingredient in Taxotere, is lipophilic and practically insoluble in water. Successful development of the molecule for intravenous administration involved formulating the active ingredient with polysorbate 80 (1:26 docetaxel:polysorbate 80), a nonionic surfactant used in parenteral drug formulations as a solvent or solubilizing agent for drugs with poor aqueous solubility, and further dilution with ethanol.

Taxotere is associated with acute hypersensitivity reactions, ranging widely in incidence and severity. Taxotere also is associated with fluid retention. Many patients suffer severe (in rare cases, fatal) hypersensitivity reactions immediately following Taxotere administration. The occurrence of hypersensitivity reactions has been attributed, in part, to the intrinsic toxic effects of polysorbate 80; more specifically, to its oxidation products, which are known to cause histamine release. Even following premedication, which is required for Taxotere therapy as discussed below, hypersensitivity reactions have been observed, including, in rare cases, fatal anaphylaxis. Notably, Taxotere is contraindicated for patients with a history of hypersensitivity reactions to drugs formulated with polysorbate 80. The occurrence of fluid retention may be explained, in part, by the fact that polysorbate 80 has been shown to increase membrane permeability.

Taxotere therapy requires premedication with corticosteroids to reduce the severity of hypersensitivity reactions and the incidence and severity of fluid retention due to the presence of polysorbate 80 in the Taxotere formulation. The recommended premedication regimen for most cancer patients consists of oral corticosteroids, such as dexamethasone at 16 mg per day (e.g., 8 mg twice a day) for three days starting one day prior to Taxotere administration. Glucocorticoids, such as dexamethasone, affect blood-glucose levels, which can be problematic for diabetic patients, and may increase the risk of diabetes, osteoporosis and infection.

In addition, we believe that ANX-514 may also have handling and administration advantages for healthcare practitioners and patients. For example, Taxotere s label indicates foaming may occur when mixing Taxotere and the accompanying diluents due to the presence of polysorbate 80. Our market research suggests foaming is frequent, which can cause delays in administering the drug or disruption during administration if too much foam is present during administration. Polysorbate 80 also is incompatible with plasticized polyvinyl chloride, or PVC, which is used in making the IV bags and tubing commonly used to infuse chemotherapy drugs. Polysorbate 80 can leach diethylhexyl phthalate, a potentially hepatotoxic and carcinogenic acid, from plasticized PVC bags and tubing, resulting in the addition of diethylhexyl phthalate into the infusion solution. Taxotere s label warns against contact between Taxotere and plasticized PVC equipment. As a result, healthcare providers must have available and remember to use more costly non-PVC supplies to prepare and administer Taxotere, the costs of which generally are not separately reimbursed.

Potential Benefits of ANX-514

ANX-514 is a novel formulation of docetaxel that has the potential to improve outcomes for cancer patients. ANX-514 was designed to have clinically comparable release of docetaxel relative to Taxotere while eliminating the presence of polysorbate 80 and ethanol, both of which are used to solubilize docetaxel in the Taxotere formulation. The ANX-514 formulation solubilizes docetaxel using oil droplets comprised of a combination of non-toxic excipients. Docetaxel is contained within these oil droplets and can be administered intravenously without using detergents as pharmaceutical vehicles. Once in central circulation, the emulsion is metabolized rapidly, leaving chemically-identical active ingredient to exert its cytotoxic effect. The rate and extent of absorption of docetaxel from ANX-514 was designed to be comparable to that of Taxotere, resulting in similar clinical outcomes attributable to the active ingredient. However, the absence of polysorbate 80 and ethanol in the ANX-514 formulation has the potential

to improve the safety profile of ANX-514 relative to Taxotere and other formulations of docetaxel that use detergents as solubilizing agents or that contain alcohol.

A detergent-free docetaxel formulation may provide benefits to cancer patients. ANX-514 may reduce the incidence and severity of hypersensitivity reactions and delay the onset of fluid retention. ANX-514 also may minimize other adverse reactions to polysorbate 80, such as neurotoxicity.

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In addition, high-dose dexamethasone premedication intended to address polysorbate 80-mediated hypersensitivity reactions and fluid retention may be unnecessary with detergent-free ANX-514. Avoiding high-dose premedication could benefit diabetics and pre-diabetics (those with impaired fasting glucose). Dexamethasone and other glucocorticoids are associated with development of hyperglycemia. A study published in 2009 in the *Journal of the National Cancer Institute* examined the effect of dexamethasone on blood glucose levels in 39 women being treated for adjuvant breast cancer. All patients received 8 mg of oral dexamethasone per cycle for antiemsis, while those in a docetaxel arm received the recommended 24 mg cumulative dose. Before chemotherapy, none of the women had blood glucose in either the impaired glucose range or the diabetic range. However, among women who received the higher dose of dexamethasone, there was a statistically significant increase in blood glucose levels in later cycles (cycle 5: $p<0.001$; cycle 6: $p=0.002$). Following the fifth cycle, six women had blood glucose levels in the impaired range and eight women had levels within the diabetic range.

