ADVENTRX PHARMACEUTICALS INC Form 424B5 May 16, 2006

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The information in this prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Filed Pursuant to rule 424(b)(5) Registration No. 333-133729

#### SUBJECT TO COMPLETION

May 16, 2006

# PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated May 8, 2006) **15,495,867 Shares** Common stock

We are offering all of the 15,495,867 shares of common stock offered by this prospectus supplement. Our common stock is quoted on the American Stock Exchange (AMEX) under the symbol ANX. On May 12, 2006, the last reported sale price of our common stock on the AMEX was \$4.84 per share.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should read the discussion of material risks of investing in our common stock in Risk factors beginning on page S-14. Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds, before expenses, to us	\$	\$

The underwriters may also purchase up to an additional 2,324,380 shares of our common stock at the public offering price, less the underwriting discounts and commissions, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

The underwriters are offering the common stock as set forth under Underwriting. Delivery of the shares will be made on or about May , 2006.

Sole Book-Running Manager

UBS Investment Bank

CIBC World Markets

Fortis Securities LLC

RBC Capital Markets

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. If information in this prospectus supplement is inconsistent with the accompanying prospectus, you should rely on the prospectus supplement. We have not and the underwriters have not authorized anyone to provide you with information that is different from or in addition to that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. We are not, and the underwriters are not, offering to sell or seeking offers to buy shares of common stock in jurisdictions where offers and sales are not permitted. You should not assume that the information provided in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference in this prospectus supplement and in the accompanying prospectus is accurate as of any date other than as of their respective dates, regardless of the time of delivery of this prospectus supplement or of any sale of our common stock. Changes may occur after those dates and we may not update this information except as required by law.

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CoFactor®, Selonetm and Thiovirtm are trademarks of ADVENTRXtm. This prospectus supplement and the accompanying prospectus contain product names, trade names and trademarks of other entities.

In this prospectus supplement, ADVENTRX, Company, we, us and our refer to ADVENTRX Pharmaceuticals, Delaware corporation, unless otherwise expressly stated or the context requires otherwise.

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# Prospectus supplement summary

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before buying our common stock in this offering. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the Risk factors, the financial data and related notes and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus before buying our stock.

# **OUR BUSINESS**

We are a biopharmaceutical research and development company focused on developing treatments for cancer and infectious diseases. We seek to develop compounds which surpass the performance and safety of existing drugs by addressing significant problems such as poor drug metabolism, toxicity, bioavailability and drug resistance. We have four cancer drug candidates, including CoFactor for metastatic colorectal cancer, breast cancer, and additional chemotherapy regimens including leucovorin/5-FU, and vinorelbine emulsion for non-small cell lung cancer. We have pending a request for a Special Protocol Assessment (SPA) for a Phase III clinical trial for CoFactor. We currently expect to initiate our CoFactor Phase III clinical trial in the second quarter of 2006, assuming we obtain clearance on our pending SPA request. If the FDA grants us the SPA and clinical results are favorable, we would intend to submit the Phase III clinical trial results for CoFactor as part of a New Drug Application, or NDA, seeking FDA approval to commercialize CoFactor as a first-line treatment of metastatic colorectal cancer. In addition, we currently expect to file an IND in the third quarter of 2006 for a bioequivalence study using vinorelbine emulsion. Our planned bioequivalence study of vinorelbine emulsion may also be the basis for regulatory approval if clinical results are favorable. In addition to CoFactor, vinorelbine emulsion and Thiovir, we have two other cancer drug candidates and two other anti-infectious disease candidates planned for clinical development. Our pipeline further includes four additional compounds on which we plan to continue preclinical testing. We have retained commercial rights to all of our product candidates in development, except as to certain rights in China, Taiwan, Hong Kong and Macau relating to the product candidates that we acquired in the SD Pharmaceuticals transaction. We intend to seek to maximize the commercial value of each of our product candidates. We may choose to do so by developing and commercializing these drug candidates ourselves or through the creation of co-development and/or co-marketing partnerships.

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# **OUR PRINCIPAL PRODUCT CANDIDATES**

The table below provides an overview of our product candidates in development.

Product/Description	Development Stage	Indication	Status
CoFactor® 5-FU Biomodulator	Phase II U.S. and Europe	Metastatic colorectal cancer	Patient dosing completed. Complete clinical trial results currently expected in 2006
	Phase IIb Europe and India	Metastatic colorectal cancer	Over 66% of patients enrolled. Clinical trial results currently expected in 2007
	Phase III U.S.	Metastatic colorectal cancer	Currently expected to begin in Q2 2006
	Phase II and III U.S.	Advanced breast cancer	Strategy and protocol currently in development with company consultants
Vinorelbine emulsion (ANX-530)	Preclinical	Non-small cell lung and other solid tumors	Currently plan to file IND in Q3 2006 for bioequivalence study
Paclitaxel emulsion (ANX-513)/Taxane	Preclinical	Breast, ovarian and non- small cell lung cancers	Currently plan to file IND in Q1 2007 for bioequivalence study
Docetaxel emulsion (ANX-514)/Taxane	Preclinical	Breast, non-small cell lung, prostate and gastric cancers	Currently plan to request foreign clinical trial approvals and/or file IND in Q1 2007 for bioequivalence study
Selone <sup>tm</sup> Alkylating agent	Preclinical	Drug resistant cancers	Continue preclinical testing in 2006
Thiovir <sup>tm</sup> Pyrophosphate analog, broad spectrum antiviral	Preclinical	HIV/AIDS	Currently plan to file IND in Q3 2006
Clarithromycin emulsion (ANX-015)/IV-macrolide antibiotic	Preclinical	Mild to moderate infections caused by certain bacteria such as streptococcus pyogenes	Currently plan to request foreign clinical trial approvals in Q2 2007
Vancomycin emulsion (ANX-016)/Glycopeptide antibiotic	Preclinical	Systemic therapy for treatment of serious infections by gram-positive bacteria which are resistant to other antibiotics	Currently plan to file IND in Q2 2007
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# **OUR ONCOLOGY PRODUCT CANDIDATES**

#### CoFactor:

CoFactor (ANX-510) is a folate-based compound that is the active form of leucovorin. CoFactor is being developed as a biomodulator of the widely used chemotherapeutic agent 5-fluorouracil (5-FU). CoFactor has been studied in the clinical setting as part of a treatment regimen for metastatic, colorectal, breast, gastric and pancreatic cancers. CoFactor is designed to be a safer and more effective form of leucovorin as the biomodulator of 5-FU. Leucovorin/5-FU is used in a number of chemotherapy regimens and is associated with multiple toxicities, including hematological and gastrointestinal toxicities. Leucovorin efficiency is limited by the requirement to undergo several metabolic steps to convert into the active form of folate. Our drug, CoFactor, bypasses the chemical pathway required for leucovorin metabolism. This biochemical strategy delivers the correct form of folate that allows 5-FU to kill cancer cells more effectively while reducing 5-FU-associated toxicity. We believe that CoFactor overcomes that limitations of leucovorin and will lead to developments that will increase patient outcomes, while reducing side effects and improving the quality of life of patients on chemotherapy.

Currently, leucovorin is a generically-available product which is also the only FDA-approved biomodulator of 5-FU. According to IMS Health Data, global sales of leucovorin exceeded \$300 million in 2005. We believe that if CoFactor shows improved clinical benefit and patient survival, it may be widely used as a replacement for leucovorin in 5-FU based cancer therapies.

#### Market

More than 11 million people worldwide are diagnosed with cancer each year and over 7 million people die each year from cancer, according to statistics published by the World Health Organization. In the U.S., cancer is responsible for approximately 25% of all deaths according to recent statistics. The American Cancer Society estimates that more than 1.3 million new cases of cancer were diagnosed and over 570,000 people died due to cancer in 2005 in the U.S. According to the National Cancer Institute s SEER program, the combined incidence of newly diagnosed cases of gastrointestinal and breast cancers in the U.S. and the EU exceeds 600,000. Colorectal cancer alone claims more than 170,000 lives annually in the U.S. and EU.

Multiple drugs are commercially available to treat first-line colorectal cancer, including; Avastin® (bevacizumab), Eloxatin® (oxaliplatin), Camptosar® (irinotecan), Xeloda® (capecitabine), 5-Fluorouracil (5-FU) and leucovorin calcium (Lv). These drugs are used in a diverse set of therapeutic regimens, most of which include 5-FU and leucovorin, including:

FOLFOX/Avastin	Oxaliplatin, 5-FU, leucovorin, Avastin
FOLFOX	Oxaliplatin, 5-FU, leucovorin
FOLFIRI	Oxaliplatin, 5-FU, leucovorin
Roswell Park	5-FU (bolus), leucovorin
Saltz	Irinotecan, 5-FU, leucovorin
Saltz/Avastin	Irinotecan, 5-FU, leucovorin, Avastin
Mayo	5-FU (bolus), leucovorin
5-FU monotherapy	Capecitabine
deGramont	5-FU (infusional), leucovorin

We believe that although there are a number of drugs being investigated to treat colorectal cancer, most of these compounds are being tested as additions to 5-FU/leucovorin-containing regimens and that 5-FU will continue to be used widely as the cytotoxic component of chemotherapy during the

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course of a patient s disease. We believe that companies which are working on improving the activity of 5-FU itself will continue to utilize leucovorin as a biomodulator of their modified 5-FU.

### **Mechanism of Action**

The enzyme thymidylate synthase (TS) acts in cells to convert deoxyuridine to deoxythymidine for incorporation into newly-replicating DNA. Inhibition of TS is a well-established and efficacious method of killing rapidly dividing cells such as tumor cells. Inhibition of TS is most frequently accomplished via the use of the anti-cancer agent

- 5-Fluorouracil (5-FU), the metabolite of which binds to TS and disrupts DNA replication. This binding event between TS and the metabolite of 5-FU can be stabilized and improved by the action of a specific folate;
- 5,10-methylenetetrahydrofolate (MTHF). Currently, the source of this important folate in the clinical setting is intravenous leucovorin calcium, which is administered prior to the administration of 5-FU. However, the limitation of leucovorin is that leucovorin must undergo at least four metabolic conversions to become the active folate MTHF. Therefore, leucovorin is an indirect source of MTHF and is often insufficient to achieve desired levels of TS inhibition in tumor cells. Even in high doses, leucovorin may not reach the desired concentration in the tumor tissue to be effective in helping 5-FU achieve its anti-tumor potential.

We are developing CoFactor, which is a stable preparation of MTHF, as a direct and superior source of the form of folate needed to achieve complete inhibition of TS. Unlike leucovorin, which must undergo chemical conversion, CoFactor directly delivers the active form of folate and improves 5-FU performance without increasing toxicity. We believe that CoFactor has the potential to replace leucovorin in cancer regimens which utilize 5-FU/leucovorin as a component of therapy.

# **Clinical Efficacy**

# **Phase II Clinical Trial in Metastatic Colorectal Cancer**

A Phase II clinical trial was conducted in 50 patients to evaluate tumor response, safety, time-to-tumor-progression and overall survival in the first-line treatment of metastatic colorectal cancer patients using CoFactor and 5-FU. The study followed an open-label, single-arm, Simon two-stage design. In January 2006, the Company announced that it had reached the efficacy and safety endpoint from this Phase II clinical trial.

The primary endpoint of the study, objective response, was prospectively set at 25%. Objective response consists of either a complete (100% regression of tumors) or partial (at least 50% regression of tumors) response lasting at least 4 weeks. Blinded, third-party radiological assessment by independent reviewers determined that 35% of patients achieved an objective response, exceeding the 25% endpoint by 10%. The Company also reported median time to tumor progression (TTP) of 163 days. This duration compares favorably to historical data from other clinical trials which used 5-FU and leucovorin, including the control arms for the pivotal registration trials of Camptosar® and Xeloda®.

CoFactor was well tolerated, with zero incidence of drug-related grade 3 or grade 4 gastrointestinal or hematological toxicity observed in this clinical trial. A single case of grade 4 hematological toxicity occurred after the completion of the trial and subsequent to treatment with new chemotherapy. Because this event occurred within 30 days of the CoFactor study, it was reported as an adverse event, even though it was attributed to the subsequent course of FOLFOX therapy received by this patient. In contrast to CoFactor, administration of other 5-FU-containing regimens typically leads to an undesirable incidence of severe gastrointestinal and hematological toxicities.

The Company is also following median overall survival, which is expected to be reported during 2006.

# Phase I/ II Clinical Trial in Metastatic Colorectal Cancer

A Phase I/ II dose-ranging clinical trial was conducted in 62 patients with colorectal, breast, gastric, pancreatic or gallbladder cancer. Varying doses of CoFactor and 5-FU were administered on a weekly

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bolus schedule with an endpoint of overall safety. Response rate, time to tumor progression and survival data were also captured. The trial indicated that CoFactor/5-FU was a safe and well-tolerated regimen. Objective responses were observed in colorectal (21%), breast (56%), gastric (33%), pancreatic (40%) cancer. Among the 24 patients who received CoFactor plus 5-FU for first-line treatment of metastatic colorectal cancer, 29% had an objective response.

#### **Preclinical Efficacy**

CoFactor has been tested extensively in preclinical models. Equal doses of CoFactor and leucovorin were compared head-to-head in various combination therapies in immunocompromised and immunocompetent mice to evaluate tumor growth, survival, and toxicity. In preclinical studies, CoFactor-containing treatment regimens in immunocompromised mice induced either equivalent or superior antitumor responses, as noted by slower tumor growth and longer mouse survival, when compared with identically-dosed leucovorin-containing combinations for all drug combinations tested. CoFactor-containing treatment regimens in immunocompetent mice induced either equivalent or diminished toxicity in the preclinical studies, as noted by greater blood cell counts or less weight loss, when compared with identically-dosed leucovorin-containing combinations for all drug combinations tested.

Results from preclinical studies using *in vivo* human tumor xenotransplant mouse models for colorectal and pancreatic cancer suggest antitumor efficacy of CoFactor/5-FU in combination with irinotecan, oxaliplatin, anti-VEGF antibody, and gemcitabine. Results also suggest antitumor activity of CoFactor in combination with the 5-FU prodrugs, including Xeloda and UFT. CoFactor-containing combination regimens induced either equivalent or better antitumor responses in preclinical studies, as noted by slower tumor growth and increased mouse survival, compared with leucovorin-containing combinations for all drug types tested.

Furthermore, in an *in vivo* immunocompetent mouse model, CoFactor/5-FU induced less systemic toxicity than 5-FU/leucovorin either alone or in combination drug regimens. Lower hematological toxicity was observed including less thrombocytopenia, leukopenia, neutropenia and lymphopenia. Furthermore, weight loss was quantitatively less severe with drug treatments containing CoFactor. Additional preclinical studies are planned for CoFactor during 2006.

# **Development plans**

#### **Phase Ilb Clinical Trial in Metastatic Colorectal Cancer**

Further clinical development for CoFactor is presently underway for the treatment of metastatic colorectal cancer. A 300-patient, multi-national, randomized clinical trial is currently being conducted in the EU and India. More than two-thirds of the patients have been enrolled and dosed in this trial. The study is designed to evaluate 5-FU/ leucovorin versus 5-FU/ CoFactor in a modified deGramont (infusional) setting. The primary endpoint of this study is a reduction of grade 3 and grade 4 toxicity. Additionally, response rate, time to tumor progression and overall survival will be monitored. We anticipate that trial enrollment will be completed during 2006.

# **Phase III Clinical Trial in Metastatic Colorectal Cancer**

A pivotal Phase III trial is planned to begin in the second quarter of 2006, assuming clearance of our pending SPA request. This 1200-patient, randomized clinical trial will be conducted in approximately 50 sites across the U.S. in patients with metastatic colorectal cancer who are receiving therapy in the first-line setting. The protocol will feature a modified Roswell Park regimen of 5-FU and Avastin® (bevacizumab) randomized to either a leucovorin control arm or a CoFactor experimental arm. CoFactor will be dosed at 60-mg/m^2 while leucovorin will be dosed at 500mg/m^2. A primary endpoint of progression-free survival will be evaluated with secondary endpoints of severity of adverse events, response rate, duration of response and overall survival.

In 2005 the company was involved in discussions with the FDA under a Special Protocol Assessment (SPA) regarding our proposed Phase III pivotal clinical trial with CoFactor for the treatment of **S-6** 

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metastatic colorectal cancer. In April 2005, we received correspondence stating that Progression Free Survival was an acceptable endpoint for the proposed study, and we announced clearance to proceed with our 600-patient Phase III trial. In addition to the FDA s acceptance of our primary endpoint, they made further comments and suggestions regarding statistical analysis procedures, acceptability of secondary endpoints, and management of potential adverse events during treatment, including those related to the use of Avastin. We accepted and incorporated all of these suggestions, but in addition, chose to request modification of the trial protocol after consultation with our consultants and advisors. In February 2006, we requested these adjustments with the FDA with respect to our protocol for this Phase III clinical trial, including increasing the trial size to 1,200 patients. We are currently waiting to receive the response to this new SPA request from the FDA. Assuming FDA clearance of the new SPA, we expect to initiate the clinical trial in the second quarter of 2006.

Additionally, we are considering clinical evaluation of CoFactor in a second indication. A breast cancer strategy and protocol is currently in development.

# **Intellectual Property**

We have licensed from the University of Southern California two U.S. patents and one Canadian patent pertaining to CoFactor. These patents expire in 2011-2013. Separately, based upon independent research and development work, the Company has filed an international patent application covering the use of CoFactor. The issue of national patents based upon this international application would provide patent protection worldwide until 2025.

# **Orphan Drug Status for Pancreatic Cancer**

Further, we have applied for and received orphan drug designation in the U.S. and the EU for the pancreatic cancer indication for CoFactor.

# **ANX-530 (Vinorelbine emulsion)**

**ANX-530** is a novel emulsion formulation of vinorelbine tartrate, a generic agent. ANX-530 is designed to reduce the incidence and severity of vein irritation from IV-delivery of the drug. Vinorelbine works by disrupting microtubule formation and is a member of the vinca alkaloid class of antineoplastic agents. Vinorelbine is indicated as a single agent or in combination with cisplatin for treatment of advanced non-small cell lung cancer. Vinorelbine has also shown activity in breast, ovarian and other cancers.

### Market

Data from IMS Health show annual vinorelbine sales by our competitors in 2005 of approximately \$160 million worldwide.

Vinorelbine packaging includes a black box warning for extravasation. The product may also cause phlebitis (vein irritation) in approximately one-third of treated patients. We believe that some clinicians elect to use a central line or a different chemotherapeutic regimen as a means to avoid phlebitis. ANX-530 was developed to reduce the vein irritation associated with administration of vinorelbine.

Vinorelbine is indicated as a single agent or in combination with cisplatin for treatment of advanced non-small cell lung cancer. However, recently published clinical studies (ANITA trial results, presented by J. Douillard at 2005 ASCO Annual Meeting and Winton, et al, published in NEJM, June 23, 2005) showed a statistically significant improvement (p=0.0131) of 22 months overall survival in patients treated with vinorelbine plus cisplatin following tumor resection (this form of chemotherapy is commonly known as adjuvant therapy). Consequently, we believe that the use of vinorelbine in the adjuvant setting may increase.

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We are aware that there are multiple suppliers of generic vinorelbine and that other vinca alkaloid and non-vinca alkaloid classes of drugs to treat non-small cell lung cancer are under development by competing companies, including firms which seek to develop liposomal formulations of vinorelbine. Furthermore, additional firms may elect to enter the generic vinorelbine market. We believe we are developing a formulation of vinorelbine which ultimately will be differentiated from generic vinorelbine.

#### **Mechanism of Action**

ANX-530 is a novel emulsion formulation of vinorelbine tartrate. This formulation emulsifies vinorelbine into a homogeneous suspension of nanoparticles and is designed to protect the venous endothelium during administration into a peripheral vein, thereby reducing associated vein irritation caused by the drug.

#### **Preclinical**

In preclinical testing, ANX-530 was compared with Navelbine<sup>®</sup>, GlaxoSmithKline s FDA-approved form of vinorelbine. In this setting, ANX-530 demonstrated a reduction in vein irritation. Vein irritation was examined in rabbits following repeated IV injections in the marginal ear vein. In two cancer model studies in rodents, conducted on behalf of SD Pharmaceuticals, ANX-530 demonstrated comparable efficacy to Navelbine.

# **Development plans**

We plan to conduct a single bioequivalence study of ANX-530. This trial was affirmed by FDA to be sufficient as a marketing-enabling trial. The proposed clinical trial will compare the bioequivalence of ANX-530 with that of vinorelbine in 28 patients with advanced solid tumors. We currently plan to file an IND application for ANX-530 in Q3 2006.

We intend to file for approval of ANX-530 via a 505(b)(2) NDA application. While we intend to further develop ANX-530 as a form of vinorelbine that reduces vein irritation, if approved for commercialization, we intend to initially market the drug as equivalent to generic vinorelbine. We may conduct additional clinical trials in order to observe the ability of ANX-530 to reduce vein irritation.