Nonclinical Efficacy and Safety

In nonclinical testing, we demonstrated that ANX-514 reduced hypersensitivity reactions without impacting pharmacokinetics or antitumor activity when compared to Taxotere. In an animal model, we observed anaphylactic reactions following Taxotere administration, including decreased respiration, swelling and tremors. Furthermore, decreases in blood pressure and increases in histamine levels were observed within 10 to 20 minutes of Taxotere administration. In contrast, we did not observe treatment-related changes in blood pressure or increases in histamine levels following administration of ANX-514. On re-challenge at three weeks, increases in histamine levels were observed only in the Taxotere-treated animals.

In addition, in two separate studies in different animal species, ANX-514 showed equivalent pharmacokinetics to Taxotere. In animal models, ANX-514 demonstrated dose-dependent inhibition of tumor growth with equivalent antitumor activity when compared to Taxotere at equal dose levels.

Planned Phase 3 Clinical Study

As with Exelbine, we expect to seek approval of ANX-514 under Section 505(b)(2) of the FDCA. Initially, we intended to demonstrate the bioequivalence of ANX-514 to Taxotere in a single bioequivalence study, which we refer to as Study 514-01, and which we completed in 2009. In May 2009, we announced that pharmacokinetic equivalence, the primary endpoint of Study 514-01, was not demonstrated based on the FDA s benchmark standards. The study data revealed higher average blood-levels of total (bound and unbound) docetaxel during and immediately following infusion of the study drug (i.e., during the first hour of treatment) in patients receiving ANX-514 relative to those receiving Taxotere, but, at 10 minutes after the completion of infusion, average total docetaxel blood-levels were comparable and remained so through the end of the observation period. Interestingly, the data also revealed lower average blood-levels of unbound, or free, docetaxel in patients receiving ANX-514 relative to those receiving Taxotere.

Following extensive analysis and modeling of the data from Study 514-01 and published results from other trials using Taxotere, we believe that comparable clinical outcomes can be expected following treatment with ANX-514 or Taxotere, despite Study 514-01 not demonstrating pharmacokinetic equivalence using FDA s benchmark standards.

In February 2011, we met with the FDA to discuss ANX-514 and the data package we presented to FDA to support approval of ANX-514. Because the Cmax for total docetaxel was higher following administration with ANX-514 in Study 514-01, the FDA indicated that a randomized safety study comparing ANX-514 and Taxotere would be required in an appropriate patient population to support approval of ANX-514. The study would be primarily descriptive but with a sample size sufficient to demonstrate a comparable safety profile. The FDA recommended that the study also collect data on response rate and duration of response. We are developing a study protocol for submission to the FDA and intend to continue discussions with the FDA regarding the phase 3 clinical study and other requirements for approval of ANX-514.

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Development Outside the U.S.

In March 2009, we announced that we and our wholly-owned subsidiary, SD Pharmaceuticals, Inc., had entered into a license agreement with respect to ANX-514 with Shin Poong Pharmaceutical Co., Ltd., a company organized under the laws of the Republic of Korea, pursuant to which we granted to Shin Poong an exclusive license, including the right to sublicense, to research, develop, make, have made, use, offer for sale, sell and import licensed products, in each case solely for the treatment of cancer by intravenous administration of formulations of docetaxel as emulsified products and solely in South Korea. Under the terms of the agreement, we received an upfront licensing fee and are entitled to receive a regulatory milestone payment upon receipt of regulatory approval for marketing a licensed product in South Korea (the amount depends on whether the Korea Food and Drug Administration requires Shin Poong to conduct a bioequivalence or clinical study in human subjects prior to receipt of regulatory approval), one-time commercial milestone payments tied to annual net sales of licensed products and royalty payments on net sales of licensed products. Shin Poong is responsible for all development and commercial activities related to ANX-514 in South Korea.

Potential New Opportunity Purified Poloxamer 188

Background

Poloxamer 188, or 188, is a nonionic block copolymer surfactant that has been used in foods, drugs and cosmetics since the 1950s. In the 1980s, extensive research on the mechanisms and potential clinical applications of 188 was conducted. Research has demonstrated that 188 adheres to hydrophobic surfaces that develop when cells are damaged and restores normal hydrated surfaces, while having little or no activity in normal, healthy tissues. Research also has demonstrated that 188 prevents adhesion and aggregation of soluble fibrin and formed elements in the blood, maintains the deformability of red blood cells, non-adhesiveness of unactiviated platelets and granulocytes and the normal viscosity of blood. In addition, it is believed that 188 is not metabolized, but is excreted unchanged in the urine with a half-life of approximately two hours. Likewise, it is believed that 188 is not absorbed following oral administration, but is recovered unchanged in the stool.

We believe that 188 has numerous potential applications as a cytoprotective, rheologic, antithrombotic and anti-inflammatory agent. 188 has been evaluated in the clinic to treat acute myocardial infarction, sickle cell disease and malaria, including a 2,950-patient, randomized, controlled study in acute myocardial infarction. The effectiveness of 188 also has been observed in studies investigating its application in stroke, hemorrhagic shock, bypass surgery, adult respiratory distress syndrome, neurologic protection in deep hypothermic circulatory arrest, vasospasm, spinal cord injury, angioplasty, frostbite, amniotic fluid embolism, acute ischemic bowel disease and burns.

Purified 188 is designed to eliminate impurities present in, and associated renal toxicity that was observed in certain prior clinical investigations of, (non-purified) 188. Purified 188 has been evaluated in multiple clinical studies, including a 255-patient, phase 3 study, in which elevated levels of renal toxicity were not observed.

Sickle Cell: Clinical History; Planned Phase 3 Clinical Study

The safety and efficacy of 188 and purified 188 in sickle cell disease have been evaluated in multiple clinical studies, including a 255-patient, randomized, double-blind, placebo-controlled phase 3 study in patients with sickle cell disease in acute vaso-occlusive crisis.

In the phase 3 study, signs of efficacy were observed in the primary endpoint, duration of crisis. However, features of the study s design and the study not enrolling the originally-planned number of patients may have diluted the treatment effect or its significance. Notably, in a planned subgroup analysis in children (n=73), in which the effect of confounding factors may have been mitigated (such as chronic pain syndrome, which is less prevalent in children), a statistically significant and greater treatment effect was observed. In terms of safety, there were no differences between the two treatment groups in the overall incidence of adverse events, for adverse events defined as serious, or for adverse events involving any body system for the groups as a whole. It was determined that renal function was not influenced by treatment with purified 188. However, the purified 188 arm did exhibit a modest but statistically significant increase in levels of alanine aminotransferase and direct bilirubin, each of which returned to its respective baseline level by the day-35 follow-up visit.

We believe that a properly designed and executed clinical study will demonstrate that purified 188 is an effective treatment for sickle cell crisis. Assuming our acquisition of SynthRx closes, we intend to develop purified 188 for the

treatment of sickle cell crisis in a pediatric population and plan to meet with the FDA to reach agreement on a phase 3 clinical trial protocol.

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Sickle Cell: Market and Opportunity

Vaso-occlusive crisis, caused by sickle-shaped red blood cells that obstruct capillaries and restrict blood flow to an organ, causes pain that is often very severe and results in ischemia (restriction of blood supply), necrosis, and often organ damage. The frequency, severity and duration of these crises can vary considerably. Once vaso-occlusive crisis occurs, treatment consists of maintenance of hydration, oxygenation and analgesia, usually using narcotics. Preventative measures for pulmonary complications, such as incentive spirometry, and blood transfusion also may be used. We are not aware of any currently available agents with demonstrated efficacy in shortening the duration of vaso-occlusive crisis. Patients with sickle cell disease experience an average life expectancy of approximately 40 years.

More than $1.0 billion is spent annually in the U.S. to treat patients with sickle cell disease. We estimate that, in the U.S., sickle cell disease results in over 95,000 hospitalizations and approximately 69,000 emergency department treat-and-release encounters each year. When a patient with sickle cell disease makes an institutional visit, vaso-occlusive crisis is the primary diagnosis in approximately 77% of hospital admissions and 64% of emergency room treat-and-release encounters. In addition, although the number of untreated crisis events is difficult to measure, we estimate that it is substantial and in the hundreds of thousands in the U.S. each year. We believe that, if purified 188 is approved, as people with sickle cell disease are made aware of the new therapy, more people who suffer from vaso-occlusive crisis will seek treatment.

Competition

If regulatory authorities approve the marketing and selling of any of our product candidates, our product candidates will face significant and long-term competition from pharmaceutical companies, pharmaceutical divisions of companies and biotechnology, biopharmaceutical and specialty pharmaceutical companies, among others. This competition likely will become more intense if any of our products or competitor products achieves significant commercial success. Most of our competitors, particularly large pharmaceutical companies, have greater clinical, regulatory, manufacturing, marketing, distribution, compliance and financial resources and experience than we do. Many of these companies have commercial arrangements with other companies to supplement their internal capabilities.

Over the longer term, our ability, independently or with a strategic or other partner, to successfully manufacture, market, distribute and sell any of our or their approved products, expand their usage and bring new products to the marketplace will depend on many factors, including, but not limited to, the effectiveness and safety of those products, FDA and foreign regulatory agencies approvals of new products and indications, the degree of patent protection afforded to particular products and the rates at which those products are reimbursed.

Exelbine and ANX-514

Exelbine and ANX-514, if approved, may compete against Navelbine and Taxotere, respectively, as well as their generic equivalents and other formulations of vinorelbine and docetaxel that may be approved by the FDA. In addition to Navelbine, in the U.S., currently there are seven commercially available generic versions of vinorelbine. With respect to docetaxel, in the U.S., we believe non-Taxotere formulations of docetaxel will be commercially available in 2011 and that generic equivalents of Taxotere will be commercially available in the near-term, possibly in 2011. However, we are not aware of any docetaxel formulation with near-market potential that is polysorbate 80-free.