Section 505(b)(2) of the U.S. Food, Drug & Cosmetic Act allows the FDA to approve a follow-on drug on the basis of data in the scientific literature or data used by the FDA in the approval of other drugs. This procedure potentially makes it easier for drug manufacturers to obtain rapid approval of new forms of drugs based on proprietary data of the original drug manufacturer.

# Paclitaxel emulsion (ANX-513)

Paclitaxel emulsion (ANX-513) is a novel formulation of the chemotherapy drug paclitaxel (brand name: Taxol®) that is intended to be non-allergenic and to obviate the need for immunosuppressant premedication. Immunosuppressant premedication is recommended for paclitaxel therapy to reduce the incidence and severity of hypersensitivity reactions. Paclitaxel is an antimicrotubule agent that inhibits the normal dynamic reorganization of the cellular microtubule network that is essential for cellular division. Paclitaxel is approved to treat breast, ovarian, Kaposi s sarcoma and non-small cell lung cancers. All taxanes, including paclitaxel and docetaxel are highly water-insoluble and therefore utilize certain non-ionic surfactants as drug formulation vehicles. Cremophor® (Polyoxyl castor oil) is used to solubilize paclitaxel and is an active compound that can cause severe hypersensitivity reactions. It is recommended that all patients be premedicated with corticosteroids or anti-histamines prior to paclitaxel administration in order to prevent severe hypersensitivity reactions. Despite premedication, fatal reactions may still occur.

ANX-513 is formulated without Cremophor or detergents and is intended to eliminate the need for premedication with immunosuppressant drugs.

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# **Docetaxel emulsion (ANX-514)**

Docetaxel emulsion (ANX-514) is a novel nano-emulsion formulation of the chemotherapy drug, docetaxel (brand name: Taxotere®) that is designed to eliminate the need for multi-day immunosuppressant premedication. Immunosuppressant premedication is recommended for Taxotere therapy to reduce the incidence and severity of allergic reactions. Docetaxel is an anti-cancer agent that acts by disrupting the cellular microtubular network that is essential for cell division. Taxotere is approved to treat breast, non-small cell lung, prostate and gastric cancers. All taxanes, including docetaxel and paclitaxel are highly water-insoluble and are formulated with certain non-ionic surfactants as drug formulation vehicles. Polysorbate 80, a detergent that is used to solubilize Taxotere, can cause severe hypersensitivity reactions. Premedication with corticosteroids is recommended for patients treated with Taxotere. Severe hypersensitivity reactions may still occur despite pretreatment with corticosteroids. ANX-514 is formulated without polysorbate 80 or other detergents and is intended to eliminate the need for multi-day immunosuppressant premedication.

#### **Selone**<sup>tm</sup>

Selone and its analogues have shown effectiveness, at even relatively low concentrations, against human ovarian, breast, lung and head/neck cancers, and against leukemias and lymphomas, based upon current in vitro screening methods. Their potency is high for their rate of alkylating activity, suggesting an increased specificity of action. Preclinical efforts have shown effectiveness of Selone in treatment of leukemia in mice at doses predicted to achieve effective blood concentrations, as well as in a variety of human tumor cell lines in laboratory testing. We intend to undertake further preclinical testing of Selone during 2006 in order to determine the potential for this drug to be moved into human testing in the future.

# OUR INFECTIOUS DISEASE PRODUCT CANDIDATES Thiovir<sup>tm</sup>

Thiovir is a broad spectrum antiviral drug that has shown in preclinical tests an ability to inhibit HIV, influenza A and herpes viruses. Thiovir is a pyrophosphate analogue and reverse transcriptase inhibitor designed for oral delivery as a component of HAART for HIV/AIDS. Thiovir is a prodrug (a compound that the body converts into active drug) for a drug called foscarnet, an IV-delivered therapy for opportunistic infections in HIV patients. Thiovir delivers both the active drug TPFA (thiophosphonoformate) and the active metabolite PFA (foscarnet). Preclinical studies suggest that Thiovir is active against HIV which is resistant to other reverse transcriptase inhibitors and exhibits strong antiviral synergy when combined with the well-known reverse transcriptase inhibitor, zidovudine (AZT) and may be synergistic with Tenofovir. We currently plan to file an IND and initiate a Phase I/II clinical trial for Thiovir in HIV/AIDS in the second half of 2006.

# **Clarithromycin emulsion (ANX-015)**

ANX-015 is a proprietary intravenous formulation of an approved antibiotic in the macrolide family known as clarithromycin. Clarithromycin is approved for mild to moderate bacterial infections such as in community-acquired pneumonia. Only oral formulations of clarithromycin are currently available in the U.S.

#### Vancomycin emulsion (ANX-016)

ANX-016 is a novel formulation of vancomycin, a parenteral glycopeptide antibiotic approved to treat gram-positive bacterial infections. ANX-016 is designed to reduce the vein irritation and phlebitis associated with the IV-delivered drug.

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#### **ADDITIONAL COMPOUNDS**

We have three additional compounds in our pipeline as a result of our recent SD Pharmaceuticals acquisition. These compounds are currently under evaluation for future preclinical and clinical development or as out-licensing opportunities. These compounds include ANX-211, an intranasal/topical antiviral gel for viral indications, ANX-575, an emulsion formulation of alpha-tocopheryl succinate, which has been shown in preclinical studies to selectively facilitate cell death in cancer cells, and ANX-570, a novel formulation of beta-elemene, a small molecule anticancer agent belonging to the triterpene family.

# **OUR CORPORATE INFORMATION**

We incorporated in the State of Delaware in December 1995. We initially incorporated under the name Victoria Enterprises, Inc. A Colorado corporation also named Victoria Enterprises, Inc. merged into us in 1996. In 1996, we acquired BioQuest, Inc., a development stage biotechnology company, and concurrently changed our name to BioQuest, Inc. In 2000, we acquired Biokeys, Inc., a privately-held biomedical research and development company based in San Diego, California. Upon completion of the acquisition, Biokeys, Inc. became our wholly-owned subsidiary and we changed our name to Biokeys Pharmaceuticals, Inc.

On May 30, 2003, we merged Biokeys into us and changed our name from Biokeys Pharmaceuticals, Inc. to ADVENTRX Pharmaceuticals, Inc.

In July 2004, we formed a wholly owned subsidiary, ADVENTRX (Europe) Ltd., in the United Kingdom for the purpose of conducting clinical trials in the European Union.

On April 26, 2006, we acquired SD Pharmaceuticals, Inc., a Delaware corporation, which became our wholly-owned subsidiary. SD Pharmaceuticals holds certain U.S. and ex-U.S. intellectual property rights to eight oncology and infectious disease product candidates, including certain ex-U.S. rights to SDP-012 (ANX-530, vinorelbine emulsion). (See Recent Developments in the accompanying prospectus.)

We began filing reports under the Securities Exchange Act of 1934, as amended, in October 2001. In April 2004, our common stock began trading on the American Stock Exchange LLC.

Our principal offices are located at 6725 Mesa Ridge Rd., San Diego, California 92121 and our telephone number is (858) 552-0866. Our web site is located at www.adventrx.com. Information contained on our website or any linked websites is not part of this prospectus supplement or the accompanying prospectus. Additional information regarding our company is set forth in documents on file with the Securities and Exchange Commission and incorporated by reference herein.

See Where You Can Find More Information About Us.

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The offering

Common stock we are offering 15,495,867 shares

Common stock to be outstanding 87,145,700 shares

after this offering

Use of proceeds We estimate that the net proceeds to us from this offering, after deducting

underwriting discounts and commissions and our estimated offering expenses, will be approximately \$69,500,000 or approximately \$81,075,000 if the underwriters exercise their over-allotment option in full. We currently intend to use the net proceeds to fund clinical and preclinical development of our products and, if approved for commercial sale by the FDA, commercial launch activities for our

lead products. See Use of Proceeds.

AMEX symbol ANX

Risk factors An investment in our common stock involves significant risks. Before making an

investment in our common stock, you should carefully review the information

under the caption Risk Factors in the accompanying prospectus.

The number of shares of our common stock to be outstanding after this offering in the table above is based on the number of shares outstanding as of May 3, 2006 and does not include, as of that date:

3,593,000 shares of our common stock issuable upon the exercise of stock options issued under our stock option plans having a weighted average exercise price of \$1.97 per share;

an additional 17,323,733 shares of common stock issuable upon the exercise of outstanding warrants having a weighted average exercise price of \$2.07 per share; and

an additional 4,754,268 shares of common stock available for future issuance under our stock option plans and employee stock purchase plan.

Unless otherwise stated, all information contained in this prospectus supplement assumes that the underwriters do not exercise their over-allotment option.

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# Summary consolidated financial data

The consolidated statement of operations data set forth below for the years ended December 31, 2003, 2004 and 2005 are derived from our audited consolidated financial statements incorporated by reference in this prospectus supplement and the accompanying prospectus. The financial data for the three-month periods ended March 31, 2005 and 2006 is derived from our unaudited financial statements. The unaudited financial data has been prepared on the same basis as the audited financial statements and the notes thereto, which include, in the opinion of management, all adjustments (consisting of normal recurring adjustments) necessary for a fair presentation of the information for the unaudited interim periods. The operating results for the three-month period ended March 31, 2006 may not be indicative of the operating results for the full year.

This summary consolidated financial data set forth below should be read in conjunction with, and is qualified in its entirety by reference to, our audited consolidated financial statements, including the related notes thereto, and

Management s discussion and analysis of financial condition and results of operations and Selected financial data in our Annual Report on Form 10-K for the year ended December 31, 2005, and our unaudited consolidated financial statements, including the related notes thereto, and Management s discussion and analysis of financial condition and results of operations in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2006, in each case incorporated by reference in this prospectus supplement and the accompanying prospectus.

This summary consolidated financial data set forth below does not include financial information reflecting our recent acquisition of SD Pharmaceuticals, Inc., which information can be found in Amendment No. 1 to our Current Report on Form 8-K dated April 1, 2006, incorporated by reference in this prospectus supplement and the accompanying prospectus. (See Where You Can Find More Information About Us in the accompanying prospectus). The as adjusted balance sheet data as of March 31, 2006 has been adjusted to give effect to the sale of the 15,495,867 shares of our common stock in this offering, assuming a public offering price of \$4.84, and receipt by us of the net proceeds therefrom, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

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	Year ended December 31			Three months ended March 31,		
Statement of operations data:	2003	2004	2005	2005	2006	
				(unau	dited)	
Revenues:				·	·	
Grant revenue	\$ 3,603	\$	\$	\$	\$	
Interest income	9,269	103,042	496,059	37,322	236,527	
Total revenues Research and development	12,872 748,997	103,042 2,744,328	496,059 8,682,498	37,322 1,704,797	236,527 2,483,858	
General and administrative	1,594,566	4,059,762	5,016,547	1,177,159	1,772,285	
Interest expense	1,386	4,037,702	3,010,347	300	1,772,203	
Total costs and operating expenses	2,344,949	6,804,090	13,699,045	2,882,256	4,256,143	
Loss from operations	(2,332,077)	(6,701,048)	(13,202,986)	(2,844,934)	(4,019,616)	
Loss on fair value of warrants			11,579,660		17,027,065	
Net loss	(2,332,077)	(6,701,048)	(24,782,646)	(2,844,934)	(21,046,681)	
Preferred stock dividends	(37,840)					
Net loss applicable to common stock Basic and diluted net loss per	(2,369,917)	(6,701,048)	(24,782,646)	(2,844,934)	(21,046,681)	
share	\$ (0.07)	\$ (0.13)	\$ (0.41)	\$ (0.05)	\$ (0.31)	
Shares used in computing basic and diluted net loss per share	31,797,986	50,720,180	59,828,357	53,967,933	67,976,352	

# As of March 31, 2006

Balance sheet data:	Actual	As Adjusted
	(unau	dited)
Cash, cash equivalents and marketable securities	22,013,996	91,513,993
Working capital	(26,613,088)	42,886,909
Total assets	23,043,477	92,543,474
Long-term obligations	57,078	57,078
Accumulated deficit	(81,011,521)	(81,011,521)
Shareholders equity (deficiency)	(25,945,510)	43,554,487

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#### Risk factors

An investment in our common stock involves a high degree of risk. Prospective investors in our common stock should carefully consider the following risk factors as well as the other information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that we are not aware of or focused on or we currently deem immaterial may also impair our business operations. All information contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference is qualified in its entirety by these risk factors. If any of the following risks actually occur, our financial condition and results of operations could be materially and adversely affected. If this were to happen, the value of our common stock could decline significantly, and you could lose all or part of your investment.

#### **RISKS RELATING TO THE COMPANY**

# We have a substantial accumulated deficit and limited working capital.

We had an accumulated deficit of \$81 million as of March 31, 2006. We have had losses from operations and negative cash flow from operations in each year since our inception. We had losses from operations of \$2.3 million, \$6.7 million and \$13.2 million in the years ended December 31, 2003, 2004 and 2005, respectively, and a loss from operations of \$4.0 million in the three months ended March 31, 2006. We used cash from operations of \$2.2 million, \$5.1 million, \$11.6 million and \$3.0 million during these same periods. Since we presently have no source of revenues and are committed to continuing our product research and development program, significant expenditures and losses will continue until development of new products is completed and such products have been clinically tested, approved by the FDA or other regulatory agencies and successfully marketed. In addition, we fund our operations primarily through the sale of equity securities, and have had limited working capital for our product development and other activities. We do not believe that debt financing from financial institutions will be available until at least the time that one of our products is approved for commercial production.

# We have no current product sales revenues or profits.

We have devoted our resources to developing a new generation of therapeutic drug products, but such products cannot be marketed until clinical testing is completed and governmental approvals have been obtained. Accordingly, there is no current source of revenues, much less profits, to sustain our present activities, and no revenues will likely be available until, and unless, the new products are clinically tested, approved by the FDA or other regulatory agencies and successfully marketed, either by us or a marketing partner, an outcome which we are not able to guarantee.

### It is uncertain that we will have access to future capital.

We do not expect to generate positive cash flow from operations for at least the next several years. As a result, substantial additional equity or debt financing for research and development or clinical development will be required to fund our activities. Although we have raised equity financing in the past, including in April 2004 and July 2005, we cannot be certain that we will be able to continue to obtain such financing on favorable or satisfactory terms, if at all, or that it will be sufficient to meet our cash requirements. Any additional equity financing could result in substantial dilution to stockholders, and debt financing, if available, would likely involve restrictive covenants that preclude us from making distributions to stockholders and taking other actions beneficial to stockholders. In

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#### **Risk factors**

connection with certain past warrant issuances by us, we have provided the warrant holders with anti-dilution protections that, among other things, protect them against subsequent issuances by us of common stock at a price per share that is less than the exercise price of the warrants. You could experience additional significant dilution in the future as a result of these provisions if we are required to issue common stock or other equity securities below the exercise prices contained in the warrants. Our ability to raise capital would most likely be impaired if we became ineligible to file shelf registration statements on Form S-3.

If adequate funds are not available, we may be required to delay or reduce the scope of our drug development program or attempt to continue development by entering into arrangements with collaborative partners or others that may require us to relinquish some or all of our rights to proprietary drugs. The inability to adequately and timely fund our capital requirements would have a material adverse effect on us. We expect that the proceeds of this offering will last for at least the next 12 months, although we cannot assure you that we will not require additional funds earlier.

# We are not certain that we will be successful in the development of our drug candidates.

The successful development of any new drug is highly uncertain and is subject to a number of significant risks. Our drug candidates, all of which are in a development stage, require significant, time-consuming and costly development, testing and regulatory clearance. This process typically takes several years and can require substantially more time. Risks include, among others, the possibility that a drug candidate will (i) be found to be ineffective or unacceptably toxic, (ii) have unacceptable side effects, (iii) fail to receive necessary regulatory clearances, (iv) not achieve broad market acceptance, (v) be subject to competition from third parties who may market equivalent or superior products, (vi) be affected by third parties holding proprietary rights that will preclude us from marketing a drug product, or (vii) not be able to be manufactured by manufacturers in a timely manner in accordance with required standards of quality. There can be no assurance that the development of our drug candidates will demonstrate the efficacy and safety of our drug candidates as therapeutic drugs, or, even if demonstrated, that there will be sufficient advantages to their use over other drugs or treatments so as to render the drug product commercially viable. In the past, we have been faced with limiting the scope and/or delaying the launch of preclinical and clinical drug trials due to limited cash and personnel resources. We have also chosen to terminate licenses of some drug candidates that were not showing sufficient promise to justify continued expense and development. In the event that we are not successful in developing and commercializing one or more drug candidates, investors are likely to realize a loss of their entire investment. We have been delayed at certain times in the past in the development of our drug products by limited funding. In addition, if certain of our scientific and technical personnel resigned at or about the same time, the development of our drug products would probably be delayed until new personnel were hired and became familiar with the development programs.

Positive results in preclinical and clinical trials do not ensure that future clinical trials will be successful or that drug candidates will receive all necessary regulatory approvals for the marketing, distribution or sale of such drug candidates.

Success in preclinical and clinical trials does not ensure that large-scale clinical trials will be successful. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly and may be difficult to predict. In the past, we have terminated licenses of drug candidates when our preclinical trials did not support or verify earlier preclinical data. There is a significant risk that any of

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#### **Risk factors**

our drug candidates could fail to show satisfactory results in continued trials, and would not justify further development.

# We will face intense competition from other companies in the pharmaceutical industry.

We are engaged in a segment of the pharmaceutical industry that is highly competitive and rapidly changing. If successfully developed and approved, any of our drug candidates will likely compete with several existing therapies. CoFactor, our leading drug candidate, would likely compete against a well-established product, leucovorin. In addition, there are numerous companies with a focus in oncology and/or anti-viral therapeutics that are pursuing the development of pharmaceuticals that target the same diseases as are targeted by the drugs being developed by us. We anticipate that we will face intense and increasing competition in the future as new products enter the market and advanced technologies become available. We cannot assure that existing products or new products developed by competitors will not be more effective, or more effectively marketed and sold than those we may market and sell. Competitive products may render our drugs obsolete or noncompetitive prior to our recovery of development and commercialization expenses.

Many of our likely competitors, such as Merck, Wyeth and Pfizer, will also have significantly greater financial, technical and human resources and will likely be better equipped to develop, manufacture and market products. In addition, many of these competitors have extensive experience in preclinical testing and clinical trials, obtaining FDA and other regulatory approvals and manufacturing and marketing pharmaceutical products. A number of these competitors also have products that have been approved or are in late-stage development and operate large, well-funded research and development programs. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. Furthermore, academic institutions, government agencies and other public and private research organizations are becoming increasingly aware of the commercial value of their inventions and are actively seeking to commercialize the technology they have developed. Companies such as Gilead, Roche and GlaxoSmithKline all have drugs in various stages of development that could become competitors. Other companies, such as Merck Eprova, with which we had a Co-Operation Agreement (2001-2003), may be developing products which could compete with CoFactor. Accordingly, competitors may succeed in commercializing products more rapidly or effectively than us, which would have a material adverse effect on us.

# There is no assurance that our products will have market acceptance.

Our success will depend in substantial part on the extent to which a drug product, if eventually approved for commercial distribution, achieves market acceptance. The degree of market acceptance will depend upon a number of factors, including (i) the receipt and scope of regulatory approvals, (ii) the establishment and demonstration in the medical community of the safety and efficacy of a drug product, (iii) the product s potential advantages over existing treatment methods and (iv) reimbursement policies of government and third party payors. We cannot predict or guarantee that physicians, patients, healthcare insurers or maintenance organizations, or the medical community in general, will accept or utilize any of our drug products.

The unavailability of health care reimbursement for any of our products will likely adversely impact our ability to effectively market such products and whether health care reimbursement will be available for any of our products is uncertain.

Our ability to commercialize our technology successfully will depend in part on the extent to which reimbursement for the costs of such products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. Significant

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uncertainty exists as to the reimbursement status of newly approved medical products. We cannot guarantee that adequate third-party insurance coverage will be available for us to establish and maintain price levels sufficient for realization of an appropriate return on our investments in developing new therapies. If we are successful in getting FDA approval for CoFactor, we will be competing against a generic drug, leucovorin, which has a lower cost and a long, established history of reimbursement. Receiving sufficient reimbursement for purchase costs of CoFactor will be necessary to make it cost effective and competitive versus the established drug, leucovorin. Government, private health insurers, and other third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement for new therapeutic products approved for marketing by the FDA. Accordingly, even if coverage and reimbursement are provided by government, private health insurers, and third-party payors for use of our products, the market acceptance of these products would be adversely affected if the amount of reimbursement available for the use of our therapies proved to be unprofitable for health care providers.

# Uncertainties related to health care reform measures may affect our success.

There have been some federal and state proposals in the past to subject the pricing of health care goods and services, including prescription drugs, to government control and to make other changes to the U.S. health care system. None of the proposals seems to have affected any of the drugs in our programs. However, it is uncertain if future legislative proposals would be adopted that might affect the drugs in our programs or what actions federal, state, or private payors for health care treatment and services may take in response to any such health care reform proposals or legislation. Any such health care reforms could have a material adverse effect on the marketability of any drugs for which we ultimately require FDA approval.