Because we have submitted our Exelbine NDA with only bioequivalence data, the ability to differentiate it from competing products will be limited. Even if we believe Exelbine demonstrates clinical, pharmacoeconomic or other benefits relative to competing products, we may be unable to market or promote it based on these benefits. If our products do not receive unique HCPCS product codes, we may be required to price our products at levels that do not cover our costs to manufacture, market and distribute the products or provide any profit, or to price our products at levels at which they are not competitive.

In addition, numerous companies are focused on reformulating currently marketed drugs. In particular, the taxanes, the class of drugs of which Taxotere is a member, have experienced substantial commercial success, in part as a result of their effectiveness in treating a wide variety of cancers. This commercial success has generated significant interest in reformulating Taxotere and other taxanes. For instance, in 2010, the FDA approved Jevtana® for treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment

regimen. The active ingredient of Jevtana is cabazitaxel, an antineoplastic agent belonging to the taxane class.

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In addition to our approach of emulsifying docetaxel, other companies may be pursuing alternative delivery vehicles, including the use of albumin nanoparticles, prodrugs, polyglutamates, analogs, co-solvents, liposomes and microspheres. Many of these or similar approaches might also be applied to vinorelbine. Relative to our formulations, formulations based on one or more of these other methods may result in greater efficacy or safety, provide better drug delivery to tumor sites or otherwise improve benefits to patients and healthcare providers. For instance, there is an oral formulation of vinorelbine approved for use in the EU against which Exelbine would compete if it were approved for use in the EU.

Purified 188 for Sickle Cell Crisis

Currently, most treatment options for sickle cell crisis are focused on symptomatic relief or treatment to address complications, such as morphine or other analgesics for pain. However, there is substantial interest in developing agents for the treatment of sickle cell crisis. In addition to for-profit commercial enterprises, numerous foundations and interest groups also are committed to treating sickle cell disease and preventing and mitigating acute crisis associated with sickle cell disease. We are aware of numerous companies with product candidates in varying stages of development for the treatment of sickle cell crisis, including mechanisms that target the sPLA2 enzyme or P2Y12 ADP receptor, increase oxygen binding of hemoglobin or stimulate production of fetal hemoglobin. Advances in the understanding of the signaling pathways associated with sickle cell disease may lead to further interest and development of treatment options.

More broadly, purified 188 would compete against agents designed to treat sickle cell disease, of which sickle cell crisis is a condition. Hydroxyurea, a form of chemotherapy used for myeloproliferative disease, has been shown to decrease the severity of sickle cell disease by reducing the frequency of crisis, but hydroxyurea does not treat the crisis itself. Blood transfusions, which carry risk of allergic reactions and iron overload, also are used to treat sickle cell disease. Bone marrow and stem cell transplantation have been shown to be effective to treat and, in some cases, cure sickle cell disease, but current methods are expensive, require a well-matched donor and come with risk of serious complications including bleeding, pneumonia, and severe infection.

In addition, there is increasing interest in developing drugs for rare diseases, which may have the effect of increasing the development of agents to treat sickle cell disease generally or sickle cell crisis in particular. GlaxoSmithKline and Pfizer each recently formed a unit focused on rare diseases. Legislative action, such as the potential to expand the priority review voucher system to rare pediatric diseases, may further generate interest.

Manufacturing

We do not have our own manufacturing facilities. We meet our nonclinical and clinical trial manufacturing requirements (including manufacturing active pharmaceutical ingredient, or API, formulating and assembling final drug product, labeling, testing and release, packaging, storing API and finished drug product and similar activities) by establishing relationships with third-party manufacturers and other service providers to perform these services for us.

In the past, with respect to Exelbine and ANX-514, we relied on individual proposals and purchase orders to meet our needs and typically relied on terms and conditions proposed by the third party or us to govern our rights and obligations under each order (including provisions with respect to intellectual property, if any). In 2008, we entered into a master services agreement with a new contract manufacturer, as well as individual work orders that are governed by the master services agreement, under which the manufacturer provided process development and scale-up activities for Exelbine. We do not have any long-term agreements or commitments for these services. Likewise, we do not have any long-term agreements or commitments with vendors to supply the underlying component materials of Exelbine, some of which are available from only a single supplier. We are in the process of entering into supply arrangements with third parties in connection with the potential commercialization of Exelbine. We also are in the process of evaluating vendors with respect to manufacturing ANX-514.

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Purified 188 is manufactured by applying a proprietary, super-critical fluid extraction (SCFE) process to commercial grade 188, which is available from several manufacturers. We believe multiple vendors have the capability to manufacture both purified 188 drug substance pursuant to this SCFE process and the final, finished drug product. However, prior to manufacturing additional purified 188, including for clinical use, we expect to evaluate critical operating parameters and ranges and, ultimately, to re-validate the SCFE process with the anticipated manufacturers.

As noted above with respect to Exelbine, should any of our product candidates obtain marketing approval, relationships with third-party manufacturers and other service providers in connection with the commercial production of our products would need to be established. There is some flexibility in securing other manufacturers to produce our product candidates; however, our alternatives may be limited due to proprietary technologies or methods used in the manufacture of some of our product candidates. In addition, if we seek to make certain changes to an approved product, such as changing vendors who supply the underlying component materials of our product candidates, we will need FDA review and approval before the change can be implemented. For example, if we change the manufacturer of a product or of the API component of a product, the FDA may require stability or other data from the new manufacturer, which data will take time and is costly to generate, and the delay associated with generating this data may cause interruptions in our ability to meet commercial demand, if any.

Intellectual Property

Exelbine (vinorelbine injectable emulsion)

We own world-wide rights (excluding China, Hong Kong, Macau and Taiwan) to patent applications covering the composition and use of our vinorelbine injectable emulsion product candidate, subject to the exclusive license we granted to Latitude Pharmaceuticals (described below under Licensing Agreement). In January 2011, the United States Patent and Trademark Office, or USPTO, issued patent claims directed to formulations of vinorelbine bitartrate that provide protection for Exelbine. U.S. Patent No. 7,871,632, entitled Compositions for Delivering Highly Water Soluble Drugs, will provide coverage for Exelbine until November 2027. In addition, in December 2010, we filed a continuation application of U.S. Patent No. 7,871,632 in the USPTO claiming a priority date of July 12, 2004 drawn to methods of treatment. With respect to patent protection outside the U.S., patents entitled Compositions for Delivering Highly Water Soluble Drugs have issued in Japan and Russia and will provide coverage for Exelbine until July 2025. In addition, patent applications entitled Compositions for Delivering Highly Water Soluble Drugs currently are pending in Canada, India, South Korea and the European Patent Office. These applications have a priority date of July 12, 2004, and any patents granted thereon will have an expected expiration date of July 2025.

ANX-514 (docetaxel emulsion for injection)

We own world-wide rights (excluding China, Hong Kong, Macau and Taiwan) to patent applications covering the composition and use of our docetaxel injectable emulsion product candidate, subject to the exclusive licenses we have granted to Latitude Pharmaceuticals (described below under Licensing Agreements) and Shin Poong Pharmaceutical Co., Ltd. (described above under ANX-514 Development Outside the U.S.). Patent applications, entitled Low Oil Emulsion Compositions for Delivering Taxoids and Other Insoluble Drugs, currently are pending in the U.S., Canada, India, Japan, South Korea, Mexico and the European Patent Office. These applications have a priority date of September 28, 2004, and any patents granted thereon will have an expected expiration date of September 2024 in the U.S. and September 2025 in the other countries.

Patent applications, entitled Vitamin E Succinate Stabilized Pharmaceutical Compositions, Methods for the Preparation and Use Thereof, currently are pending in the U.S., Canada, Australia, India, Japan, South Korea, Mexico, New Zealand, the European Patent Office and the Eurasian Patent Office. These applications have a priority date of February 1, 2006, and any patents granted thereon will have an expected expiration date of February 2027 in the U.S. and in the other countries.

Purified 188 for Sickle Cell Crisis

Assuming our acquisition of SynthRx closes, pursuant to an agreement with CytRx Corporation (described below under Licensing Agreements), we will acquire exclusive rights to a variety of issued patents related to poloxamers and their uses. The issued patents cover, among other things, 188, purified 188, methods of treating sickle cell anemia using 188 and methods of preparing purified 188. However, we expect many of the patents covering purified 188 for the treatment of sickle cell crisis will expire prior to regulatory approval of purified 188 for that indication.

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We believe the primary method of exclusivity for purified 188 for the treatment of sickle cell crisis will be the orphan drug designation that the FDA has granted for 188. Accordingly, as described below under Government Regulations, if our product candidate receives the first FDA approval for sickle cell crisis, the FDA may not approve any other application to market 188 for sickle cell crisis for a period of seven years, except in limited circumstances, such as another product showing clinical superiority to 188. However, orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. In addition, competitors may receive approval of different drugs or biologics for sickle cell crisis or sickle cell disease generally. In addition, if we and the FDA reach agreement that the planned phase 3 study in a pediatric population will satisfy the requirements for pediatric exclusivity, upon FDA approval, we may be granted an additional six months of marketing exclusivity.

Assuming our acquisition of SynthRx closes, we also will acquire ownership of certain patent applications related to 188 for the treatment and diagnosis of chronic inflammation due to chronic microvascular diseases and use in increasing the safety and efficacy of blood transfusions and improving oxygenation of jeopardized tissue.

We are aware of a substantial number of patents issued and patent applications filed in our technical areas or fields. There is a risk that third parties may allege that they have patent rights encompassing our product candidates or methods and no assurance can be given that patents do not exist, have not been filed, or could not be filed or issued, that contain claims covering our product candidates or methods.