# Further testing of our drug candidates will be required and there is no assurance of FDA approval.

The FDA and comparable agencies in foreign countries impose substantial requirements upon the introduction of medical products, through lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures. Satisfaction of these requirements typically takes several years or more and varies substantially based upon the type, complexity, and novelty of the product.

The effect of government regulation and the need for FDA approval will delay marketing of new products for a considerable period of time, impose costly procedures upon our activities, and provide an advantage to larger companies that compete with us. There can be no assurance that the FDA or other regulatory approval for any products developed by us will be granted on a timely basis or at all. Any such delay in obtaining or failure to obtain, such approvals would materially and adversely affect the marketing of any contemplated products and the ability to earn product revenue. Further, regulation of manufacturing facilities by state, local, and other authorities is subject to change. Any additional regulation could result in limitations or restrictions on our ability to utilize any of our technologies, thereby adversely affecting our operations.

Human pharmaceutical products are subject to rigorous preclinical testing and clinical trials and other approval procedures mandated by the FDA and foreign regulatory authorities. Various federal and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical products. The process of obtaining these approvals and the subsequent compliance with appropriate U.S. and foreign statutes and regulations are time-consuming and require the expenditure of substantial resources. In addition, these requirements and processes vary widely from country to country.

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Among the uncertainties and risks of the FDA approval process are the following: (i) the possibility that studies and clinical trials will fail to prove the safety and efficacy of the drug, or that any demonstrated efficacy will be so limited as to significantly reduce or altogether eliminate the acceptability of the drug in the marketplace, (ii) the possibility that the costs of development, which can far exceed the best of estimates, may render commercialization of the drug marginally profitable or altogether unprofitable, (iii) the possibility of additional delays in the development of CoFactor, despite the fact that we expect that the FDA will approve our SPA for our proposed Phase III clinical and that we will be able to commence the trial in the second quarter of 2006, and (iv) the possibility that the amount of time required for FDA approval of a drug may extend for years beyond that which is originally estimated. In addition, the FDA or similar foreign regulatory authorities may require additional clinical trials, which could result in increased costs and significant development delays. Delays or rejections may also be encountered based upon changes in FDA policy and the establishment of additional regulations during the period of product development and FDA review. Similar delays or rejections may be encountered in other countries.

# We may not achieve our projected development goals in the time frames we announce and expect.

We set goals for and make public statements regarding timing of the accomplishment of objectives material to our success, such as the commencement and completion of clinical trials. The actual timing of these events can vary dramatically due to factors such as delays or failures in our clinical trials, and the uncertainties inherent in the regulatory approval process. There can be no assurance that our clinical trials will commence or be completed, that we will make regulatory submissions or receive regulatory approvals as planned or that we will be able to adhere to our current schedule for the launch of any of our products. If we fail to achieve one or more of these milestones as planned, the market price of our shares could decline.

# Our success will depend on licenses and proprietary rights we receive from other parties, and on any patents we may obtain.

Our success will depend in large part on our ability and our licensors ability to (i) maintain patent protection with respect to drug products, (ii) our ability to maintain our licenses, (iii) defend patents and licenses once obtained, (iv) maintain trade secrets, (v) operate without infringing upon the patents and proprietary rights of others and (vi) obtain appropriate licenses to patents or proprietary rights held by third parties if infringement would otherwise occur, both in the U.S. and in foreign countries.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. There is no guarantee that we or our licensors have or will develop or obtain the rights to products or processes that are patentable, that patents will issue from any of the pending applications or that claims allowed will be sufficient to protect the technology licensed to us. In addition, we cannot be certain that any patents issued to or licensed by us will not be challenged, invalidated, infringed or circumvented, including by our competitors, or that the rights granted thereunder will provide competitive advantages to us.

Litigation, which could result in substantial cost, may also be necessary to enforce any patents to which we have rights, or to determine the scope, validity and unenforceability of other parties proprietary rights, which may affect our rights. There can be no assurance that our owned or licensed patents would be held valid by a court or administrative body or that an alleged infringer would be found to be infringing. The uncertainty resulting from the mere institution and continuation of any technology-related litigation or interference proceeding could have a material adverse effect on us pending resolution of the disputed matters.

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We may also rely on unpatented trade secrets and know-how to maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with employees, consultants and others. There can be no assurance that these agreements will not be breached, invalidated or terminated, that we will have adequate remedies for any breach, or that trade secrets will not otherwise become known or be independently discovered by competitors.

# A third party may have an interest in two issued U.S. patents licensed to us by the University of Southern California (USC), which could adversely affect our intellectual property position with respect to CoFactor.

We have recently become aware of the possibility that Mr. Goran Carlsson, a named inventor in the Canadian patent pertaining to CoFactor licensed to us by USC, may also be a co-inventor of the two corresponding U.S. patents licensed to us by USC. The facts are currently under investigation. We believe that if Mr. Carlsson is found to be a proper co-inventor of the U.S. patents, he may be under contractual obligation to assign to USC his ownership rights in these U.S. patents.

USC may not be successful in acquiring ownership rights, if any, that Mr. Carlsson may have in the patents. In such case, we will consider all our alternatives, including seeking remedies from the courts. Any such action is likely to be expensive and consume management s attention, and we may not be successful. Although we believe Mr. Carlsson s possible ownership rights do not limit our ability to make use of our technology, Mr. Carlsson may attempt to license any rights he may have to third parties, including our competitors. While we believe our other intellectual property is sufficient to preclude others from making, using, or selling aspects of our CoFactor (ANX-510) technology, if Mr. Carlsson is able to establish inventorship rights in the relevant patents, and if his rights are not licensed to us through USC, the value of our current intellectual property could be materially diminished.

# Our license agreements can be terminated in the event of a breach.

The license agreements pursuant to which we license our core technologies for CoFactor and Thiovir permit the licensor, the University of Southern California, to terminate the agreements under certain circumstances, such as the failure by us to use our reasonable best efforts to commercialize the subject drug or the occurrence of any other uncured material breach by us. The license agreements also provide that the licensor is primarily responsible for obtaining patent protection for the technology licensed, and we are required to reimburse the licensor for the costs it incurs in performing these activities. The license agreements also require the payment of specified royalties. Any inability or failure to observe these terms or pay these costs or royalties could result in the termination of the applicable license agreement in certain cases. In the past, we have let lapse certain licenses for drug candidates when we determined that the expense and risk of continued development outweighed the likely benefits of that continued development. The termination of any license agreement could have a material adverse effect on us.

# The United States government and the University of Southern California retain certain rights in the technologies we have licensed from them.

The technologies developed by the University of Southern California were developed in part through funding provided by the United States government. Therefore, in addition to the University of Southern California s termination rights described above, our licenses are subject to a non-exclusive, non-transferable, royalty-free right of the United States government and the University of Southern California to practice the licensed technologies for research and, in the case of the United States government, other governmental purposes on behalf of the United States and on behalf of any foreign government or international organization pursuant to any existing or future treaty or agreement with the United States, but only to the extent the government funded the research. The government also

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reserves the right to require us to grant sublicenses to third parties when necessary to fulfill public health and safety needs or if we do not reasonably satisfy government requirements for public use of the technology. Although we are currently the only parties licensed to actively develop the technology, we cannot assure you that the government will not in the future require us to sublicense the technology. Any action by the government to force us to issue such sublicenses or development activities pursuant to its reserved rights in the technology would erode our ability to exclusively develop products based on the technology and could materially harm our financial condition and operating results.

Licenses of technology developed through funding provided by the United States government, including the University of Southern California licenses, require that licensees in this case, us and our affiliates and sub-licensees agree that products covered by the licenses will be manufactured substantially in the United States. We cannot assure you that we will be able to contract for manufacturing facilities in the United States on favorable terms or obtain waivers of such requirement, or that such requirement will not impede our ability to license our products to others. If we are unable to contract for management facilities in the United States or obtain an appropriate waiver, we risk losing our rights under the University of Southern California licenses, which could materially harm our financial condition and operating results.

# Protecting our proprietary rights may be difficult and costly.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. Accordingly, we cannot predict the breadth of claims allowed in these companies patents or whether we may infringe or be infringing these claims. Although we have not been notified of any patent infringement, nor notified others of patent infringement, such patent disputes are common and could preclude the commercialization of our products. Patent litigation is costly in its own right and could subject us to significant liabilities to third parties. In addition, an adverse decision could force us to either obtain third-party licenses at a material cost or cease using the technology or product in dispute.

# If a trademark infringement action is commenced against us regarding the use of our corporate name, we could be required to pay monetary damages and/or change our name.

In March of 2005, we received correspondence from Aventis Pharmaceuticals, Inc. and its parent, Sanofi-Aventis (collectively, Sanofi) in which Sanofi asserted that our use of the word ADVENTRX infringes upon their trademark AVENTIS and demanded that we discontinue use of the word ADVENTRX. In May of 2005, we responded with a letter in which we outlined reasons why we do not believe that our name, ADVENTRX, infringes on Sanofi s trademark, AVENTIS. Since our response, counsel for both parties have exchanged further communications and Sanofi has made further inquiries regarding our use of the ADVENTRX mark. These communications are continuing. Sanofi may take legal action in the future, including proceeding with an action for trademark infringement. Depending upon the circumstances, an adverse result in a trademark infringement action could require the payment of monetary damages by us and/or changing our corporate name.

# We may be unable to retain skilled personnel and maintain key relationships.

The success of our business depends, in large part, on our ability to attract and retain highly qualified management, scientific and other personnel, and on our ability to develop and maintain important relationships with leading research institutions and consultants and advisors. Competition for these types of personnel and relationships is intense from numerous pharmaceutical and biotechnology companies, universities and other research institutions. We are currently dependent upon our scientific staff, which has a deep background in our drug candidates and the ongoing preclinical and clinical

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trials. Recruiting and retaining senior employees with relevant drug development experience in oncology and anti-viral therapeutics is costly and time-consuming. There can be no assurance that we will be able to attract and retain such individuals on an uninterrupted basis and on commercially acceptable terms, and the failure to do so could have a material adverse effect on us by significantly delaying one or more of our drug development programs. The loss of any of our senior executive officers, including our chief executive officer and chief financial officer, in particular, could have a material adverse effect on the company and the market for our common stock, particularly if such loss was abrupt or unexpected. All of our employees are employed on an at-will basis under offer letters. We do not have non-competition agreements with any of our employees.

# We currently have no sales capability, and limited marketing capability.

We currently do not have sales personnel. We have limited marketing and business development personnel. We will have to develop a sales force, or rely on marketing partners or other arrangements with third parties for the marketing, distribution and sale of any drug product which is ready for distribution. There is no guarantee that we will be able to establish marketing, distribution or sales capabilities or make arrangements with third parties to perform those activities on terms satisfactory to us, or that any internal capabilities or third party arrangements will be cost-effective. In addition, any third parties with which we may establish marketing, distribution or sales arrangements may have significant control over important aspects of the commercialization of a drug product, including market identification, marketing methods, pricing, composition of sales force and promotional activities. There can be no assurance that we will be able to control the amount and timing of resources that any third party may devote to our products or prevent any third party from pursuing alternative technologies or products that could result in the development of products that compete with, or the withdrawal of support for, our products.

# We do not have manufacturing capabilities and may not be able to efficiently develop manufacturing capabilities or contract for such services from third parties on commercially acceptable terms.

We do not have any manufacturing capacity. When and if required, we will seek to establish relationships with third-party manufacturers for the manufacture of clinical trial material and the commercial production of drug products as we have with our current manufacturing partners. There can be no assurance that we will be able to establish relationships with third-party manufacturers on commercially acceptable terms or that third-party manufacturers will be able to manufacture a drug product on a cost-effective basis in commercial quantities under good manufacturing practices mandated by the FDA or other regulatory matters.

The dependence upon third parties for the manufacture of products may adversely affect future costs and the ability to develop and commercialize a drug product on a timely and competitive basis. Further, there can be no assurance that manufacturing or quality control problems will not arise in connection with the manufacture of our drug products or that third party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such products. Any failure to establish relationships with third parties for our manufacturing requirements on commercially acceptable terms would have a material adverse effect on us.

# We are dependent in part on third parties for drug development and research facilities.

We do not possess research and development facilities necessary to conduct all of our drug development activities. We engage consultants and independent contract research organizations to design and conduct clinical trials in connection with the development of our drugs. As a result, these

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important aspects of a drug s development will be outside our direct control. In addition, there can be no assurance that such third parties will perform all of their obligations under arrangements with us or will perform those obligations satisfactorily.

In the future, we anticipate that we will need to obtain additional or increased product liability insurance coverage and it is uncertain that such increased or additional insurance coverage can be obtained on commercially reasonable terms.

Our business will expose us to potential product liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical products. There can be no assurance that product liability claims will not be asserted against us. We intend to obtain additional limited product liability insurance for our clinical trials, directly or through our marketing development partners or contract research organization (CRO) partners, when they begin in the U.S. and to expand our insurance coverage if and when we begin marketing commercial products. However, there can be no assurance that we will be able to obtain product liability insurance on commercially acceptable terms or that we will be able to maintain such insurance at a reasonable cost or in sufficient amounts to protect against potential losses. A successful product liability claim or series of claims brought against us could have a material adverse effect on us.

The market price of our shares, like that of many biotechnology companies, is highly volatile. Market prices for our common stock and the securities of other medical and biomedical technology companies have been highly volatile and may continue to be highly volatile in the future. Factors such as announcements of technological innovations or new products by us or our competitors, government regulatory action, litigation, patent or

proprietary rights developments, and market conditions for medical and high technology stocks in general can have a significant impact on any future market for our common stock.

If we cannot satisfy AMEX s listing requirements, it may delist our common stock and we may not have an active public market for our common stock. The absence of an active trading market would likely make the common stock an illiquid investment.

Our common stock is quoted on the American Stock Exchange. To continue to be listed, we are required to maintain shareholders equity of \$6,000,000 among other requirements. We do not satisfy that requirement as of March 31, 2006. However, the Exchange will not normally consider suspending dealings in, or removing from the list, the securities of a company if the company has a total value of market capitalization of at least \$50,000,000 and has at least 1,100,000 shares publicly held, with a market value of publicly held shares of at least \$15,000,000 and 400 round lot shareholders. We currently meet these criteria. If the Exchange were to delist our common stock and suspend trading in our common stock, our common stock would likely trade in the over-the-counter market in the so-called pink sheets or, if available, the OTC Bulletin Board Service. As a result, an investor would likely find it significantly more difficult to dispose of, or to obtain accurate quotations as to the value of, our shares.

If our common stock is delisted, it may become subject to the SEC s penny stock rules and more difficult to sell.

SEC rules require brokers to provide information to purchasers of securities traded at less than \$5.00 and not traded on a national securities exchange or quoted on the Nasdaq Stock Market. If our common stock becomes a penny stock that is not exempt from these SEC rules, these disclosure requirements may have the effect of reducing trading activity in our common stock and making it more difficult for investors to sell. The rules require a broker-dealer to deliver a standardized risk

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disclosure document prepared by the SEC that provides information about penny stocks and the nature and level of risks in the penny market. The broker must also give bid and offer quotations and broker and salesperson compensation information to the customer orally or in writing before or with the confirmation. The SEC rules also require a broker to make a special written determination that the penny stock is a suitable investment for the purchaser and receive the purchaser s written agreement to the transaction before a transaction in a penny stock.

# Changes in laws and regulations that affect the governance of public companies has increased our operating expenses and will continue to do so.

Recently enacted changes in the laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002 and the listing requirements for American Stock Exchange, have imposed new duties on us and on our executives, directors, attorneys and independent accountants. In order to comply with these new rules, we have hired and expect to hire additional personnel and use additional outside legal, accounting and advisory services, which have increased and are likely to continue increasing our operating expenses. In particular, we expect to incur additional administrative expenses as we continue compliance with Section 404 of the Sarbanes-Oxley Act, which requires management to extensively evaluate and report on, and our independent registered public accounting firm to attest to, our internal controls. For example, we have incurred significant expenses, and expect to incur additional expenses, in connection with the evaluation, implementation, documentation and testing of our existing and newly implemented control systems. Management time associated with these compliance efforts necessarily reduces time available for other operating activities, which could adversely affect operating results. If we are unable to achieve full and timely compliance with these regulatory requirements, we could be required to incur additional costs, expend additional money and management time on additional remedial efforts which could adversely affect our results of operations.

# Failure to implement effective control systems, or failure to complete our assessment of the effectiveness of our internal control over financial reporting, may subject us to regulatory sanctions and could result in a loss of public confidence, which could harm our operating results.

Pursuant to Section 404 of the Sarbanes-Oxley Act, beginning with our fiscal year ending December 31, 2005, we are required to include in our annual report our assessment of the effectiveness of our internal control over financial reporting. Furthermore, our independent registered public accounting firm is required to issue an opinion on whether our assessment of the effectiveness of our internal control over financial reporting is fairly stated in all material respects and separately report on whether it believes we maintained, in all material respects, effective internal control over financial reporting on an annual basis.

In connection with their required assessment under Section 404 of the Sarbanes-Oxley Act of 2002, our management concluded that our internal controls over financial reporting were effective as of December 31, 2005, and our independent public accountants were able to attest to that assessment. However, in connection with the 2005 year-end audit, our independent public accountants identified certain internal control weaknesses that, although not rising to the level of material weaknesses, were significant deficiencies. Additionally, in prior years (most recently 2004), certain material weaknesses in our internal controls over financial reporting were identified in connection with our annual financial audits. While we believe we remediated the material weaknesses from prior years, including through adopting a new financial accounting system and adding a financial controller to our accounting staff, any failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our operating results or cause us to fail to meet our reporting obligations. Inferior internal controls could also cause investors to lose confidence.

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#### **Risk factors**

If we fail to remedy any material weaknesses which are uncovered in the future, fail to timely complete our assessment, or if our independent registered public accounting firm cannot timely attest to our assessment, we could be subject to regulatory sanctions and a loss of public confidence in our internal control. In addition, any failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our operating results or cause us to fail to timely meet our regulatory reporting obligations.

Our early corporate records are incomplete. As a result, we might have difficulty in assessing and defending against any claims relating to our common stock purportedly issued during, or corporate actions taken during, periods for which our records are incomplete.

We were initially incorporated in 1995. All of our current senior management have joined our company since 2002 and our corporate records prior to 2002, including minutes of board meetings and stock transfer records, are incomplete. As a result, if claims were to be asserted against us relating to our common stock purportedly issued during, or corporate actions taken during, this time, we might have difficulty in assessing and defending them.

# We have engaged in and may continue to engage in further expansion through mergers and acquisitions, which could negatively affect our business and earnings.

We have engaged in and may continue to engage in expansion through mergers and acquisitions. There are risks associated with such expansion. These risks include, among others, incorrectly assessing the asset quality of a prospective merger partner, encountering greater than anticipated costs in integrating acquired businesses, facing resistance from customers or employees, and being unable to profitably deploy assets acquired in the transaction. Additional country- and region-specific risks are associated with transactions outside the United States. To the extent we issue capital stock in connection with additional transactions, these transactions and related stock issuances may have a dilutive effect on earnings per share and share ownership.

Our earnings, financial condition, and prospects after a merger or acquisition depend in part on our ability to successfully integrate the operations of the acquired company. We may be unable to integrate operations successfully or to achieve expected cost savings. Any cost savings which are realized may be offset by losses in revenues or other charges to earnings.

# RISKS RELATED TO OUR COMMON STOCK AND THE OFFERING

# The price of our common stock has been and is likely to continue to be volatile, and your investment could suffer a decline in value.

The trading price of our common stock has been, and is likely to be, volatile and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control, including:

the timing and the results from our clinical trial programs;

FDA or international regulatory actions;

failure of any of our product candidates, if approved, to achieve commercial success;

announcements of clinical trial results or new product introductions by our competitors;

market conditions in the pharmaceutical, biopharmaceutical and biotechnology sectors;

developments concerning intellectual property rights;

litigation or public concern about the safety of our potential products;

deviations in our business and the trading price of our common stock from the estimates of securities analysts;

#### **Risk factors**

additions or departures of key personnel; and

third party reimbursement policies.

As a result, you could lose all or part of your investment. In addition, the stock market in general experiences extreme price and volume fluctuations that are often unrelated and disproportionate to the operating performance of companies.

# Investors in this offering will experience immediate and substantial dilution.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will incur immediate and substantial dilution in the pro forma net tangible book value per share of common stock from the price per share that you pay for the common stock. If the holders of outstanding options or warrants exercise those options or warrants at prices below the public offering price, you will incur further dilution. See Dilution.

# Sales of substantial amounts of our common stock or the perception that such sales may occur could cause the market price of our common stock to drop significantly, even if our business is performing well.

The market price of our common stock could decline as a result of sales by, or the perceived possibility of sales by, our existing stockholders of shares of common stock in the market after this offering. These sales might also make it more difficult for us to sell equity securities at a time and price that we deem appropriate. The lock-up agreements delivered by our directors and officers to the underwriters in connection with the offering generally provide that they will not dispose of their shares for a period of 90 days after the date of this prospectus supplement. Our underwriters have no pre-established conditions to waiving the terms of the lock-up agreements, and any decision by them to waive those conditions would depend on a number of factors, which may include market conditions, the performance of the common stock in the market and our financial condition at that time. In addition, we have filed resale shelf registration statements to register shares of our common stock that may be sold by certain of our stockholders.

# We will have broad discretion in how we use the proceeds of this offering, and we may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering. We currently intend to use the net proceeds of this offering to fund clinical and preclinical developments of our product candidates and commercial launch activities for our lead product candidates. However, our management has broad discretion over how these proceeds are used and could spend the proceeds in ways with which you may not agree. We may not invest the proceeds of this offering effectively or in a manner that yields a favorable or any return, and consequently, this could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline or delay the development of our product candidates.

# Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult, which could depress our stock price.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of our company more difficult, even if a change in control would be beneficial to the stockholders. Our charter documents provide that our board of directors may issue, without a vote of our stockholders, one or more series of preferred stock

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#### **Risk factors**

that has more than one vote per share. This could permit our board of directors to issue preferred stock to investors who support our management and give effective control of our business to our management. Additionally, issuance of preferred stock could block an acquisition resulting in both a drop in the price of our common stock and a decline in interest in the stock, which could make it more difficult for stockholders to sell their shares. This could cause the market price of our common stock to drop significantly, even if our business is performing well. Our bylaws also limit who may call a special meeting of stockholders and establish advance notice requirements for nomination for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, the board of directors approves the transaction. Our board of directors may use these provisions to prevent changes in the management and control of our company. Also, under applicable Delaware law, our board of directors may adopt additional anti-takeover measures in the future. In addition, provisions of certain contracts, such as employment agreements with our executive officers, may have an anti-takeover effect. In connection with a July 2005 private placement, we agreed with the investors in that transaction that we would not implement certain additional measures that would have an anti-takeover effect, as described under Certain Relationships and Related Transactions .

# Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Upon completion of this offering, our executive officers, directors and beneficial owners of 5% or more of our common stock and their affiliates will, in aggregate, beneficially own approximately 27.04% of our outstanding common stock or 26.33% if the underwriters exercise their over-allotment option in full. These persons, acting together, will be able to exercise significant influence over all matters requiring stockholder approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. This concentration of ownership may harm the market price of our common stock by delaying or preventing a change in control of our company at a premium price even if beneficial to our other stockholders.

# Because we do not expect to pay dividends in the foreseeable future, you must rely on stock appreciation for any return on your investment.

We have paid no cash dividends on any of our capital stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future, and payment of cash dividends, if any, will also depend on our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we may in the future become subject to contractual restrictions on, or prohibitions against, the payment of dividends. Accordingly, the success of your investment in our common stock will likely depend entirely upon any future appreciation. There is no guarantee that our common stock will appreciate in value after the offering or even maintain the price at which you purchased your shares, and you may not realize a return on your investment in our common stock.

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#### Special note regarding forward-looking statements

Many of the statements under the sections titled Prospectus supplement summary, Risk factors and elsewhere in this prospectus supplement and the accompanying prospectus, including the incorporated by reference documents, constitute forward-looking statements. These statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results and/or the timing of events, among other things, to be materially different from projected results or events expressed or implied by the forward-looking statements. These factors include, among others, those listed under Risk factors and elsewhere in this prospectus supplement and the accompanying prospectus. In some cases, you can identify forward-looking statements by terms such as may, will. should. expects. plans, believes, estimates, predicts, potential, or continue or similar terms. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Our actual results could differ materially from those expressed or implied by these forward-looking statements as a result of various factors, including the risk factors described under the heading Risk factors and elsewhere in this prospectus supplement and the accompanying prospectus. We undertake no obligation to update publicly any forward-looking statements for any reason, except as required by law, even as new information becomes available or other events occur in the future.

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# Use of proceeds

We estimate the net proceeds of this offering at an assumed public offering price of \$4.84 per share, will be approximately \$69,500,000, after deducting payment of underwriting discounts and commissions and estimated expenses of this offering payable by us. If the underwriters over-allotment option is exercised in full, we anticipate that the net proceeds will be approximately \$81,075,000. An increase (or decrease) in the public offering price from the assumed public offering price of \$4.84 per share by \$1.00 would increase (or decrease) the net proceeds to us from this offering by approximately \$15.566 million, after deducting the estimated underwriting discounts and commissions and estimated aggregate offering expenses payable by us and assuming no exercise of the underwriters over-allotment option and no other change to the number of shares offered by us as set forth on the cover page of this prospectus. We currently intend to use the net proceeds from the sale of the shares of common stock in this offering to fund preclinical and clinical testing and other product developments as well as possibly for commercial launch preparation. We have no current agreements or commitments with respect to any acquisition.

The timing and amount of our actual expenditures will be based on many factors, including our ability to identify drug candidates to develop, technologies or companies to acquire, and to negotiate and enter into definitive agreements with respect to any acquisitions.

Until we use the net proceeds of this offering for the above purposes, we intend to invest the funds in short-term, investment grade, interest-bearing securities. We cannot predict whether the proceeds invested will yield a favorable return.

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# Capitalization

The following table sets forth our cash, cash equivalents and short-term investments and capitalization as of March 31, 2006:

on an actual basis; and

on an as adjusted basis to give effect to our sale of 15,495,867 shares of common stock in this offering at an assumed public offering price of \$4.84 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the table above in conjunction with Management's discussion and analysis of financial condition and results of operation and our consolidated financial statements and the related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of March 31, 2006			
	Actual		As adjusted	
	(unaudited) (in thousands, except share and per share data)			
Cash, cash equivalents and short-term investments	\$	22,014	\$	91,514
Warrant liability Current liabilities Long-term obligations		46,723 2,209 57		46,723 2,209 57
Shareholders equity:				
Temporary equity:				
Common stock subject to continuing registration, \$.001 par value; 10,810,809 shares issued and outstanding, actual; 10,810,809 shares issued				
and outstanding, as adjusted				
Shareholders deficiency:				
Common stock, \$0.001 par value. Authorized 200,000,000 shares; 58,317,667 shares issued and outstanding, actual; 73,813,534 shares issued				
and outstanding, as adjusted		69		84
Additional paid in capital		55,034		124,519
Accumulated other comprehensive loss		(3)		(3)
Deficit accumulated during the development stage		(81,011)		(81,011)
Treasury stock, 23,165 shares at cost		(35)		(35)
Total shareholders equity (deficiency)		(25,946)		43,554
Total capitalization	\$	23,043	\$	92,543

The number of shares of our common stock in the actual and as adjusted columns in the table above excludes as of March 31, 2006:

3,113,000 shares of our common stock issuable upon the exercise of stock options issued under our stock option plans having a weighted average exercise price of \$2.13 per share;

an additional 17,737,100 shares of common stock issuable upon the exercise of outstanding warrants having a weighted average exercise price of \$2.06 per share; and

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# Capitalization

an additional 5,234,268 shares of common stock available for future issuance under our stock option plans and employee stock purchase plan.

To the extent we change the number of shares of common stock we sell in this offering from the 15,495,867 shares we expect to sell or the public offering price varies from the \$4.84 per share assumed public offering price, or any combination of these events occurs, our net proceeds from this offering and as adjusted additional paid-in capital may increase or decrease. An increase (or decrease) of \$1.00 from the assumed public offering price, assuming no change in the number of shares of common stock to be sold, would increase (or decrease) our net proceeds from this offering and our as adjusted additional paid-in capital by approximately \$15.566 million and an increase (or decrease) of 1,000,000 shares from the expected number of shares to be sold in the offering, assuming no change in the assumed public offering price, would increase (or decrease) our net proceeds from this offering and our as adjusted additional paid-in capital by approximately \$4.5 million.

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# Price range of common stock

Since April 2004, our common stock has been trading publicly on the American Stock Exchange under the symbol ANX. Our common stock traded on the OTC Bulletin Board from June 2002 to April 2004, and in the Pink Sheets prior to that time. The following table presents quarterly information on the price range of our common stock. This information indicates the high and low sales prices reported by the AMEX.

	High	Low
Fiscal year ending December 31, 2004		
First quarter	\$ 2.40	\$ 0.85
Second quarter	2.39	1.45
Third quarter	1.80	0.90
Fourth quarter	1.35	0.78
Fiscal year ended December 31, 2005		
First quarter	\$ 1.69	\$ 0.87
Second quarter	3.39	1.55
Third quarter	4.16	2.17
Fourth quarter	3.77	2.50
Fiscal year ended December 31, 2006		
First quarter	\$ 5.20	\$ 3.16
Second quarter (through May 12)	\$ 5.38	\$ 4.28

On May 12, 2006, the last sale price reported on the AMEX for our common stock was \$4.84 per share. As of May 12, 2006, there were approximately 7,021 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

### Dividend policy

We have not declared or paid cash dividends on our common stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain future earnings, if any, to fund the development and growth of our business. Our board of directors will determine future dividends, if any.

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### Dilution

If you invest in our common stock, your interest will be diluted to the extent of the difference between the public offering price per share you pay in this offering and the net tangible book value per share of our common stock immediately after this offering.

Our net tangible book value on March 31, 2006 was approximately (\$25,945,510), or approximately \$(0.38) per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding. As adjusted net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after completion of this offering. After giving effect to the sale of 15,495,867 shares of our common stock in this offering at an assumed public offering price of \$4.84 per share and after deducting underwriting discounts and commissions and our estimated offering expenses, our as adjusted net tangible book value as of March 31, 2006 would have been \$0.51 per share. This amount represents an immediate increase in net tangible book value of \$0.89 per share to existing shareholders and an immediate dilution in net tangible book value of \$4.33 per share to purchasers of common stock in this offering, as illustrated in the following table:

Assumed public offering price per share			\$ 4.84
Net tangible book value per share as of March 31, 2006	(\$	0.38)	
Increase in net tangible book value per share attributable to new investors		0.89	
As adjusted net tangible book value per share after this offering			0.51
Dilution per share to new investors			\$ 4.33

If the underwriters exercise their over-allotment option in full, the as adjusted net tangible book value as of March 31, 2006 would have been \$0.63 per share, representing an increase to existing shareholders of \$1.01 per share, and there will be an immediate dilution of \$4.21 per share to new investors. The number of shares of our common stock in the table above excludes as of March 31, 2006:

3,113,000 shares of our common stock issuable upon the exercise of stock options issued under our stock option plans having a weighted average exercise price of \$2.13 per share;

an additional 17,737,100 shares of our common stock issuable upon the exercise of outstanding warrants having a weighted average exercise price of \$2.06 per share; and

an additional 5,234,268 shares of common stock available for future issuance under our stock option plans and employee stock purchase plan.

To the extent that these options are exercised, there could be further dilution to new investors.

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### Board of directors and executive officers

The names of each of our directors and executive officers at May 12, 2006 and certain information about them are set forth below.

The Board of Directors is currently composed of six members. Directors are elected annually. Each director s term is subject to the election and qualification of his successor, or his earlier death, resignation or removal. The authorized number of directors may not be less than three or more than nine and may be established within that range by our Board of Directors. There are no family relationships among any of our directors or executive officers.

Name	Age	Position	Director Since
Mark Bagnall, CPA <sup>(1)</sup>	49	Director	2004
Mark Cantwell	36	Vice President, Research & Development	
Carrie E. Carlander	35	Chief Financial Officer, Senior Vice President,	
		Finance, Secretary and Treasurer	
Brian Culley	35	Senior Vice President, Business Development	
Michael M. Goldberg, M.D. <sup>(1)</sup>	47	Director	2004
M. Ross Johnson, Ph.D.	61	Chairman of the Board	2002
Evan M. Levine	40	Director, Chief Executive Officer, President	2002
Keith Meister <sup>(2)</sup>	33	Director	2005
Mark J. Pykett, V.M.D., Ph.D. <sup>(1)</sup>	42	Director	2004
Joan M. Robbins	46	Executive Vice President and Chief Science	
		Officer	

- (1) Member of the Audit Committee, the Compensation Committee and the Nominating and Governance Committee of the Board of Directors.
- (2) *Member of the Compensation Committee of the Board of Directors.*

Mark Bagnall, CPA. Mr. Bagnall has served as a Director since February 2004. Mr. Bagnall is currently Senior Vice President and Chief Finance and Operations Officer of Metabolex, Inc., a privately held pharmaceutical company focused on the development of drugs to treat diabetes and related metabolic disorders, where he has served since June 2000. Mr. Bagnall has been in the biotechnology industry for over 17 years. In the 12 years prior to joining Metabolex, Mr. Bagnall held the top financial position at four life science companies: Metrika, Inc., a privately held diagnostics company, and three public biotechnology companies, Progenitor, Inc., Somatix Therapy Corporation, and Hana Biologics, Inc. During his career in biotechnology, he has managed several private and public financings, merger and acquisition transactions and corporate licensing agreements. Mr. Bagnall received his Bachelor of Science degree in Business Administration from the U.C. Berkeley Business School and is a Certified Public Accountant. Mark J. Cantwell, Ph.D. Dr. Cantwell is Vice President, Research and Development and has served in this role since January 2006. Dr. Cantwell joined the Company as Director of Preclinical Programs in November 2003. From 1998 to 2003, Dr. Cantwell was employed at Tragen Pharmaceuticals, formerly Immunogenex Inc., a company specializing in immune therapies for cancer and autoimmune diseases. While at Tragen, Dr. Cantwell was a staff scientist involved in the preclinical development of Tragen s drug candidates. Prior to joining Tragen, Dr. Cantwell received his Ph.D. in Biomedical Sciences at the University of California, San Diego in the lab of Thomas J. Kipps, M.D., Ph.D. Dr. Cantwell received his B.S. in Applied Biology at Georgia Institute of Technology.

Carrie E. Carlander. Ms. Carlander has served as our Vice President, Finance and Treasurer since November 2004 and was appointed Chief Financial Officer in December 2004. Furthermore,

### Board of directors and executive officers

Ms. Carlander was appointed Senior Vice President, Finance in January 2005. From August 2004 to December 2004, Ms. Carlander served in a consulting capacity as Chief Financial Officer of Singlefin, Inc., an email/internet security software company. From December 2003 to December 2004, Ms. Carlander served in a consulting capacity as Chief Financial Officer of SofLinx, Inc., a wireless sensor network and software company. From December 2002 to June 2004, Ms. Carlander served as Vice President of Finance of V-Enable, Inc., a software company specializing in multimodal software for wireless devices. From December 1996 to May 2000, Ms. Carlander served first as Director of Finance and Human Resources, and then as Vice President, Finance and Administration, of Websense Inc., a publicly traded company that provides software products that analyze, report and manage computing resource use by employees. Ms. Carlander received her B.A. in Political Science from University of California, San Diego, her MBA from San Diego State University and a Certified Management Accountant designation from the IMA. Brian M. Culley, MS, MBA. Mr. Culley is our Senior Vice President, Business Development. He has served as Vice President, Business Development since joining us in December 2004, and was appointed Senior Vice President, Business Development in January 2006. From 2002 until 2004, Mr. Culley managed all strategic collaborations and licensing agreements for Immusol, Inc. in San Diego, where his most recent title was Director of Business Development and Marketing. From 1999 until 2000, he was a licensing and marketing associate at the University of California, San Diego Department of Technology Transfer & Intellectual Property Services and from 1996 to 1999, he was a research associate for Neurocrine Biosciences, Inc., where he performed drug discovery research. Mr. Culley has over 12 years of experience in the biotechnology industry, including deal structure and negotiation, licensing, due diligence, market and competitive research, and venture funding. He received a MS in Biochemistry from the University of California Santa Barbara and an MBA from The Johnson School of Business at Cornell University with an emphasis on private equity and entrepreneurship.

Michael M. Goldberg, M.D. Dr. Goldberg has served as a Director since January 2004. Dr. Goldberg is currently Chairman and Chief Executive Officer of Emisphere Technologies, Inc. where he has served since August 1990. Emisphere is a biopharmaceutical company specializing in the oral delivery of therapeutic macromolecules and other compounds that are not currently deliverable by oral means. Dr. Goldberg was previously a Vice President for The First Boston Corporation, where he was a founding member of the Healthcare Banking Group. He received a B.S. from Rensselaer Polytechnic Institute, an M.D. from Albany Medical College of Union University and an M.B.A. from Columbia University Graduate School of Business.

M. Ross Johnson, Ph.D. Dr. Johnson has served as our Chairman of the Board since October 2002. Dr. Johnson is also currently Chief Executive Officer, Director and Co-Founder of Parion Sciences, Inc. where he has served since February 2001. He has served on numerous boards and currently holds additional board positions with Cortex Pharmaceuticals, Inc. (COR) and the University of North Carolina Education Advancement Board. He also currently serves on the Advisory Board of the Chemistry Department at the University of California at Berkley and the University of North Carolina at Chapel Hill. From 1995 to 1999, he was President, Chief Executive Officer and Chief Scientific Officer of Trimeris, Inc. (TRMS), a company which went public in 1997. From 1987 to 1994, he was Vice President of Chemistry at Glaxo Inc. (GSK) where he was part of the original scientific founding team for Glaxo s research entry in the U.S. From 1971 to 1987, Dr. Johnson served in key scientific and research management positions with Pfizer Central Research (PFE). He has also served as a Special Advisor to Nobex Corporation, Ceretec, AtheroGenics, Inc. (AGIX) and Albany Molecular Research, Inc. (AMRI). Dr. Johnson received his B.S. in Chemistry from the University of California at Berkeley in 1967 and a Ph.D. in organic chemistry from the University of California at Santa Barbara in 1970.

*Evan M. Levine.* Mr. Levine has served as our President and Chief Executive Officer since September 2004 and as a member of our Board of Directors since October 2002. From January 2004 until

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### Board of directors and executive officers

August 2005, Mr. Levine served as Vice Chairman of the Board and from October 2002 until August 2005 Mr. Levine served as Chief Operating Officer and Secretary of the Company. From March 2002 to June 2002, Mr. Levine served as the Interim Chief Executive Officer of Digital Courier Technologies, Inc., a provider of advanced e-payment services for businesses, merchants and financial institutions. From 1997 to 2001, he served as Managing Principal and Portfolio Manager of Brown Simpson Asset Management, a private equity fund, specializing in structured finance for public companies. From 1996 to 1997, he served as Senior Vice President of Convertible Sales and Trading at Dillon Read & Company, a financial services company, managing a proprietary convertible portfolio and supervising all institutional sales and trading activity. From 1993 to 1996, he served as Vice President of Convertible Sales and Trading at Hambrecht & Quist, a financial services company, where he handled all convertible operations and augmented investment banking and corporate finance revenues through his involvement in the placement of convertible products. From 1992 to 1993, he served as a Global Arbitrage Trader at Spectrum Trading Partners, a financial derivatives trading company, where he was responsible for maintaining market neutral and currency neutral hedges for an international convertible securities portfolio. Mr. Levine has over 18 years of investment banking, venture capital, institutional trading, arbitrage dealing, and senior corporate management experience. Mr. Levine received his B.A. in Economics and Finance from Rutgers University and has completed graduate coursework for his MBA at New York University s Stern School of Business.

Keith Meister. Mr. Meister was appointed Director in August 2005. Since June 2002, Mr. Meister has been a Senior Investment Analyst of High River Limited Partnership, a company owned and controlled by Mr. Carl C. Icahn that is primarily engaged in the business of holding and investing in securities. Mr. Meister is also a Senior Investment Analyst of Icahn Partners LP and Icahn Partners Master Fund LP, private investment funds controlled by Mr. Icahn. He is also a director of Icahn Fund Ltd., which is the feeder fund of Icahn Partners Master Fund LP. Since August 2003, Mr. Meister has served as the Chief Executive Officer of American Property Investors, Inc. (API), which is the general partner of American Real Estate Partners, L.P., a public limited partnership controlled by Mr. Icahn that invests in real estate and holds various other interests, including the interests in its subsidiaries that are engaged, among other things, in the oil and gas business, the casino entertainment business and the textile business. Mr. Meister served as API s President from August 2003 to April 2005. From March 2000 through the end of 2001, Mr. Meister co-founded and served as co-president of J Net Ventures, a venture capital fund focused on investments in information technology and enterprise software businesses. From 1997 through 1999, Mr. Meister served as an investment professional at Northstar Capital Partners, an opportunistic real estate investment partnership. Prior to his work at Northstar, Mr. Meister served as an investment analyst in the investment banking group at Lazard Freres. Mr. Meister also is a director of American Entertainment Properties Corp. and American Casino & Entertainment Properties Finance Corp., which are gaming companies, and Scientia Corporation, a private health care venture company, all of which are companies controlled by American Real Estate Partners, L.P., which is controlled by Mr. Icahn. In August 2005, Mr. Meister became a director of American Railcar Industries, Inc., a company of which Mr. Icahn is a principal beneficial stockholder, that is primarily engaged in the business of manufacturing covered hopper and tank railcars. Mr. Meister has been a director of XO Holdings, Inc. since February 2006 and was a member of XO Communications, Inc. s (XO Holdings predecessor) Board of Directors from January 2003 to February 2006. XO Holdings is a publicly traded telecommunications services provider controlled by Mr. Icahn. In addition, in January 2006, Mr. Meister became a director of BKF Capital Group Inc., a publicly traded investment firm. Mr. Meister received his A.B. in Government, cum laude, from Harvard College.