We cannot provide assurance that our pending patent applications will issue as patents, that any issued patents will provide us with significant competitive advantages, or that the validity or enforceability of any of our patents will not be challenged or, if instituted, that these challenges will not be successful. The cost of litigation to uphold the validity and prevent infringement of our patents could be substantial. Furthermore, we cannot provide assurance that others will not independently develop similar technologies or duplicate our technologies or design around the patented aspects of our technologies. We can provide no assurance that our proposed technologies will not infringe patents or rights owned by others, licenses to which might not be available to us.

In addition, the approval process for patent applications in different countries may differ significantly. The patent authorities in each country administer that country s laws and regulations relating to patents independently of the laws and regulations of any other country and the patents must be sought and obtained separately, which can add substantial cost and expense. In addition, a favorable outcome or approval in one country does not necessarily indicate that a favorable outcome or approval can be obtained in other countries.

Trademarks

We have applied for trademark registration for EXELBINE in the U.S. We are developing commercial names for our other product candidates. All other trademarks, service marks or trade names appearing in this report, including but not limited to Navelbine® and Taxotere®, are the property of their respective owners. Use or display by us of other parties trademarks, service marks, trade names, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, service mark, trade name, trade dress or product owners.

Research and Development

Our research and development expenses were $3.7 million in 2010 and $6.5 million in 2009. Our research and development expenses consist primarily of costs associated with nonclinical activities, such as research-related manufacturing, nonclinical research studies, quality assurance and regulatory activities, salaries and related employee benefits, and costs associated with bioequivalence and clinical trials managed by contract research organizations, or CROs. In 2010, our most significant costs were for consulting services related to the November 2010 Exelbine NDA, stability testing for Exelbine and consulting services related to evaluation of the data from Study 514-01 and research-related manufacturing for ANX-514. In 2009, our most significant costs were for manufacturing, analytical and stability testing for Exelbine and consulting services related to the December 2009 Exelbine NDA. Our research-related manufacturing expenses include purchasing API, manufacturing materials for bioequivalence and clinical trials and stability testing to support regulatory filings, related labeling, testing and release, packaging and storing and related consulting fees. Our bioequivalence and clinical trial expenses include payments to vendors such as CROs, investigators, clinical suppliers and related consulting fees.

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Licensing Agreements

SD Pharmaceuticals

In April 2006, we acquired SD Pharmaceuticals, Inc. in exchange for shares of our common stock. Under a prior license agreement between SD Pharmaceuticals, Latitude Pharmaceuticals, Inc. and Andrew X. Chen, the sole owner of Latitude Pharmaceuticals, Dr. Chen had assigned to SD Pharmaceuticals all rights and interests of Dr. Chen and Latitude Pharmaceuticals to certain patents throughout the world other than in China, Hong Kong, Macau and Taiwan. Under this agreement, SD Pharmaceuticals granted back to Latitude Pharmaceuticals a worldwide, exclusive, royalty-free and irrevocable license to use the assigned patents in all fields of use other than certain excluded fields as specified in the agreement. Our rights in Exelbine and ANX-514 arise through our interest in SD Pharmaceuticals. Accordingly, we have no rights in these product candidates in China, Hong Kong, Macau and Taiwan, and our rights under the assigned patents in the rest of the world are limited to the following fields:

For Exelbine, vinca alkaloid intravenous emulsion formulation for cancer treatment and any other disease indication.

For ANX-514, docetaxel intravenous emulsion formulation for cancer treatment and any other disease indication.

CytRx Corporation

Assuming our acquisition of SynthRx closes, we will acquire a 2004 license agreement between CytRx Corporation and SynthRx. Under the agreement, as amended, CytRx granted to SynthRx an exclusive license, with the right to grant sublicenses, under specified patents to use, offer and sell licensed products in all of the countries in the world and in all fields, except those fields that, at the time of the agreement, were or will be licensed pursuant to certain identified agreements. We believe that the field limitation does not prevent us from developing or commercializing purified 188 for the treatment of sickle cell crisis.

In partial consideration of the license grant, SynthRx agreed to pay CytRx certain non-refundable and non-creditable milestone payments based on the approval of each product in a major market, which includes the U.S. The amount of each milestone is in the low single-digit millions, half of which is due on the first commercial sale of the approved product and half of which is due as a royalty on net sales. In addition, SynthRx would pay a single-digit royalty on net sales of licensed products. However, in the event of a sublicense under the specified patents, in lieu of the foregoing milestone and royalty payments, SynthRx, in its sole discretion, may elect to pay CytRx an amount equal to 20% of any sublicensing income received by SynthRx within 30 days of receipt thereof. Sublicense income includes, without limitation, license fees, royalties, milestone payments, license maintenance fees and strategic alliance payments, whether in cash, equity or other property, with the payment to be in the same form as the payment received by SynthRx.