*Mark J. Pykett, V.M.D.*, *Ph.D.* Dr. Pykett has served as a Director since February 2004. Dr. Pykett is currently the President and Chief Operating Officer of Boston Life Sciences, Inc. where he has served since November 2004. From May 1996 until April 2003, Dr. Pykett served as President and Chief

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### Board of directors and executive officers

Executive Officer and a Director of Cytomatrix, LLC, a private biotechnology company focused on the research, development and commercialization of novel cell-based therapies that Dr. Pykett co-founded. Cytomatrix was acquired by Cordlife, Pte. Ltd., a subsidiary of CyGenics Ltd., a public biotechnology company listed on the Australian Stock Exchange. From April 2003 to February 2004, Dr. Pykett served as President of Cordlife and then as President and Director of CyGenics from February 2004 until November 2004. Dr. Pykett graduated Phi Beta Kappa, Summa Cum Laude from Amherst College, holds a veterinary degree, Phi Zeta, Summa Cum Laude, and doctorate in molecular biology from the University of Pennsylvania, and received an M.B.A. degree Beta Gamma Sigma from Northeastern University. He completed post-doctoral fellowships at the University of Pennsylvania and Harvard University. In his research in academia, Dr. Pykett focused on understanding the molecular basis of cancer. Dr. Pykett also held an adjunct faculty position at the Harvard School of Public Health from 1997 to 2004. Joan M. Robbins, Ph.D. Dr. Robbins is our Executive Vice President and Chief Science Officer. She served as our Chief Technical Officer from March 2003 to January 2006, and was appointed Executive Vice President and Chief Science Officer in January 2006. From 1996 to 2003, Dr. Robbins was employed by Immusol, Inc., a biopharmaceutical company specializing in anticancer and antiviral therapeutics in addition to certain dermatologic and ophthalmic disorders. At Immusol, she held several positions, including Vice President, Product Development, Senior Director, Product Development, and Director, Therapeutics. Dr. Robbins has directed drug discovery and development resulting in the advancement of drug candidates into Phase I, II and III human trials, including the development of clinical protocols with the FDA. She has also led programs for formulation, manufacturing, toxicology and pharmacology development. From 1994 to 1995, she was Research Scientist and Project Leader for Cancer Research at Chiron where she developed gamma-IFN recombinant retroviral immuno-gene therapy for cancer, and tk-recombinant retroviral gene therapy for brain tumors. From 1992 to 1993, Dr. Robbins was a Post Graduate Researcher at University of California, San Diego, where she developed a novel DNA-based immunotherapeutic for treatment of Her2/neu expressing tumors. From 1990 to 1991, she was a Research Fellow at the Garvin Institute for Medical Research, Centre for Immunology in Sydney, Australia, and from 1981 to 1989, Dr. Robbins was a Microbiologist at the Laboratory of Tumor Immunology and Biology at the National Cancer Institute in Bethesda, Maryland. Dr. Robbins received her B.S. degree in genetics from the University of California, Davis, and a Ph.D. degree in genetics from George Washington University, Washington D.C.

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# Certain relationships and related transactions

Since January 1, 2003, we have not entered into any material transaction with any of our directors, executive officers or holders of more than 5% of our common stock, or with any persons in which directors, executive officers or such stockholders have direct or indirect material interests, except as described below.

In July 2005, we entered into a Securities Purchase Agreement (the Purchase Agreement ) with (i) Icahn Partners LP, Icahn Partners Master Fund LP and High River Limited Partnership (the Icahn Funds ); (ii) Viking Global Equities LP and VGE III Portfolio Ltd. (the Viking Funds ), and (iii) certain other investors (the Purchase Agreement ). Pursuant to the Purchase Agreement, we sold 4,324,324 shares of our common stock to the Icahn Funds for an aggregate purchase price of approximately \$8,000,000 and issued to the Icahn Funds warrants to purchase 4,324,324 shares of our common stock at an exercise price of \$2.26 per share. Pursuant to the Purchase Agreement, we also sold 3,783,783 shares of our common stock to the Viking Funds for an aggregate purchase price of approximately \$7,000,000 and issued to the Viking Funds warrants to purchase 3,783,783 shares of our common stock at an exercise price of \$2.26 per share. We believe that the Icahn Funds and the Viking Funds are each the beneficial holder of more than five percent of our outstanding common stock. We believe that Keith Meister, a member of our Board of Directors who was appointed pursuant to our agreements with the Icahn Funds and the Viking Funds, may be deemed to be the beneficial owner of the shares beneficially owned by the Icahn Funds.

In the Purchase Agreement, we agreed to enter into a Rights Agreement (the Icahn/ Viking Agreement ) upon the closing of the transaction with the Icahn Funds and the Viking Funds (together, the Icahn/ Viking Investors ). Pursuant to the Icahn/ Viking Agreement, which is dated July 27, 2005, we agreed to propose to our stockholders the approval of the Classified Board Prohibition Amendment and the Poison Pill Prohibition Amendment, both of which were approved by our stockholders.

The Classified Board Prohibition Amendment prohibits us from dividing our Board of Directors into classes. Each of our directors, whether elected or appointed to our Board of Directors, would hold office until our next annual meeting of stockholders following such election or appointment. The prohibition would cease upon the earlier of (i) July 27, 2012; (ii) the date that the Icahn/Viking Investors, collectively, hold less than 4,054,053 of our shares (subject to certain adjustments) that the Icahn/Viking Investors purchased (or for which they exercise warrants for common stock issued) pursuant to the Securities Purchase Agreement, dated July 21, 2005; and (iii) the time of (A) any acquisition of us by means of merger, consolidation or other form of corporate reorganization (other than a reincorporation transaction or change of domicile) following which the holders of our outstanding voting securities immediately prior to the transaction do not hold equity securities representing a majority of the voting power of the surviving or resulting entity immediately following the transaction or (B) a sale of all or substantially all of our assets other than to a buyer in which the holders of our outstanding voting securities immediately prior to such sale hold (in their capacity as such) equity securities representing a majority of the voting power immediately following such sale (such earlier date set forth in (i), (ii) and (iii), the Prohibition Termination Date ).

A classified board of directors could serve to protect our stockholders against unfair treatment in takeover situations, by making it more difficult and time-consuming for a potential acquirer to take control of our Board of Directors. A company may also adopt a classified board of directors to ensure stability in the board of directors and thereby improve long-term planning which arguably benefits stockholders. Any benefit to us and our stockholders from instituting a classified board in these and other circumstances would be unavailable while the Classified Board Prohibition Amendment remains a part of our restated certificate of incorporation.

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# Certain relationships and related transactions

The Poison Pill Prohibition Amendment prohibits us from adopting or approving any rights plan, poison pill or other similar plan, agreement or device (a Poison Pill ) designed to prevent or make more difficult a hostile takeover of us by increasing the cost to a potential acquirer of such a takeover either through the issuance of new rights, shares of common stock or preferred stock or any other security or device that may be issued to stockholders of our company, other than all of our stockholders, that carry severe redemption provisions, favorable purchase provisions or otherwise. The foregoing provisions would cease to be of any force or effect upon the Prohibition Termination Date. Poison Pills are adopted for the purpose of making a hostile takeover prohibitively expensive for a hostile acquirer. Customarily, Poison Pills provide that the company issue a large number of new shares of capital stock, often preferred stock, to existing stockholders other than the hostile acquirer when the hostile acquirer has acquired a certain percentage of the outstanding stock often 15%. The newly issued shares customarily have harsh redemption and/or conversion features that would cause an immediate dilution of the target company s outstanding stock to the detriment of the hostile acquirer. Because of these severe redemption and/or conversion features, customarily a potential acquirer will not acquire a number of shares that would trigger the Poison Pill and would instead negotiate with the board of directors of the target company to amend the Poison Pill so that it will not apply to the acquirer s attempt to take over the target company or terminate the Poison Pill. Any benefit to us and our stockholders from adopting a poison pill in these and other circumstances would be unavailable while the Poison Pill Prohibition Amendment remains a part of our restated certificate of incorporation.

Pursuant to the Icahn Viking Agreement with the Icahn/Viking Investors, we also agreed to the following:

to grant the Icahn/Viking Investors the right to consent to any issuance of securities by us at a per share price lower than the Warrant exercise price for up to one year, with certain enumerated exceptions;

to grant the Icahn/Viking Investors the right to participate in sales of securities for the next seven years, with certain enumerated exceptions set forth in the Icahn/Viking Agreement, including the right to purchase (i) up to 50% of securities sold in a public offering if the offering price is equal to or below \$8.00 per share, (ii) up to 20% of the securities sold in a public offering if the offering price is above \$8.00 per share, and (iii) up to 50% of the securities sold in a private offering;

to obtain stockholder approval of any change of control transaction; and

to expand the size of the Board of Directors by one member and appoint a nominee of the Icahn/Viking Investors. Thereafter, for so long as the Icahn/Viking Investors hold the participation rights described above, we are required to nominate a nominee selected by them to our Board of Directors.

At a meeting on August 9, 2005, our Board of Directors expanded the size of our Board from five (5) to six (6) and appointed Mr. Keith Meister, the designee of the Icahn/Viking Investors, to our Board of Directors. (See Board of Directors and executive officers for information regarding Mr. Meister.)

In connection with this offering, the Icahn/ Viking Investors have waived their rights to participate in this offering. During 2004, we engaged Burnham Hill Partners to provide placement agent services to us in connection with the sale of certain of our securities. In consideration of the services Burnham Hill Partners provided to us, we paid Burnham Hill Partners \$874,532 and issued to Burnham Hill Partners and certain other persons designated by Burnham Hill Partners warrants to purchase up to an aggregate of 612,547 shares of common stock at \$2.00 per share. In connection with that engagement,

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# Certain relationships and related transactions

we agreed to pay to Burnham Hill Partners a four percent cash commission on each cash exercise of warrants to purchase up to an aggregate of (i) 3,125,272 shares of Common Stock at \$2.00 per share and (ii) 2,083,518 shares of Common Stock at \$2.50 per share, which warrants were acquired by investors in transactions for which Burnham Hill Partners acted as placement agent. During 2005, we paid \$84,378 to Burnham Hill Partners as cash commissions in connection with the cash exercise of a portion of these warrants. We believe that Matthew Balk, a person we believe is the beneficial holder of more than five percent of our outstanding Common Stock, is a partner of Burnham Hill Partners and therefore may have an indirect material interest in the amounts we paid to Burnham Hill Partners. We do not know the nature or extent of Mr. Balk s indirect interest in the amounts we paid to Burnham Hill Partners, except that Burnham Hill Partners directed us to issue a warrant to purchase up to 184,447 shares of Common Stock directly to Mr. Balk from the warrants we were obligated to issue to Burnham Hill Partners.

SD Pharmaceuticals, which we acquired on April 26, 2006, is party to an agreement pursuant to which SD Pharmaceuticals has agreed to offer any formulation developmental work it requires to Latitude Pharmaceuticals, Inc. before it may contract with any other third party for these services. We are not required to use Latitude Pharmaceuticals to provide these services if we determine in good faith that Latitude Pharmaceuticals cannot provide the services on a competitive, cost effective, timely and quality basis comparable to what other third parties are able to provide, and also in certain other circumstances. Latitude Pharmaceuticals is a company controlled by Mr. Andrew Chen, who was a principal of SD Pharmaceuticals prior to its acquisition by us and is currently one of our consultants. As a result of the acquisition, we issued 962,860 shares to The Chen Family Trust, for which Mr. Chen is a Trustee, representing less than 2% of our outstanding common stock.

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## Principal stockholders

The following table sets forth certain information as of May 3, 2006, concerning the ownership of common stock by (i) each of our stockholders that we believe is the beneficial owner of more than 5% of the outstanding shares of common stock, (ii) each current member of our Board of Directors, (iii) each of our executive officers and (iv) all directors and executive officers as a group. This information does not give effect to the sale of shares in this offering. or any other changes in our outstanding securities or in the holdings of the named security holders after May 3, 2006. We determined beneficial ownership in accordance with Rule 13d-3 under the Exchange Act and included all shares over which the beneficial owner exercises voting or investment power. Options and warrants to purchase common stock that are presently exercisable or exercisable within 60 days of May 3, 2006 that are held by any person listed below are included in the total number of shares beneficially owned for such person and are considered outstanding for the purpose of calculating the percentage ownership only of such holder. We have relied on information supplied by our officers, directors and certain stockholders and on information contained in filings with the SEC in completing the table below. Except as otherwise indicated, and subject to community property laws where applicable, we believe, based on information provided by these persons or contained in filings with the SEC, that the persons named in the table have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them. The percentage of beneficial ownership of common stock is based on 71,649,833 shares of common stock outstanding as of May 3, 2006 and for any particular stockholder, the options or warrants described above held by that holder.

Name and Address of Beneficial Owner <sup>(1)</sup>	Beneficial Ownership as of May 3, 2006	Percent of Outstanding Before Offering
Carl Icahn Related Funds <sup>(2)</sup>	8,648,648	12.07%
c/o Icahn Associates Corp.		
767 Fifth Avenue		
New York, NY 10153		
Viking Global Funds <sup>(3)</sup>	6,911,366	9.65%
c/o Viking Global Investors LP		
55 Railroad Avenue		
Greenwich, CT 06830		
Mark Capital LLC <sup>(4)</sup>	4,320,000	6.03%
<b>Current Directors</b>		
M. Ross Johnson, Ph.D. <sup>(5)</sup>	2,297,592	3.21%
Evan M. Levine <sup>(6)</sup>	4,570,000	6.78%
Mark Bagnall <sup>(7)</sup>	100,000	*
Michael Goldberg <sup>(8)</sup>	176,000	*
Mark Pykett <sup>(9)</sup>	100,000	*
Keith Meister <sup>(10)</sup>	8,648,648	12.07%

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# **Principal stockholders**

Name and Address of Beneficial Owner <sup>(1)</sup>	Beneficial Ownership as of May 3, 2006	Percent of Outstanding Before Offering
Executive Officers who are not Directors		
Joan Robbins, Ph.D. <sup>(11)</sup>	500,000	*
Carrie Carlander <sup>(12)</sup>	136,111	*
Brian Culley <sup>(13)</sup>	52,778	*
Mark J. Cantwell <sup>(14)</sup>	68,750	*
All directors and executive officers as a group	16,649,879	23.24%

- \* Less than one percent.
- (1) Unless indicated otherwise, the address of each person listed in the table is c/o ADVENTRX Pharmaceuticals, Inc.; 6725 Mesa Ridge Road, Suite 100; San Diego, California 92121
- Includes 864,865 shares of common stock held by High River Limited Partnership (High River), 1,660,540 shares of common stock held by Icahn Partners LP ( Icahn Partners ) and 1,798,919 shares of common stock held by Icahn Partners Master Fund LP ( Icahn Master ). Also includes 864,865 shares of common stock issuable upon exercise of warrants held by High River, 1,660,540 shares of common stock issuable upon exercise of warrants held by Icahn Partners and 1,798,919 shares of common stock issuable upon exercise of warrants held by Icahn Master. Based on our review of a Schedule 13D filed with the Commission on August 5, 2005 (the Icahn 13D) by High River, Hopper Investments, LLC (Hopper), Barberry Corp. (Barberry), Icahn Master, Icahn Offshore LP ( Icahn Offshore ), CCI Offshore Corp. ( CCI Offshore ), Icahn Partners, Icahn Onshore LP ( Icahn Onshore ), CCI Onshore Corp. ( CCI Onshore ) and Mr. Carl C. Icahn, we believe that each of (i) Barberry, Hopper and Mr. Icahn may be deemed to beneficially own (as that term is defined in Rule 13d-3 under the Exchange Act) the shares (including warrant shares) held by High River; (ii) CCI Onshore, Icahn Onshore and Mr. Icahn may be deemed to beneficially own (as that term is defined in Rule 13d-3 under the Exchange Act) the shares (including warrant shares) directly held by Icahn Partners; and (iii) CCI Offshore, Icahn Offshore and Mr. Icahn may be deemed to beneficially own (as that term is defined in Rule 13d-3 under the Exchange Act) the shares (including warrant shares) directly held by Icahn Master because in each of the foregoing cases such referenced persons are in a position to directly or indirectly determine the investment and voting decisions of the holder referenced. Barberry, Hopper, CCI Onshore, Icahn Onshore, CCI Offshore, Icahn Offshore and Mr. Icahn each disclaim beneficial ownership of such shares they may be deemed the beneficial owner of for all other purposes.
- (3) Includes 1,609,700 shares of common stock held by VGE III Portfolio Ltd. ( VGE III ) and 1,517,883 shares of common stock held by Viking Global Equities LP ( VGE Global ). Also includes 1,951,300 shares of common stock issuable upon exercise of warrants held by VGE III and 1,832,483 shares of common stock issuable upon exercise of warrants held by Viking Global. Based on our review of a Schedule 13G filed with the Commission on August 5, 2005 (the Viking 13G ) by Viking Global Performance LLC ( VGP ), Viking Global Investors LP ( VGI ), VGE Global, O. Andreas Halvorsen, Brian T. Olson and David C. Ott, we believe that each of VGP, VGI and Messrs. Halvorsen, Olson and Ott may be deemed to beneficially own (as that term is defined in Rule 13d-3 under the Exchange Act) the shares (including warrant shares) directly held by VGE III and VGE

Global because such persons are in a position to directly or indirectly determine the investment and voting decisions of VGE III and VGE Global.

(footnotes continued on following page)

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# **Principal stockholders**

- (4) Includes 100,000 shares of common stock subject to a warrant.
- (5) Includes 550,000 shares of common stock exercisable under an option and exercisable warrants to purchase 532,528 shares of common stock.
- (6) Includes 4,220,000 shares of common stock held by Mark Capital LLC and 100,000 shares of common stock subject to a warrant held by Mark Capital LLC. Mr. Levine is the managing member of Mark Capital LLC. Includes 250,000 shares of common stock exercisable under an option.
- (7) Includes 100,000 shares of common stock subject to options that are exercisable within 60 days of May 3, 2006.
- (8) Includes 100,000 shares of common stock subject to options that are exercisable within 60 days of May 3, 2006; a warrant to purchase 6,000 shares of common stock; and a warrant to purchase 50,000 shares of common stock held by Emisphere Technologies, Inc. of which Mr. Goldberg is the President and Chief Executive Officer.
- (9) Includes 100,000 shares of common stock subject to options that are exercisable within 60 days of May 3, 2006.
- (10) Based on our review of a Form 3 filed with the Commission on August 16, 2005 (the Form 3) by Keith Meister, a member of our Board of Directors, and the information disclosed in the Icahn 13D, we believe that because Mr. Meister is a limited partner of Icahn Onshore and has an interest in the fees, including the performance fees, relating to Icahn Onshore and Icahn Offshore, he may be deemed to beneficially own (as that term is defined in Rule 13d-3 under the Exchange Act) the shares (including warrant shares) beneficially owned by Icahn Onshore and Icahn Offshore. Mr. Meister disclaims beneficial ownership of all such shares (including warrant shares) in the Form 3.
- (11) Includes 500,000 shares of common stock subject to an option that is exercisable within 60 days of May 3, 2006; and 162,500 shares of common stock held by Dr. Robbins husband.
- (12) Includes 111,111 shares of common stock subject to an option that is exercisable within 60 days of May 3, 2006.
- (13) Consists of 52,778 shares of common stock subject to options that are exercisable within 60 days of May 3, 2006.
- (14) Consists of 68,750 shares of common stock subject to options that are exercisable within 60 days of May 3, 2006

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Material United States federal income and estate tax consequences to non-United States holders. The following is a general discussion of the material U.S. federal income and estate tax consequences of the ownership and disposition of our common stock by a non-U.S. holder that acquires our common stock pursuant to this offering. The discussion is based on provisions of the Internal Revenue Code of 1986, as amended (the Code), applicable U.S. Treasury regulations promulgated thereunder and administrative and judicial interpretations, all as in effect on the date of this prospectus, and all of which are subject to change, possibly on a retroactive basis. The discussion is limited to non-U.S. holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). As used in this discussion, the term non-U.S. holder means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

an individual who is a citizen or resident of the United States;

a corporation or partnership (including any entity treated as a corporation or partnership for U.S. federal income tax purposes) created or organized in or under the laws of the United States or any State of the United States or the District of Columbia, other than a partnership treated as foreign under U.S. Treasury regulations;

an estate the income of which is includible in gross income for U.S. federal income tax purposes regardless of its source; or

a trust (1) if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust, or (2) that has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

This discussion does not consider:

U.S. federal gift tax consequences, or U.S. state or local or non-U.S. tax consequences;

specific facts and circumstances that may be relevant to a particular non-U.S. holder s tax position, including, if the non-U.S. holder is a partnership, that the U.S. tax consequences of holding and disposing of our common stock may be affected by certain determinations made at the partner level;

the tax consequences for partnerships or persons who hold their interests through a partnership or other entity classified as a partnership for U.S. federal income tax purposes;

the tax consequences for the stockholders or beneficiaries of a non-U.S. holder;

all of the U.S. federal tax considerations that may be relevant to a non-U.S. holder in light of its particular circumstances or to non-U.S. holders that may be subject to special treatment under U.S. federal tax laws, such as financial institutions, insurance companies, tax-exempt organizations, certain trusts, hybrid entities, certain former citizens or residents of the United States, holders subject to U.S. federal alternative minimum tax, broker-dealers, and traders in securities; or

special tax rules that may apply to a non-U.S. holder that holds our common stock as part of a straddle, hedge, conversion transaction, synthetic security, or other integrated investment.

This discussion is for general purposes only. Prospective investors are urged to consult their own tax advisors regarding the application of the U.S. federal income and estate tax laws to their particular situations and the consequences under U.S. federal gift tax laws, as well as foreign, state, and local laws and tax treaties.

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# Material United States federal income and estate tax consequences to non-United States holders

### **Dividends**

As previously discussed, we do not anticipate paying dividends on our common stock in the foreseeable future. See Dividend Policy. If we pay dividends on our common stock, those payments will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those dividends exceed our current and accumulated earnings and profits, the dividends will constitute a return of capital and first reduce the non-U.S. holder s basis, but not below zero, and then will be treated as gain from the sale of stock.

We will have to withhold U.S. federal income tax at a rate of 30%, or a lower rate under an applicable income tax treaty, from the gross amount of the dividends paid to a non-U.S. holder, unless the dividend is effectively connected with the conduct of a trade or business of the non-U.S. holder within the United States or, if an income tax treaty applies, attributable to a permanent establishment of the non-U.S. holder within the United States. Under applicable U.S. Treasury regulations, a non-U.S. holder (including, in certain cases of non-U.S. holders that are entities, the owner or owners of such entities) will be required to satisfy certain certification requirements in order to claim a reduced rate of withholding pursuant to an applicable income tax treaty. Non-U.S. holders should consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

Dividends that are effectively connected with a non-U.S. holder s conduct of a trade or business in the United States or, if an income tax treaty applies, attributable to a permanent establishment in the United States, are taxed on a net income basis at the regular graduated U.S. federal income tax rates in the same manner as if the non-U.S. holder were a resident of the United States. In such cases, we will not have to withhold U.S. federal income tax if the non-U.S. holder complies with applicable certification and disclosure requirements. In addition, a branch profits tax may be imposed at a 30% rate, or a lower rate under an applicable income tax treaty, on dividends received by a foreign corporation that are effectively connected with the conduct of a trade or business in the United States. In order to claim the benefit of an income tax treaty or to claim exemption from withholding because the income is effectively connected with the conduct of a trade or business in the United States, the non-U.S. holder must provide a properly executed IRS Form W-8BEN, for treaty benefits, or W-8ECI, for effectively connected income, respectively (or such successor forms as the IRS designates), prior to the payment of dividends. These forms must be periodically undated.

A non-U.S. holder that is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for a refund together with the required information with the IRS.

# **Gain on Disposition of Common Stock**

A non-U.S. holder generally will not be subject to U.S. federal income or withholding tax with respect to gain realized on a sale or other disposition of our common stock unless one of the following applies:

the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the United States or, alternatively, if an income tax treaty applies, is attributable to a permanent establishment maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the regular graduated rates and in the manner applicable to U.S. persons and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above may also apply;

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# Material United States federal income and estate tax consequences to non-United States holders

the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met; in this case, the non-U.S. holder will be subject to a 30% tax on the gain derived from the disposition; or

our common stock constitutes a United States real property interest by reason of our status as a United States real property holding corporation, or a USRPHC, for U.S. federal income tax purposes at any time during the shorter of the 5-year period ending on the date of such disposition or the period that the non-U.S. holder held our common stock. We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our United States real property interests relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. As long as our common stock is regularly traded on an established securities market within the meaning of Section 897(c)(3) of the Code, however, such common stock will be treated as United States real property interests only if a non-U.S. holder owned directly or indirectly more than 5 percent of such regularly traded common stock during the shorter of the 5-year period ending on the date of disposition or the period that the non-U.S. holder held our common stock and we were a USRPHC during such period. If we are or were to become a USRPHC and a non-U.S. holder owned directly or indirectly more than 5 percent of our common stock during the period described above or our common stock is not regularly traded on an established securities market, then a non-U.S. holder would generally be subject to U.S. federal income tax on its net gain derived from the disposition of our common stock at regular graduated rates.

# **Federal Estate Tax**

Common stock owned or treated as owned by an individual who is a non-U.S. holder at the time of death will be included in the individual s gross estate for U.S. federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise and, therefore, may be subject to U.S. federal estate tax.

# **Information Reporting and Backup Withholding Tax**

We must report annually to the IRS and to each non-U.S. holder the amount of dividends paid to that holder and the tax withheld from those dividends. These reporting requirements apply regardless of whether withholding was reduced or eliminated by an applicable income tax treaty. Copies of the information returns reporting those dividends and withholding may also be made available under the provisions of an applicable income tax treaty or agreement to the tax authorities in the country in which the non-U.S. holder is a resident.

Under some circumstances, U.S. Treasury regulations require backup withholding and additional information reporting on reportable payments on common stock. The gross amount of dividends paid to a non-U.S. holder that fails to certify its non-U.S. holder status in accordance with applicable U.S. Treasury regulations generally will be reduced by backup withholding at the applicable rate (currently 28%).

The payment of the proceeds of the sale or other disposition of common stock made to a non-U.S. holder by or through the U.S. office of any broker, U.S. or non-U.S., generally will be reported to the IRS and reduced by backup withholding, unless the non-U.S. holder either certifies its status as a non-U.S. holder under penalties of perjury or otherwise establishes an exemption. The payment of the proceeds from the disposition of common stock made to a non-U.S. holder by or through a non-U.S. office of a non-U.S. broker will not be reduced by backup withholding or reported

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# Material United States federal income and estate tax consequences to non-United States holders

to the IRS, unless the non-U.S. broker has certain enumerated connections with the United States. In general, the payment of proceeds from the disposition of common stock made to a non-U.S. holder by or through a non-U.S. office of a broker that is a U.S. person or has certain enumerated connections with the United States will be reported to the IRS and may be reduced by backup withholding unless the broker receives a statement from the non-U.S. holder that certifies its status as a non-U.S. holder under penalties of perjury or the broker has documentary evidence in its files that the holder is a non-U.S. holder.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder s U.S. federal income tax liability, if any, provided that the required information is furnished to the IRS in a timely manner. These backup withholding and information reporting rules are complex and non-U.S. holders are urged to consult their own tax advisors regarding the application of these rules to them.

The foregoing discussion of U.S. federal income and estate tax considerations is not tax advice. Accordingly, each prospective non-U.S. holder of our common stock should consult that holder s own tax advisor with respect to the federal, state, local and non-U.S. tax consequences of the ownership and disposition of our common stock.

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# Underwriting

We are offering the shares of our common stock described in this prospectus supplement through the underwriters named below. UBS Securities LLC is the sole book-running manager of this offering. UBS Securities LLC, CIBC World Markets Corp., RBC Capital Markets Corporation and Fortis Securities LLC are the representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, each of the underwriters has severally agreed to purchase the number of shares of common stock listed next to its name in the following table:

Underwriters Number of shares

**UBS Securities LLC** 

CIBC World Markets Corp.

**RBC** Capital Markets Corporation

Fortis Securities LLC

Total 15,495,867

The underwriting agreement provides that the underwriters must buy all of the shares if they buy any of them. However, the underwriters are not required to take or pay for the shares covered by the underwriters over-allotment option described below.

Our common stock is offered subject to a number of conditions, including:

receipt and acceptance of our common stock by the underwriters; and

the underwriters right to reject orders in whole or in part.

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses electronically.

# **OVER-ALLOTMENT OPTION**

We have granted the underwriters an option to buy up to 2,324,380 additional shares of our common stock. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with this offering. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If the underwriters exercise this option, they will each purchase additional shares approximately in proportion to the amounts specified in the table above.

# **COMMISSIONS AND DISCOUNTS**

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$ per share from the public offering price. Any of these securities dealers may resell any shares purchased from the underwriters to other brokers or dealers at a discount of up to \$ per share from the public offering price. If all the shares are not sold at the public offering price, the representatives may change the public offering price and the other selling terms. Upon execution of the underwriting agreement, the underwriters will be obligated to purchase the shares at the prices and upon the terms stated therein and, as a result, will thereafter bear any risk associated with changing the offering price to the public or other selling terms. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

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# **Underwriting**

The following table shows the per share and total underwriting discounts and commissions we will pay to the underwriters, assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 2,324,380 shares:

	No exercise	Full exercise
Per share	\$	\$
Total	\$	\$

We estimate that the total expenses of this offering payable by us, not including the underwriting discounts and commissions, will be approximately \$1,000,000.

# **NO SALES OF SIMILAR SECURITIES**

We and our executive officers and directors have entered into lock-up agreements with the underwriters. Under these lock-up agreements, we and each of these persons may not, without the prior written approval of UBS Securities LLC, subject to limited exceptions, offer, sell, contract to sell, or otherwise dispose of, directly or indirectly, or hedge our common stock or securities convertible into or exercisable or exchangeable for our common stock. These restrictions will be in effect for a period of 90 days after the date of this prospectus supplement. The 90-day lock-up period may be extended under certain circumstances where we announce or pre-announce earnings or material news or a material event within approximately 18 days prior to, or approximately 16 days after, the termination of the 90-day period. At any time and without public notice, UBS Securities LLC may, in its sole discretion, release all or some of the securities from these lock-up agreements.

# INDEMNIFICATION AND CONTRIBUTION

We have agreed to indemnify the underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we will contribute to payments the underwriters and their controlling persons may be required to make in respect of those liabilities.

# AMERICAN STOCK EXCHANGE QUOTATION

Our common stock is quoted on the American Stock Exchange under the symbol ANX.

# PRICE STABILIZATION, SHORT POSITIONS

In connection with this offering, the underwriters may engage in activities that stabilize, maintain or otherwise affect the price of our common stock, including:

stabilizing transactions;
short sales;
purchases to cover positions created by short sales;

syndicate covering transactions.

imposition of penalty bids; and

Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of our common stock while this offering is in progress. These transactions may also include making short sales of our common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering. Short sales may be covered short sales, which are short positions in an amount not greater than the

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# **Underwriting**

underwriters over-allotment option referred to above, or may be naked short sales, which are short positions in excess of that amount.

The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which they may purchase shares through the over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchased in this offering.

The underwriters also may impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of that underwriter in stabilizing or short covering transactions.

As a result of these activities, the price of our common stock may be higher than the price that otherwise might exist in the open market. If these activities are commenced, they may be discontinued by the underwriters at any time. The underwriters may carry out these transactions on the AMEX, in the over-the-counter market or otherwise.

### **AFFILIATIONS**

Certain of the underwriters and their affiliates have provided and may provide certain commercial banking, financial advisory and investment banking services for us for which they receive fees. The underwriters and their affiliates may from time to time in the future engage in transactions with us and perform services for us in the ordinary course of their business.

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### Notice to investors

# European economic area

In relation to each Member State of the European Economic Area ( EEA ) which has implemented the Prospectus Directive (each, a Relevant Member State ), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date ) our common stock will not be offered to the public in that Relevant Member State prior to the publication of a prospectus in relation to our common stock that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, our common stock may be offered to the public in that Relevant Member State at any time:

- (a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts; or
- (c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive.

As used above, the expression offered to the public in relation to any of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common stock to be offered so as to enable an investor to decide to purchase or subscribe for our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression Prospectus Directive means Directive 2003/71/ EC and includes any relevant implementing measure in each Relevant Member State.

The EEA selling restriction is in addition to any other selling restrictions set out below.

# **United Kingdom**

Our common stock may not be offered or sold and will not be offered or sold to any persons in the United Kingdom other than to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or as agent) for the purposes of their businesses and in compliance with all applicable provisions of the Financial Services and Markets Act 2000 ( FSMA ) with respect to anything done in relation to our common stock in, from or otherwise involving the United Kingdom. In addition, each underwriter has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us. Without limitation to the other restrictions referred to herein, this prospectus supplement and the accompanying prospectus is directed only at (1) persons outside the United Kingdom, (2) persons having professional experience in matters relating to investments who fall within the definition of investment professionals in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005; or (3) high net worth bodies corporate, unincorporated associations and partnerships and trustees of high value trusts as described in

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### **Notice to investors**

Article 49(2) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005. Without limitation to the other restrictions referred to herein, any investment or investment activity to which this prospectus supplement and the accompanying prospectus relate is available only to, and will be engaged in only with, such persons, and persons within the United Kingdom who receive this communication (other than persons who fall within (2) or (3) above) should not rely or act upon this communication.

### **France**

No prospectus (including any amendment, supplement or replacement thereto) has been prepared in connection with the offering of our common stock that has been approved by the *Autorité des marchés financiers* or by the competent authority of another State that is a contracting party to the Agreement on the European Economic Area and notified to the *Autorité des marchés financiers*; no common stock has been offered or sold and will be offered or sold, directly or indirectly, to the public in France except to permitted investors ( *Permitted Investors* ) consisting of persons licensed to provide the investment service of portfolio management for the account of third parties, qualified investors (*investisseurs qualifiés*) acting for their own account and/or corporate investors meeting one of the four criteria provided in Article 1 of Decree N° 2004-1019 of September 28, 2004 and belonging to a limited circle of investors (*cercle restreint d investisseurs*) acting for their own account, with qualified investors and limited circle of investors having the meaning ascribed to them in Article L. 411-2 of the French *Code Monétaire et Financier* and applicable regulations thereunder; none of this prospectus supplement and the accompanying prospectus or any other materials related to the offer or information contained therein relating to our common stock has been released, issued or distributed to the public in France except to Permitted Investors; and the direct or indirect resale to the public in France of any common stock acquired by any Permitted Investors may be made only as provided by articles L. 412-1 and L. 621-8 of the French *Code Monétaire et Financier* and applicable regulations thereunder.

# Italy

The offering of shares of our common stock has not been cleared by the Italian Securities Exchange Commission (*Commissione Nazionale per le Società e la Borsa*, the CONSOB) pursuant to Italian securities legislation and, accordingly, shares of our common stock may not and will not be offered, sold or delivered, nor may or will copies of this prospectus supplement and the accompanying prospectus or any other documents relating to shares of our common stock or the offering be distributed in Italy other than to professional investors (*operatori qualificati*), as defined in Article 31, paragraph 2 of CONSOB Regulation No. 11522 of July 1, 1998, as amended ( *Regulation No. 11522* ).

Any offer, sale or delivery of shares of our common stock or distribution of copies of this prospectus supplement and the accompanying prospectus or any other document relating to shares of our common stock or the offering in Italy may and will be effected in accordance with all Italian securities, tax, exchange control and other applicable laws and regulations, and, in particular, will be: (i) made by an investment firm, bank or financial intermediary permitted to conduct such activities in Italy in accordance with the Legislative Decree No. 385 of September 1, 1993, as amended (the *Italian Banking Law*), Legislative Decree No. 58 of February 24, 1998, as amended, Regulation No. 11522, and any other applicable laws and regulations; (ii) in compliance with Article 129 of the Italian Banking Law and the implementing guidelines of the Bank of Italy; and (iii) in compliance with any other applicable notification requirement or limitation which may be imposed by CONSOB or the Bank of Italy.

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### **Notice to investors**

Any investor purchasing shares of our common stock in the offering is solely responsible for ensuring that any offer or resale of shares of common stock it purchased in the offering occurs in compliance with applicable laws and regulations.

This prospectus supplement and the accompanying prospectus and the information contained herein are intended only for the use of its recipient and are not to be distributed to any third party resident or located in Italy for any reason. No person resident or located in Italy other than the original recipients of this document may rely on it or its content. In addition to the above (which shall continue to apply to the extent not inconsistent with the implementing measures of the Prospective Directive in Italy), after the implementation of the Prospectus Directive in Italy, the restrictions, warranties and representations set out under the heading European Economic Area above shall apply to Italy.

# **Spain**

Neither the common stock nor this prospectus supplement and the accompanying prospectus have been approved or registered in the administrative registries of the Spanish National Securities Exchange Commission (*Comisión Nacional del Mercado de Valores*). Accordingly, our common stock may not be offered in Spain except in circumstances which do not constitute a public offer of securities in Spain within the meaning of articles 30bis of the Spanish Securities Markets Law of 28 July 1988 (*Ley 24/1988, de 28 de Julio, del Marcado de Valores*), as amended and restated, and supplemental rules enacted thereunder.

### Sweden

This is not a prospectus under, and has not been prepared in accordance with the prospectus requirements provided for in, the Swedish Financial Instruments Trading Act (*lagen* (1991:980) *om handel med finasiella instrument*) nor any other Swedish enactment. Neither the Swedish Financial Supervisory Authority nor any other Swedish public body has examined, approved, or registered this document.

### **Switzerland**

The common stock may not and will not be publicly offered, distributed or re-distributed on a professional basis in or from Switzerland and neither this prospectus supplement and the accompanying prospectus nor any other solicitation for investments in our common stock may be communicated or distributed in Switzerland in any way that could constitute a public offering within the meaning of Articles 1156 or 652a of the Swiss Code of Obligations or of Article 2 of the Federal Act on Investment Funds of March 18, 1994. This prospectus supplement and the accompanying prospectus may not be copied, reproduced, distributed or passed on to others without the underwriter s prior written consent. This prospectus supplement and the accompanying prospectus is not a prospectus within the meaning of Articles 1156 and 652a of the Swiss Code of Obligations or a listing prospectus according to article 32 of the Listing Rules of the Swiss Exchange and may not comply with the information standards required thereunder. We will not apply for a listing of our common stock on any Swiss stock exchange or other Swiss regulated market and this prospectus supplement and the accompanying prospectus may not comply with the information required under the relevant listing rules. The common stock offered hereby has not and will not be registered with the Swiss Federal Banking Commission and has not and will not be authorized under the Federal Act on Investment Funds of March 18, 1994. The investor protection afforded to acquirers of investment fund certificates by the Federal Act on Investment Funds of March 18, 1994 does not extend to acquirers of our common stock.

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# Legal matters

The validity of the issuance of shares of common stock we are offering under this prospectus will be passed upon for us by Bingham McCutchen LLP, San Francisco, California. Dewey Ballantine LLP, New York, New York, is counsel to the underwriters in connection with this offering.

# **Experts**

Our consolidated balance sheets as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders—equity (deficit) and cash flows for each of the years in the three-year period ended December 31, 2005, and for the period from June 12, 1996 (date of inception) through December 31, 2005, and management—s assessment of the effectiveness of internal control over financial reporting as of December 31, 2005, have been incorporated by reference in this prospectus and in the registration statement in reliance on the reports of J.H. Cohn LLP, independent registered public accounting firm, given upon the authority of that firm as experts in accounting and auditing. The report of J.H. Cohn LLP notes that the consolidated financial statements for the period from June 12, 1996 (date of inception) through December 31, 2001, were audited by other auditors. J.H. Cohn LLP—s opinion insofar as it relates to the period from June 12, 1996 to December 31, 2001, is based solely on the report of such other auditors.

The financial statements of SD Pharmaceuticals, Inc. as of December 31, 2005 and 2004 and for the year ended December 31, 2005 and for the period from June 16, 2004 (date of inception) to December 31, 2004 have been incorporated by reference in this prospectus and in the registration statement in reliance on the report, which includes an explanatory paragraph relating to the ability of SD Pharmaceuticals, Inc. to continue as a going concern, of J.H. Cohn LLP, independent registered public accounting firm, given upon the authority of that firm as experts in accounting and auditing.