Material Terms of the Pending Acquisition of SynthRx

Under the terms of our merger agreement with SynthRx, in connection with consummation of the merger we would issue 2,938,773 shares of our common stock to SynthRx s stakeholders, of which 200,000 shares would be placed in escrow for 12 months following the closing of the merger to indemnify us against breaches of SynthRx s representations and warranties, and 1,938,773 shares would be subject to repurchase rights by us pending achievement of the first development milestone described below. We would issue up to an aggregate of 13,478,050 additional shares of our common stock to SynthRx s stakeholders if the development of purified 188 achieves certain milestones, as described below, and our stockholders approve the issuance of such milestone-related shares, as required by NYSE Amex rules. If our stockholders do not approve the issuance of the milestone-related shares, under the terms of the merger agreement, we would be required to pay SynthRx s stakeholders in cash the value of the milestone-related shares we would have otherwise issued, with all such cash payments made in quarterly installments and, with respect to the cash value associated with 12,478,050 of the milestone-related shares, payable based on net sales of purified 188. We cannot determine with any degree of certainty the amount of our potential cash payments to SynthRx s stakeholders because the amount of such payments, if applicable, will depend on the 10-day volume weighted average of the closing price of our common stock at the time a milestone is achieved and the market price of our common stock historically has been, and likely will continue to be, highly volatile. Of the shares issuable in connection with achievement of milestones, up to 1,000,000 shares would be issuable upon the dosing of the first patient in a phase 3

clinical study that the FDA has indicated may be sufficient to support approval of a new drug application covering the use of purified 188 for the treatment of sickle cell crisis in children, or the 188 NDA, which we refer to as the First Milestone; 3,839,400 shares would be issuable upon acceptance for review of the 188 NDA by the FDA, which we refer to as the Second Milestone; and 8,638,650 shares would be issuable upon approval by the FDA of the 188 NDA, which we refer to as the Third Milestone.

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Under the terms of the merger agreement, we have agreed to use commercially reasonable efforts (a) to request a meeting with the FDA to occur within nine months of the closing of the merger for the purpose of discussing clinical development and regulatory approval of an intravenous injection product in which a purified form of 188 is an active ingredient and (b) during the one-year period following the closing of the merger, to conduct certain activities related to the development of purified 188; provided that the aggregate cost of such activities does not exceed $1.5 million. We have also agreed to use commercially reasonable efforts to develop an intravenous injection product in which a purified form of 188 is an active ingredient until the earlier of achievement of the Third Milestone or the date that is four years after February 12, 2011. In addition, we have agreed not to consummate a change of control with a third party that involves all or substantially all of SynthRx s assets until the earlier of the achievement of the Third Milestone and the date that is four years following February 12, 2011, except (x) in connection with an Exempt Transaction (as described below) or (y) with the written consent of SynthRx, which consent shall not be unreasonably withheld, conditioned or delayed. Under the merger agreement, an Exempt Transaction is a change of control that closes prior to achievement of the Third Milestone in which the acquiror agrees in writing to submit the 188 NDA to the FDA for FDA approval (or, if there are unexpected safety or regulatory issues, to conduct activities to address or resolve such issues) until the earlier of (i) the date that, beginning at the effective time of the merger and thereafter, the aggregate expenditure related to the program involving the product candidate on which the 188 NDA is to be based is at least $15,000,000 and (ii) the fourth anniversary of the effective time of the merger; provided, however, such acquiror shall be relieved of such obligations under certain specified conditions.

In connection with our execution of the merger agreement, each of SynthRx s stockholders entered into a voting and transfer restriction agreement with us, the term of which will commence at the effective time of the merger. Under the voting and transfer restriction agreement, each SynthRx stockholder has agreed to vote all shares of our common stock beneficially owned by that stockholder with respect to every action or approval by written consent of our stockholders in such manner as directed by us. Notwithstanding the foregoing, until the earlier of: (a) achievement of the Third Milestone and (b) the four year anniversary of the closing of the merger, each SynthRx stockholder will be permitted to vote any shares of our common stock beneficially owned by that stockholder in such stockholder s sole discretion solely with respect to a change of control that involves the transfer of SynthRx s assets to a third party and in which at least 80% of the consideration received by our company (or our stockholders) is non-contingent and paid in cash. In addition, pursuant to the voting and transfer restriction agreement, SynthRx stockholders may not transfer any shares of our common stock that are subject to vesting or that are held in escrow. We refer to shares of our common stock issued to SynthRx stockholders that have vested and/or been released from escrow as Transferable Shares. Transferable Shares may be transferred by their holder to an affiliate of such holder in accordance with applicable securities laws, provided that any such transferee becomes a party to the voting and transfer restriction agreement. The voting and transfer restriction agreement also provides that SynthRx s stockholders, as a group, will have the right to transfer Transferable Shares to non-affiliates pursuant to an effective resale registration statement, which we agreed to file within 120 days of the effective time of the merger, or in compliance with Rule 144 of the Securities Act of 1933, (a) on each trading day, such aggregate number of Transferable Shares as is equal to or less than 10% of the average daily trading volume of our common stock, and (b) not more than once in any 12-month period, such aggregate amount of Transferable Shares as is equal to five times the average daily trading volume of our common stock.

Prior Cost-Containment and Fundraising Activities

In the past, we spent significant resources on the development of ANX-510, or CoFactor®, including a 300-patient phase 2b clinical trial and a discontinued phase 3 clinical trial. Following our October 2007 announcement that CoFactor did not meet the primary endpoint in the phase 2b clinical trial, in October 2008, we discontinued active work on our CoFactor program. In June 2010, we granted an exclusive worldwide license for CoFactor to Theragence, Inc., which includes the right to grant sublicenses under certain circumstances, to conduct research on and to develop, make, have made, use, offer for sale, sell, have sold and import licensed products in any field or use.

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Beginning in October 2008 and through June 2009, we implemented numerous restructuring, cost-cutting and re-prioritization initiatives to reduce operating costs and to focus on those of our options that we believed maximized the overall value of our company. For instance, in October 2008, in addition to the discontinuation of our CoFactor program, we discontinued active work on all compounds to which we have or had rights and on which we may have previously spent resources developing, other than Exelbine and ANX-514. In addition, during that period, we suspended substantially all fundamental business operations and effected three reductions in our full-time employee workforce while we explored options for capital-raising and/or strategic transactions as well as liquidating our assets and winding-up our operations.

Since June 2009, we have completed seven registered direct financing transactions, raising an aggregate of approximately $56.7 million in net proceeds, after deducting our aggregate dividend and related payment obligations, the fees and expenses of our placement agent and financial advisor in those financings and our other estimated offering expenses. In addition, in December 2009 and January 2010, we raised an aggregate of approximately $3.3 million in net proceeds in connection with the exercise of warrants issued in connection with certain of these financings.

Government Regulations

Governmental authorities in the U.S. and other countries extensively regulate the testing, manufacturing, labeling, storage, recordkeeping, advertising, promotion, export, marketing and distribution, among other things, of pharmaceutical products. In the U.S., the FDA, under the FDCA and other federal statutes and regulations, subjects pharmaceutical products to rigorous review. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our products, and we may be criminally prosecuted.

We and our third-party manufacturers, distributors and CROs may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, the Health Insurance Portability and Accountability Act, privacy laws and import, export and customs regulations, as well as the laws and regulations of other countries.

FDA Approval Process

To obtain approval of a new product from the FDA, we must, among other requirements, submit data supporting safety and efficacy, as well as detailed information on the manufacture and composition of the product and proposed labeling. The testing and collection of data and the preparation of necessary applications are expensive and time-consuming. The FDA may not act quickly or favorably in reviewing these applications, and we may encounter significant difficulties or costs in our efforts to obtain FDA approvals that could delay or preclude us from marketing our products.

The process required by the FDA before a new drug may be marketed in the U.S. generally involves the following: (i) completion of nonclinical laboratory and animal testing in compliance with FDA regulations; (ii) submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin; (iii) performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use; and (iv) submission and approval of an NDA by the FDA. The sponsor typically conducts human clinical trials in three sequential phases, but the phases may overlap. In phase 1 clinical trials, the product is tested in a small number of patients or healthy volunteers, primarily for safety at one or more doses. In phase 2, in addition to safety, the sponsor evaluates the efficacy of the product on targeted indications, and identifies possible adverse effects and safety risks, in a patient population somewhat larger than in phase 1 clinical trials. Phase 3 clinical trials typically involve additional testing for safety and clinical efficacy in an expanded population at geographically-dispersed test sites. A clinical trial may combine the elements of more than one phase and, typically, two or more phase 3 studies are required. A company s designation of a clinical trial as being of a particular phase is not necessarily indicative that the trial will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. In addition, a clinical trial may contain elements of more than one phase notwithstanding the designation of the trial as being of a particular phase.

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As a product candidate moves through the clinical phases, manufacturing processes are further defined, refined, controlled and validated. The level of control and validation required by the FDA increases as clinical studies progress.

Clinical trials must be conducted in accordance with the FDA s good clinical practices requirements. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. An institutional review board, or IRB, generally must approve the clinical trial design and patient informed consent at each clinical site and may also require the clinical trial at that site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions. It is not possible to estimate with any certainty the time required to complete phase 1, 2 and 3 studies with respect to a given product candidate.

The applicant must submit to the FDA the results of the nonclinical studies and clinical trials, together with, among other things, detailed information on the manufacture and composition of the product and proposed labeling, in the form of an NDA, including payment of a user fee, unless waived. The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting an NDA for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under PDUFA, the FDA ordinarily has 10 months in which to complete its initial review of the NDA and respond to the applicant. However, the PDUFA goal dates are not legal mandates and the FDA response often occurs several months beyond the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the NDA submission. The NDA review process can, accordingly, be very lengthy. During its review of an NDA, the FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. Data from clinical trials are not always conclusive and the FDA and/or any advisory committee it appoints may interpret data differently than we or any future partner of ours interprets data.