# Where you can find more information about us

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file with the Commission at the Public Reference Room at the Commission, 100 F Street, N.E., Washington, D.C. 20549. Please call 1-800-SEC-0330 for further information concerning the Public Reference Room. The Commission also makes these documents and other information available on its website at http://www.sec.gov. We also maintain a website at http://www.adventrx.com. The material on our website is not a part of this prospectus supplement or the accompanying prospectus. We have filed with the Commission a registration statement under the Securities Act on Form S-3 relating to the common stock offered by this prospectus supplement. This prospectus supplement and the accompanying prospectus constitute a part of the registration statement but do not contain all of the information set forth in the registration statement and its exhibits. For further information, we refer you to the registration statement and its exhibits. The Commission allows us to incorporate by reference the information we file with it, which means that we can disclose certain information to you by referring you to another document we have filed with the Commission. We may furnish other information to the Commission which is not considered to be filed and is therefore not incorporated by reference into or otherwise a part of this prospectus supplement and the accompanying prospectus, unless we indicate to the contrary. The information incorporated by reference is an important part of this prospectus supplement and the accompanying

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# Where you can find more information about us

prospectus and information that we file later with the Commission will automatically update this prospectus supplement and the accompanying prospectus and replace any outdated information. We incorporate by reference the following:

- (a) the section entitled Description of Registrant's Securities contained in the Registrant's Registration Statement on Form 8-A (file No. 001-32157) filed with the Commission on April 27, 2004;
- (b) our Annual Report on Form 10-K for the fiscal year ended December 31, 2005 filed with the Commission on March 16, 2006:
  - (c) our Current Report on Form 8-K filed with the Commission on January 30, 2006;
  - (d) our Current Report on Form 8-K filed with the Commission on January 31, 2006;
  - (e) our Current Report on Form 8-K filed with the Commission on February 6, 2006;
  - (f) our Current Report on Form 8-K filed with the Commission on February 15, 2006;
  - (g) our Current Report on Form 8-K filed with the Commission on March 1, 2006;
- (h) our Current Report on Form 8-K filed with the Commission on March 20, 2006 (Items 4.02, 8.01 and 9.01), as amended by Amendment No. 1 filed with the Commission on March 27, 2006;
  - (i) our Current Report on Form 8-K filed with the Commission on March 20, 2006 (Items 8.01 and 9.01);
  - (j) our Current Report on Form 8-K filed with the Commission on April 6, 2006;
- (k) our Current Report on Form 8-K filed with the Commission on April 11, 2006 as amended by Amendment No. 1 filed with the Commission on May 1, 2006;
- (l) our Quarterly Report on Form 10-Q for the quarter ended March 31, 2006 filed with the Commission on May 10, 2006; and
- (m) any future filings we make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act prior to the termination of the offering of the securities made by this prospectus supplement and the accompanying prospectus.

You may request a copy of these filings, at no cost, by writing or telephoning:

Carrie E. Carlander Chief Financial Officer ADVENTRX Pharmaceuticals, Inc. 6725 Mesa Ridge Road, Suite 100 San Diego, California 92121 (858) 552-0866

We will provide exhibits to these filings at no cost only if they are specifically incorporated into those filings.

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### **PROSPECTUS**

\$100,000,000 Common Stock ADVENTRX Pharmaceuticals, Inc. 6725 Mesa Ridge Road, Suite 100 San Diego, California 92121 (858) 558-0866

ADVENTRX Pharmaceuticals, Inc. (the Company ) is offering an aggregate of up to \$100,000,000 of its common stock.

We may sell the shares covered by this prospectus from time to time in transactions on the American Stock Exchange LLC, in the over-the-counter market or in negotiated transactions. We may sell directly, or through agents or dealers designated from time to time, at fixed prices, at prevailing market prices at the time of sale, at varying prices determined at the time of sale or at negotiated prices.

Our common stock is listed on the American Stock Exchange LLC under the symbol ANX. On May 8, 2006, the last reported sale price of our common stock on the American Stock Exchange LLC was \$4.93 per share.

Investing In Our Common Stock Involves Risks. See Risk Factors beginning on page 7.

Neither the Securities and Exchange Commission nor any state securities regulator has approved or disapproved the shares of common stock covered by this prospectus, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 8, 2006

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## **Important Information About This Prospectus**

This prospectus is part of a shelf registration statement that we filed with the SEC. By using a shelf registration statement, we may sell our common stock, as described in this prospectus, from time to time in one or more offerings. Each time we sell our common stock, we will provide a supplement to this prospectus that contains specific information about the terms of that offering. The supplement may also add, update or change information contained in this prospectus. Before purchasing any of our common stock, you should carefully read both this prospectus and any supplement, together with the additional information incorporated into this prospectus or described under the heading Where You Can Find More Information.

You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell our common stock in any jurisdiction where the offer or sale is not permitted. The information in this prospectus and any prospectus supplement is accurate as of the date on the front cover of this prospectus or any prospectus supplement, and the information in documents we file with the SEC and incorporate by reference into this prospectus or any prospectus supplement, is accurate as of the date on those documents.

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In this prospectus, ADVENTRX, the company, we, us, and our refer to ADVENTRX Pharmaceuticals, Inc.

# **Special Note Regarding Forward-Looking Statements**

Some of the statements under Our Company, Risk Factors and elsewhere in this prospectus constitute forward-looking statements. These statements involve known and unknown risks, uncertainties, and other factors that may cause our actual results to be materially different from projected results expressed or implied by the forward-looking statements. These factors include, among others, those listed under Risk Factors and elsewhere in this prospectus. In some cases, you can identify forward-looking statements by terms such as may, plans, anticipates, believes, estimates, predicts, potential, or continue or similar terms. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements. Our actual results could differ materially from those expressed or implied by these forward-looking statements as a result of various factors, including the risk factors described under the heading Risk Factors and elsewhere in this prospectus. We undertake no obligation to update publicly any forward-looking statements for any reason, except as required by law, even as new information becomes available or other events occur in the future.

### Where You Can Find More Information About Us

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file with the Commission at the Public Reference Room at the Commission, 100 F Street, N.E., Washington, D.C. 20549. Please call 1-800-SEC-0330 for further information concerning the Public Reference Room. The Commission also makes these documents and other information available on its website at http://www.sec.gov. We also maintain a website at http://www.adventrx.com. The material on our website is not a part of this prospectus or any prospectus supplement.

We have filed with the Commission a registration statement under the Securities Act on Form S-3 relating to the common stock offered by this prospectus. This prospectus and any prospectus supplement constitute a part of the registration statement but do not contain all of the information set forth in the registration statement and its exhibits. For further information, we refer you to the registration statement and its exhibits.

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The Commission allows us to incorporate by reference the information we file with it, which means that we can disclose certain information to you by referring you to another document we have filed with the Commission. We may furnish other information to the Commission which is not considered to be filed and is therefore not incorporated by reference into or otherwise a part of this prospectus, unless we indicate to the contrary. The information incorporated by reference is an important part of this prospectus and information that we file later with the Commission will automatically update this prospectus and replace any outdated information. We incorporate by reference the following:

- (a) the section entitled Description of Registrant's Securities contained in the Registrant's Registration Statement on Form 8-A (file No. 001-32157) filed with the Commission on April 27, 2004;
- (b) our Annual Report on Form 10-K for the fiscal year ended December 31, 2005 filed with the Commission on March 16, 2006;
  - (c) our Current Report on Form 8-K filed with the Commission on January 30, 2006;
  - (d) our Current Report on Form 8-K filed with the Commission on January 31, 2006;
  - (e) our Current Report on Form 8-K filed with the Commission on February 6, 2006;
  - (f) our Current Report on Form 8-K filed with the Commission on February 15, 2006;
  - (g) our Current Report on Form 8-K filed with the Commission on March 1, 2006;
- (h) our Current Report on Form 8-K filed with the Commission on March 20, 2006 (Items 4.02, 8.01 and 9.01), as amended by Amendment No. 1 filed with the Commission on March 27, 2006;
  - (i) our Current Report on Form 8-K filed with the Commission on March 20, 2006 (Items 8.01 and 9.01);
  - (j) our Current Report on Form 8-K filed with the Commission on April 6, 2006;
- (k) our Current Report on Form 8-K filed with the Commission on April 11, 2006 as amended by Amendment No. 1 filed with the Commission on May 1, 2006; and
- (l) any future filings we make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act after the date of the initial registration statement and prior to effectiveness of the registration statement, and until we file a post-effective amendment which indicates the termination of the offering of the securities made by this prospectus.

You may request a copy of these filings, at no cost, by writing or telephoning:

Carrie E. Carlander Chief Financial Officer ADVENTRX Pharmaceuticals, Inc. 6725 Mesa Ridge Road, Suite 100 San Diego, California 92121 (858) 552-0866

We will provide exhibits to these filings at no cost only if they are specifically incorporated into those filings.

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## **Our Company**

We are a biopharmaceutical research and development company focused on introducing new technologies for anticancer and antiviral treatments that improve the performance and safety of existing drugs by addressing significant problems such as drug metabolism, toxicity, bioavailability and resistance. We do not manufacture, market, sell or distribute any product. Pursuant to license agreements with University of Southern California and SD Pharmaceuticals, Inc., we have rights to drug candidates in varying stages of development. Our current drug candidates are CoFactor, ANX-530, Selone and Thiovir. All of these drug candidates are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2005.

On May 30, 2003, we merged our wholly-owned subsidiary, Biokeys, Inc., into the Company and changed our name from Biokeys Pharmaceuticals, Inc. to ADVENTRX Pharmaceuticals, Inc. The merger had no effect on our financial statements.

In July 2004, we formed a wholly-owned subsidiary, ADVENTRX (Europe) Ltd., in the United Kingdom for the purpose of conducting drug trials in the European Union.

We have incurred net losses since our inception. As of December 31, 2005, our accumulated deficit was approximately \$59,964,840. We expect to incur substantial and increasing losses for the next several years as we continue development and possible commercialization of new products.

To date, we have funded our operations primarily through sales of equity securities.

Our business is subject to significant risks, including risks inherent in our ongoing clinical trials, the regulatory approval processes, the results of our research and development efforts, commercialization, and competition from other pharmaceutical companies.

### **Recent Developments**

On April 7, 2006, we entered into an Agreement and Plan of Merger (the Merger Agreement ) among the Company, SD Pharmaceuticals, Inc., a Delaware corporation (SDP), Speed Acquisition, Inc., a Delaware corporation and a wholly-owned subsidiary of the Company (Merger Sub), Paul Marangos and Andrew X. Chen, each as stockholders of SDP and Paul Marangos, as an individual acting as the stockholder representative. Pursuant to the Merger Agreement, we will acquire SDP through the merger of Merger Sub into SDP and SDP will continue as the surviving corporation and as a wholly-owned subsidiary of the Company (the Merger).

Upon the closing of the transaction on April 26, 2006, ADVENTRX acquired certain U.S. and ex-U.S. intellectual property rights to eight oncology and infectious disease product candidates, including certain ex-U.S. rights to SDP-012 (ANX-530, vinorelbine emulsion). In October 2005, ADVENTRX announced it had licensed U.S. development and marketing rights to SDP-012 (ANX-530) from SD Pharma. Certain product candidates that ADVENTRX acquired as a result of the merger are based on a nano-emulsion technology for both soluble and insoluble parenteral drugs. The nano-emulsion technology was developed by Dr. Andrew Chen and is designed to enable the delivery of vein irritating or difficult to dissolve drugs without excipient-induced adverse effects. Many of the product candidates are based on currently approved drugs and may qualify for the 505(b)(2) regulatory process. Certain product candidates obtained in the transaction are being evaluated by ADVENTRX as possible out-licensing opportunities.

The SD Pharma product portfolio consists of five anticancer and three anti-infective therapies which are listed below:

SDP-013 A non-allergenic, non cremophor-containing emulsion formulation of paclitaxel (Tax&P) designed to eliminate the need for immunosuppressant premedication, which is recommended for paclitaxel therapy to reduce the incidence and severity of severe hypersensitivity

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reaction. Paclitaxel is approved to treat breast, ovarian and non-small cell lung cancers. Taxol<sup>tm</sup> worldwide sales were approximately \$750 million in 2005. (Source: Bristol-Myers Squibb).

SDP-014 A novel docetaxel (Taxoter on the containing polysorbate 80 or other detergents, intended to eliminate the need for multiday immunosuppressant premedication, which is recommended for docetaxel therapy to reduce the incidence and severity of allergic reaction. Taxotere is approved to treat breast, non-small cell lung, prostate and gastric cancers. Worldwide Taxotere sales were approximately \$1.6 billion in 2005. (Source: Sanofi-Aventis)

SDP-012 (vinorelbine emulsion) A novel emulsion formulation of vinorelbine tartrate designed to reduce vein irritation associated with the drug. Vinorelbine is approved to treat non-small cell lung cancer. According to IMS Health, worldwide sales of vinorelbine in 2005 were over \$150 million.

- SDP-111 A novel formulation of beta-elemene, a small molecule anticancer agent belonging to the triterpene family and currently approved in China for a variety of cancers.
- SDP-112 An emulsion formulation of alpha-tocopheryl succinate, a form of vitamin E which has been shown to selectively facilitate apoptosis, or cell death, in cancer cells.
- SDP-015 A proprietary intravenous formulation of an approved antibiotic in the macrolide family known as clarithromycin. Clarithromycin is approved for mild to moderate bacterial infections such as in community-acquired pneumonia. Only oral formulations of clarithromycin are currently available in the U.S.
- SDP-011 A broad spectrum intranasal/topical anti-viral gel intended for use in cold and flu and other viral indications as an over-the-counter (OTC) product.
- SDP-016 A novel formulation of vancomycin, a parenteral glycopeptide antibiotic approved to treat gram-positive bacterial infections. SDP-016 is designed to reduce the vein irritation and phlebitis associated with the IV-delivered drug.

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### **Risk Factors**

Readers and prospective investors in our securities should carefully consider the following risk factors as well as the other information contained or incorporated by reference in this report. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that management is not aware of or focused on or that management currently deems immaterial may also impair our business operations. This report is qualified in its entirety by these risk factors.

If any of the following risks actually occur, the Company s financial condition and results of operations could be materially and adversely affected. If this were to happen, the value of the Company s securities could decline significantly, and you could lose all or part of your investment.

# We have a substantial accumulated deficit and limited working capital.

We had an accumulated deficit of \$59,964,840 as of December 31, 2005. Since we presently have no source of revenues and are committed to continuing our product research and development program, significant expenditures and losses will continue until development of new products is completed and such products have been clinically tested, approved by the FDA or other regulatory agencies and successfully marketed. In addition, we fund our operations primarily through the sale of equity securities, and have had limited working capital for our product development and other activities. We do not believe that debt financing from financial institutions will be available until at least the time that one of our products is approved for commercial production.

# We have no current product sales revenues or profits.

We have devoted our resources to developing a new generation of therapeutic drug products, but such products cannot be marketed until clinical testing is completed and governmental approvals have been obtained. Accordingly, there is no current source of revenues, much less profits, to sustain our present activities, and no revenues will likely be available until, and unless, the new products are clinically tested, approved by the FDA or other regulatory agencies and successfully marketed, either by us or a marketing partner, an outcome which we are not able to guarantee.

# It is uncertain that we will have access to future capital.

We do not expect to generate positive cash flow from operations for at least the next several years. As a result, substantial additional equity or debt financing for research and development or clinical development will be required to fund our activities. Although we have raised equity financing in the past, including in April 2004 and July 2005, we cannot be certain that we will be able to continue to obtain such financing on favorable or satisfactory terms, if at all, or that it will be sufficient to meet our cash requirements. Any additional equity financing could result in substantial dilution to stockholders, and debt financing, if available, would likely involve restrictive covenants that preclude us from making distributions to stockholders and taking other actions beneficial to stockholders. If adequate funds are not available, we may be required to delay or reduce the scope of our drug development program or attempt to continue development by entering into arrangements with collaborative partners or others that may require us to relinquish some or all of our rights to proprietary drugs. The inability to adequately and timely fund our capital requirements would have a material adverse effect on us.

# We are not certain that we will be successful in the development of our drug candidates.

The successful development of any new drug is highly uncertain and is subject to a number of significant risks. Our drug candidates, all of which are in a development stage, require significant, time-consuming and costly development, testing and regulatory clearance. This process typically takes several years and can require substantially more time. Risks include, among others, the possibility that a drug candidate will (i) be found to be ineffective or unacceptably toxic, (ii) have unacceptable side

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effects, (iii) fail to receive necessary regulatory clearances, (iv) not achieve broad market acceptance, (v) be subject to competition from third parties who may market equivalent or superior products, (vi) be affected by third parties holding proprietary rights that will preclude us from marketing a drug product, or (vii) not be able to be manufactured by manufacturers in a timely manner in accordance with required standards of quality. There can be no assurance that the development of our drug candidates will demonstrate the efficacy and safety of our drug candidates as therapeutic drugs, or, even if demonstrated, that there will be sufficient advantages to their use over other drugs or treatments so as to render the drug product commercially viable. In the past, we have been faced with limiting the scope and/or delaying the launch of preclinical and clinical drug trials due to limited cash and personnel resources. We have also chosen to terminate licenses of some drug candidates that were not showing sufficient promise to justify continued expense and development. In the event that we are not successful in developing and commercializing one or more drug candidates, investors are likely to realize a loss of their entire investment.

We have been delayed at certain times in the past in the development of our drug products by limited funding. In addition, if certain of our scientific and technical personnel resigned at or about the same time, the development of our drug products would probably be delayed until new personnel were hired and became familiar with the development programs.

Positive results in preclinical and clinical trials do not ensure that future clinical trials will be successful or that drug candidates will receive all necessary regulatory approvals for the marketing, distribution or sale of such drug candidates.

Success in preclinical and clinical trials does not ensure that large-scale clinical trials will be successful. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. The length of time necessary to complete clinical trials and to submit an application for marketing approval for a final decision by a regulatory authority varies significantly and may be difficult to predict. In the past, we have terminated licenses of drug candidates when our preclinical trials did not support or verify earlier preclinical data. There is a significant risk that any of our drug candidates could fail to show satisfactory results in continued trials, and would not justify further development.

# We will face intense competition from other companies in the pharmaceutical industry.

We are engaged in a segment of the pharmaceutical industry that is highly competitive and rapidly changing. If successfully developed and approved, any of our drug candidates will likely compete with several existing therapies. CoFactor, our leading drug candidate, would likely compete against a well-established product, leucovorin. In addition, there are numerous companies with a focus in oncology and/or anti-viral therapeutics that are pursuing the development of pharmaceuticals that target the same diseases as are targeted by the drugs being developed by us. We anticipate that we will face intense and increasing competition in the future as new products enter the market and advanced technologies become available. We cannot assure that existing products or new products developed by competitors will not be more effective, or more effectively marketed and sold than those we may market and sell. Competitive products may render our drugs obsolete or noncompetitive prior to our recovery of development and commercialization expenses.

Many of our likely competitors such as Merck and Pfizer, will also have significantly greater financial, technical and human resources and will likely be better equipped to develop, manufacture and market products. In addition, many of these competitors have extensive experience in preclinical testing and clinical trials, obtaining FDA and other regulatory approvals and manufacturing and marketing pharmaceutical products. A number of these competitors also have products that have been approved or are in late-stage development and operate large, well-funded research and development programs. Smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical and biotechnology companies. Furthermore, academic

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institutions, government agencies and other public and private research organizations are becoming increasingly aware of the commercial value of their inventions and are actively seeking to commercialize the technology they have developed. Companies such as Gilead, Roche and GlaxoSmithKline all have drugs in various stages of development that could become competitors. Accordingly, competitors may succeed in commercializing products more rapidly or effectively than us, which would have a material adverse effect on us.

# There is no assurance that our products will have market acceptance.

Our success will depend in substantial part on the extent to which a drug product, if eventually approved for commercial distribution, achieves market acceptance. The degree of market acceptance will depend upon a number of factors, including (i) the receipt and scope of regulatory approvals, (ii) the establishment and demonstration in the medical community of the safety and efficacy of a drug product, (iii) the product s potential advantages over existing treatment methods and (iv) reimbursement policies of government and third party payors. We cannot predict or guarantee that physicians, patients, healthcare insurers or maintenance organizations, or the medical community in general, will accept or utilize any of our drug products.

The unavailability of health care reimbursement for any of our products will likely adversely impact our ability to effectively market such products and whether health care reimbursement will be available for any of our products is uncertain.

Our ability to commercialize our technology successfully will depend in part on the extent to which reimbursement for the costs of such products and related treatments will be available from government health administration authorities, private health insurers and other third-party payors. Significant uncertainty exists as to the reimbursement status of newly approved medical products. We cannot guarantee that adequate third-party insurance coverage will be available for us to establish and maintain price levels sufficient for realization of an appropriate return on our investments in developing new therapies. If we are successful in getting FDA approval for CoFactor, we will be competing against a generic drug, leucovorin, which has a lower cost and a long, established history of reimbursement. Receiving sufficient reimbursement for purchase costs of CoFactor will be necessary to make it cost effective and competitive versus the established drug, leucovorin. Government, private health insurers, and other third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement for new therapeutic products approved for marketing by the FDA. Accordingly, even if coverage and reimbursement are provided by government, private health insurers, and third-party payors for use of our products, the market acceptance of these products would be adversely affected if the amount of reimbursement available for the use of our therapies proved to be unprofitable for health care providers.

# Uncertainties related to health care reform measures may affect our success.

There have been some federal and state proposals in the past to subject the pricing of health care goods and services, including prescription drugs, to government control and to make other changes to the U.S. health care system. None of the proposals seems to have affected any of the drugs in our programs. However, it is uncertain if future legislative proposals would be adopted that might affect the drugs in our programs or what actions federal, state, or private payors for health care treatment and services may take in response to any such health care reform proposals or legislation. Any such health care reforms could have a material adverse effect on the marketability of any drugs for which we ultimately require FDA approval.

Further testing of our drug candidates will be required and there is no assurance of FDA approval. The FDA and comparable agencies in foreign countries impose substantial requirements upon the introduction of medical products, through lengthy and detailed laboratory and clinical testing

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procedures, sampling activities and other costly and time-consuming procedures. Satisfaction of these requirements typically takes several years or more and varies substantially based upon the type, complexity, and novelty of the product.

The effect of government regulation and the need for FDA approval will delay marketing of new products for a considerable period of time, impose costly procedures upon our activities, and provide an advantage to larger companies that compete with us. There can be no assurance that the FDA or other regulatory approval for any products developed by us will be granted on a timely basis or at all. Any such delay in obtaining or failure to obtain, such approvals would materially and adversely affect the marketing of any contemplated products and the ability to earn product revenue. Further, regulation of manufacturing facilities by state, local, and other authorities is subject to change. Any additional regulation could result in limitations or restrictions on our ability to utilize any of our technologies, thereby adversely affecting our operations.

Human pharmaceutical products are subject to rigorous preclinical testing and clinical trials and other approval procedures mandated by the FDA and foreign regulatory authorities. Various federal and foreign statutes and regulations also govern or influence the manufacturing, safety, labeling, storage, record keeping and marketing of pharmaceutical products. The process of obtaining these approvals and the subsequent compliance with appropriate U.S. and foreign statutes and regulations are time-consuming and require the expenditure of substantial resources. In addition, these requirements and processes vary widely from country to country.

Among the uncertainties and risks of the FDA approval process are the following: (i) the possibility that studies and clinical trials will fail to prove the safety and efficacy of the drug, or that any demonstrated efficacy will be so limited as to significantly reduce or altogether eliminate the acceptability of the drug in the marketplace, (ii) the possibility that the costs of development, which can far exceed the best of estimates, may render commercialization of the drug marginally profitable or altogether unprofitable, and (iii) the possibility that the amount of time required for FDA approval of a drug may extend for years beyond that which is originally estimated. In addition, the FDA or similar foreign regulatory authorities may require additional clinical trials, which could result in increased costs and significant development delays. Delays or rejections may also be encountered based upon changes in FDA policy and the establishment of additional regulations during the period of product development and FDA review. Similar delays or rejections may be encountered in other countries.

# Our success will depend on licenses and proprietary rights we receive from other parties, and on any patents we may obtain.

Our success will depend in large part on our ability and our licensors ability to (i) maintain license and patent protection with respect to their drug products, (ii) defend patents and licenses once obtained, (iii) maintain trade secrets, (iv) operate without infringing upon the patents and proprietary rights of others and (iv) obtain appropriate licenses to patents or proprietary rights held by third parties if infringement would otherwise occur, both in the U.S. and in foreign countries. We have obtained licenses to patents and other proprietary rights from the University of Southern California.

The patent positions of pharmaceutical companies, including ours, are uncertain and involve complex legal and factual questions. There is no guarantee that we or our licensors have or will develop or obtain the rights to products or processes that are patentable, that patents will issue from any of the pending applications or that claims allowed will be sufficient to protect the technology licensed to us. In addition, we cannot be certain that any patents issued to or licensed by us will not be challenged, invalidated, infringed or circumvented, or that the rights granted thereunder will provide competitive disadvantages to us.

Litigation, which could result in substantial cost, may also be necessary to enforce any patents to which we have rights, or to determine the scope, validity and unenforceability of other parties proprietary rights, which may affect our rights. U.S. patents carry a presumption of validity and

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generally can be invalidated only through clear and convincing evidence. There can be no assurance that our licensed patents would be held valid by a court or administrative body or that an alleged infringer would be found to be infringing. The mere uncertainty resulting from the institution and continuation of any technology-related litigation or interference proceeding could have a material adverse effect on us pending resolution of the disputed matters. We may also rely on unpatented trade secrets and know-how to maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with employees, consultants and others. There can be no assurance that these agreements will not be breached or terminated, that we will have adequate remedies for any breach, or that trade secrets will not otherwise become known or be independently discovered by competitors.

# Our license agreements can be terminated in the event of a breach.

The license agreements pursuant to which we license our core technologies for our potential drug products permit the licensors, to terminate the agreement under certain circumstances, such as the failure by us to use our reasonable best efforts to commercialize the subject drug or the occurrence of any other uncured material breach by us. The license agreements also provide that the licensor is primarily responsible for obtaining patent protection for the technology licensed, and we are required to reimburse the licensor for the costs it incurs in performing these activities. The license agreements also require the payment of specified royalties. Any inability or failure to observe these terms or pay these costs or royalties could result in the termination of the applicable license agreement in certain cases. In the past, we have let lapse certain licenses for drug candidates when we determined that the expense and risk of continued development outweighed the likely benefits of that continued development. The termination of any license agreement could have a material adverse effect on us.

# Protecting our proprietary rights is difficult and costly.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. Accordingly, we cannot predict the breadth of claims allowed in these companies patents or whether we may infringe or be infringing these claims. Although we have not been notified of any patent infringement, nor notified others of patent infringement, such patent disputes are common and could preclude the commercialization of our products. Patent litigation is costly in its own right and could subject us to significant liabilities to third parties. In addition, an adverse decision could force us to either obtain third-party licenses at a material cost or cease using the technology or product in dispute.

# We may be unable to retain skilled personnel and maintain key relationships.

The success of our business depends, in large part, on our ability to attract and retain highly qualified management, scientific and other personnel, and on our ability to develop and maintain important relationships with leading research institutions and consultants and advisors. Competition for these types of personnel and relationships is intense from numerous pharmaceutical and biotechnology companies, universities and other research institutions. We are currently dependent upon our scientific staff, which has a deep background in our drug candidates and the ongoing preclinical and clinical trials. Recruiting and retaining senior employees with relevant drug development experience in oncology and anti-viral therapeutics is costly and time-consuming. There can be no assurance that we will be able to attract and retain such individuals on an uninterrupted basis and on commercially acceptable terms, and the failure to do so could have a material adverse effect on us by significantly delaying one or more of our drug development programs. The loss of any of our senior executive officers, including our chief executive officer and chief financial officer, in particular, could have a material adverse effect on the company and the market for our common stock, particularly if such loss was abrupt or unexpected. All of our employees are employed on an at-will basis under offer letters. We do not have non-competition agreements with any of our employees.

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## We currently have no sales capability, and limited marketing capability.

We currently do not have sales personnel. We have limited marketing and business development personnel. We will have to develop a sales force, or rely on marketing partners or other arrangements with third parties for the marketing, distribution and sale of any drug product which is ready for distribution. There is no guarantee that we will be able to establish marketing, distribution or sales capabilities or make arrangements with third parties to perform those activities on terms satisfactory to us, or that any internal capabilities or third party arrangements will be cost-effective. In addition, any third parties with which we may establish marketing, distribution or sales arrangements may have significant control over important aspects of the commercialization of a drug product, including market identification, marketing methods, pricing, composition of sales force and promotional activities. There can be no assurance that we will be able to control the amount and timing of resources that any third party may devote to our products or prevent any third party from pursuing alternative technologies or products that could result in the development of products that compete with, or the withdrawal of support for, our products.

# We do not have manufacturing capabilities and may not be able to efficiently develop manufacturing capabilities or contract for such services from third parties on commercially acceptable terms.

We do not have any manufacturing capacity. When and if required, we will seek to establish relationships with third-party manufacturers for the manufacture of clinical trial material and the commercial production of drug products as we have with our current manufacturing partners. There can be no assurance that we will be able to establish relationships with third-party manufacturers on commercially acceptable terms or that third-party manufacturers will be able to manufacture a drug product on a cost-effective basis in commercial quantities under good manufacturing practices mandated by the FDA or other regulatory matters.

The dependence upon third parties for the manufacture of products may adversely affect future costs and the ability to develop and commercialize a drug product on a timely and competitive basis. Further, there can be no assurance that manufacturing or quality control problems will not arise in connection with the manufacture of our drug products or that third party manufacturers will be able to maintain the necessary governmental licenses and approvals to continue manufacturing such products. Any failure to establish relationships with third parties for our manufacturing requirements on commercially acceptable terms would have a material adverse effect on us.

# We are dependent in part on third parties for drug development and research facilities.

We do not possess research and development facilities necessary to conduct all of our drug development activities. We engage consultants and independent contract research organizations to design and conduct clinical trials in connection with the development of our drugs. As a result, these important aspects of a drug s development will be outside our direct control. In addition, there can be no assurance that such third parties will perform all of their obligations under arrangements with us or will perform those obligations satisfactorily.

In the future, we anticipate that we will need to obtain additional or increased product liability insurance coverage and it is uncertain that such increased or additional insurance coverage can be obtained on commercially reasonable terms.

Our business will expose us to potential product liability risks that are inherent in the testing, manufacturing and marketing of pharmaceutical products. There can be no assurance that product liability claims will not be asserted against us. We intend to obtain additional limited product liability insurance for our clinical trials, directly or through our marketing development partners or contract research organization (CRO) partners, when they begin in the U.S. and to expand our insurance

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coverage if and when we begin marketing commercial products. However, there can be no assurance that we will be able to obtain product liability insurance on commercially acceptable terms or that we will be able to maintain such insurance at a reasonable cost or in sufficient amounts to protect against potential losses. A successful product liability claim or series of claims brought against us could have a material adverse effect on us.

# The market price of our shares, like that of many biotechnology companies, is highly volatile.

Market prices for our common stock and the securities of other medical and biomedical technology companies have been highly volatile and may continue to be highly volatile in the future. Factors such as announcements of technological innovations or new products by us or our competitors, government regulatory action, litigation, patent or proprietary rights developments, and market conditions for medical and high technology stocks in general can have a significant impact on any future market for our common stock.

If we cannot satisfy AMEX s listing requirements, it may delist our common stock and we may not have an active public market for our common stock. The absence of an active trading market would likely make the common stock an illiquid investment.

Our common stock is quoted on the American Stock Exchange. To continue to be listed, we are required to maintain shareholders equity of \$6,000,000 among other requirements. We do not satisfy that requirement as of December 31, 2005. The AMEX may consider delisting our common stock and suspend trading in the common stock in which case our common stock would likely trade in the over-the-counter market in the so-called pink sheets or, if available, the OTC Bulletin Board Service. As a result, an investor would likely find it significantly more difficult to dispose of, or to obtain accurate quotations as to the value of, our shares. Our ability to raise capital would most likely also be impaired due to our ineligibility to file resale registration statements under the Securities Act.

# If our common stock is delisted, it may become subject to the SEC s penny stock rules and more difficult to sell.

SEC rules require brokers to provide information to purchasers of securities traded at less than \$5.00 and not traded on a national securities exchange or quoted on the Nasdaq Stock Market. If our common stock becomes a penny stock that is not exempt from these SEC rules, these disclosure requirements may have the effect of reducing trading activity in our common stock and making it more difficult for investors to sell. The rules require a broker-dealer to deliver a standardized risk disclosure document prepared by the SEC that provides information about penny stocks and the nature and level of risks in the penny market. The broker must also give bid and offer quotations and broker and salesperson compensation information to the customer orally or in writing before or with the confirmation. The SEC rules also require a broker to make a special written determination that the penny stock is a suitable investment for the purchaser and receive the purchaser s written agreement to the transaction before a transaction in a penny stock.

# Changes in laws and regulations that affect the governance of public companies has increased our operating expenses and will continue to do so.

Recently enacted changes in the laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act of 2002 and the listing requirements for American Stock Exchange have imposed new duties on us and on our executives, directors, attorneys and independent accountants. In order to comply with these new rules, we have hired and expect to hire additional personnel and use additional outside legal, accounting and advisory services, which have increased and are likely to continue increasing our operating expenses. In particular, we expect to incur additional administrative expenses as we implement Section 404 of the Sarbanes-Oxley Act, which requires management to extensively evaluate and report on, and our independent registered public accounting

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firm to attest to, our internal controls. For example, we have incurred significant expenses, and expect to incur additional expenses, in connection with the evaluation, implementation, documentation and testing of our existing and newly implemented control systems. Management time associated with these compliance efforts necessarily reduces time available for other operating activities, which could adversely affect operating results. If we are unable to achieve full and timely compliance with these regulatory requirements, we could be required to incur additional costs, expend additional money and management time on additional remedial efforts which could adversely affect our results of operations.

Failure to implement effective control systems, or failure to complete our assessment of the effectiveness of our internal control over financial reporting, may subject us to regulatory sanctions and could result in a loss of public confidence, which could harm our operating results.

Pursuant to Section 404 of the Sarbanes-Oxley Act, beginning with our fiscal year ended December 31, 2005, we are required to include in our annual report our assessment of the effectiveness of our internal control over financial reporting. Furthermore, our independent registered public accounting firm is required to issue an opinion on whether our assessment of the effectiveness of our internal control over financial reporting is fairly stated in all material respects and separately report on whether it believes we maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005.

If we fail to remedy any material weaknesses which are uncovered, fail to timely complete our assessment, or if our independent registered public accounting firm cannot timely attest to our assessment, we could be subject to regulatory sanctions and a loss of public confidence in our internal control. In addition, any failure to implement required new or improved controls, or difficulties encountered in their implementation, could harm our operating results or cause us to fail to timely meet our regulatory reporting obligations.

We have engaged in and may continue to engage in further expansion through mergers and acquisitions, which could negatively affect our business and earnings.

We have engaged in and may continue to engage in expansion through mergers and acquisitions. There are risks associated with such expansion. These risks include, among others, incorrectly assessing the asset quality of a prospective merger partner, encountering greater than anticipated costs in integrating acquired businesses, facing resistance from customers or employees, and being unable to profitably deploy assets acquired in the transaction. Additional country- and region-specific risks are associated with transactions outside the United States. To the extent we issue capital stock in connection with additional transactions, these transactions and related stock issuances may have a dilutive effect on earnings per share and share ownership.

Our earnings, financial condition, and prospects after a merger or acquisition depend in part on our ability to successfully integrate the operations of the acquired company. We may be unable to integrate operations successfully or to achieve expected cost savings. Any cost savings which are realized may be offset by losses in revenues or other charges to earnings.

# **Description Of Capital Stock**

Our authorized capital stock consists of 1,000,000 shares of Preferred Stock, \$0.01 par value, and 200,000,000 shares of common stock, \$0.001 par value.

### **Common Stock**

Our common stock is quoted on the American Stock Exchange LLC under the symbol ANX.

We have never paid cash dividends on any of our securities and do not currently expect to pay any cash dividends on our securities in the foreseeable future. There are no restrictions that limit our

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ability to pay dividends on our common stock or that are likely to do so in the future other than restrictions under the Delaware General Corporation Law and other applicable law.

As of May 3, 2006, there were 71,649,833 shares of common stock issued and outstanding which were held of record by approximately 7,021 stockholders.

The holders of our common stock are entitled to one vote per share held of record on all matters submitted to a vote of the stockholders. Our certificate of incorporation does not provide for cumulative voting in the election of directors. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our Board of Directors out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock, if any, then outstanding. Holders of our common stock have no preemptive or other subscription or conversion rights. There are no redemption or sinking fund provisions applicable to our common stock.

In the event of our voluntary or involuntary liquidation, dissolution or winding up, the owners of shares of common stock will be entitled to share equally in any assets available for distribution after the payment in full of all debts and distributions and after the owners of any of our outstanding preferred stock have received their liquidation preferences in full.

American Stock Transfer & Trust Company is our stock transfer agent and it maintains all our stockholder records. If you have questions regarding ADVENTRX stock you own, stock transfers, address or name changes, lost stock certificates, or duplicate mailings, please contact American Stock Transfer & Trust Transfer Company directly at the address below. If your shares are held with a stockbroker, please contact your broker.

American Stock Transfer & Trust Company 59 Maiden Lane, Plaza Level New York, NY 10038 (800) 937-5449 www.amstock.com email address - info@amstock.com

### Preferred Stock

Our Board of Directors is authorized, without action by the stockholders, to issue preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges may include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, all or any of which may be greater than the rights of the common stock.

## **Use of Proceeds**

We intend to add the net proceeds from the sale of the common stock to our general funds to be used to fund research and development and clinical trials and for general corporate purposes, which may include investment in subsidiaries, working capital, capital expenditures, repayment of short-term borrowings, refinancing of existing long-term debt, acquisitions and other business opportunities.

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### **Plan Of Distribution**

We may sell the common stock through one or more of the following ways:

directly to purchasers;

to or through one or more underwriters or dealers; or

through agents.

A prospectus supplement with respect to a particular issuance of securities will set forth the terms of the offering of those securities, including the following:

name or names of any underwriters, dealers or agents;

the purchase price of the securities and the estimated amount we will receive;

underwriting discounts and commissions; and

any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers. If we use underwriters in the sale, the underwriters will acquire the securities for their own account and they may resell them from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriting syndicates represented by one or more managing underwriters or one or more independent firms acting as underwriters may offer the securities to the public. In connection with the sale of securities, we may compensate the underwriters in the form of underwriting discounts or commissions. The purchasers of the securities for whom the underwriters may act as agent may also pay them commissions. Underwriters may sell the securities to or through dealers, and these dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Unless otherwise set forth in the applicable prospectus supplement, the obligations of any underwriters to purchase the securities will be subject to conditions precedent, and the underwriters will be obligated to purchase all of the securities if any are purchased.

If we use dealers in the sale of the securities, we will sell the securities to the dealers as principals. The dealers may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. The applicable prospectus supplement will name any dealer, who may be deemed to be an underwriter, as that term is defined in the Securities Act, involved in the offer or sale of securities, and set forth any commissions or discounts we grant to the dealer.

If we use agents in the sales of the securities, the agents may solicit offers to purchase the securities from time to time. Any of these agents, who may be deemed to be an underwriter, as that term is defined in the Securities Act, involved in the offer or sale of the securities will be named, and any commissions payable by us to such agent set forth, in the applicable prospectus supplement. Any agent will be acting on a reasonable efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

We may also sell securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to resales. The terms of those sales would be described in the prospectus supplement.

If the prospectus supplement so indicates, we will authorize agents, underwriters or dealers to solicit offers to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to stock purchase or delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth the commission payable for solicitation of the contracts.

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Agents, dealers and underwriters may be entitled under agreements with us to indemnification against some civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents, dealers or underwriters may be required to make. Agents, dealers and underwriters or their affiliates may engage in transactions with, or perform services for, us or our subsidiaries for customary compensation.

If indicated in the applicable prospectus supplement, one or more firms may offer and sell securities in connection with a remarketing upon their purchase, in accordance with their terms, acting as principals for their own accounts or as our agents. Any remarketing firm will be identified and the terms of its agreement, if any, with us will be described in the applicable prospectus supplement. We may be obligated to indemnify the remarketing firm against some liabilities, including liabilities under the Securities Act, and the remarketing firm may engage in transactions with or perform services for us or our subsidiaries for customary compensation.

Any underwriter may engage in over-allotment, stabilizing and syndicate short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Over-allotment involves sales in excess of the offering size, which creates a short position. Stabilizing transactions involve bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate short covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the underwriters to reclaim selling concessions from dealers when the securities originally sold by the dealers are purchased in covering transactions to cover syndicate short positions. These transactions may cause the price of the securities sold in an offering to be higher than it would otherwise be. These transactions, if commenced, may be discontinued by the underwriters at any time.

The prospectus supplement relating to each offering will set forth the anticipated date of delivery of the securities.

## **Legal Matters**

The validity of the issuance of shares of common stock we are offering under this prospectus will be passed upon for us by Bingham McCutchen LLP, San Francisco, California.

### Experts

Our consolidated balance sheets as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders—equity (deficit) and cash flows for each of the years in the three-year period ended December 31, 2005, and for the period from June 12, 1996 (date of inception) through December 31, 2005, and management—s assessment of the effectiveness of internal control over financial reporting as of December 31, 2005, have been incorporated by reference in this prospectus and in the registration statement in reliance on the reports of J.H. Cohn LLP, independent registered public accounting firm, given upon the authority of that firm as experts in accounting and auditing. The report of J.H. Cohn LLP notes that the consolidated financial statements for the period from June 12, 1996 (date of inception) through December 31, 2001, were audited by other auditors. J.H. Cohn LLP—s opinion insofar as it relates to the period from June 12, 1996 to December 31, 2001, is based solely on the report of such other auditors.

The financial statements of SD Pharmaceuticals, Inc. as of December 31, 2005 and 2004 and for the year ended December 31, 2005 and for the period from June 16, 2004 (date of inception) to December 31, 2004 have been incorporated by reference in this prospectus and in the registration statement in reliance on the report, which includes an explanatory paragraph relating to the ability of SD Pharmaceuticals, Inc. to continue as a going concern, of J.H. Cohn LLP, independent registered public accounting firm, given upon the authority of that firm as experts in accounting and auditing.

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