

INTROGEN THERAPEUTICS INC

Form S-3/A

April 17, 2007

**Table of Contents**

As filed with the Securities and Exchange Commission on April 17, 2007

Registration No. 333-140424

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

**Amendment No. 1 to  
FORM S-3  
REGISTRATION STATEMENT  
*Under*  
*The Securities Act of 1933***

**INTROGEN THERAPEUTICS, INC.  
(Exact name of Registrant as specified in its charter)**

**Delaware  
(State or other jurisdiction of  
incorporation or organization)**

**74-2704230  
(I.R.S. Employer  
Identification Number)**

**301 Congress Avenue, Suite 1850  
Austin, Texas 78701  
(512) 708-9310**

**(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)**

**David G. Nance  
Chief Executive Officer  
Introgen Therapeutics, Inc.  
301 Congress Avenue, Suite 1850  
Austin, Texas 78701  
(512) 708-9310**

**(Name, address, including zip code, and telephone number, including area code, of agent for service)**

*Copies to:*

**Paul R. Tobias, Esq.  
Wilson Sonsini Goodrich & Rosati,  
Professional Corporation  
8911 Capital of Texas Highway  
Westech 360, Suite 3350  
Austin, Texas 78759-7247  
(512) 338-5400**

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box.

Edgar Filing: INTROGEN THERAPEUTICS INC - Form S-3/A

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to 462(e) under the Securities Act, check the following box. o

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. o

CALCULATION OF REGISTRATION FEE

Amount of Each Class of Securities to be Registered(1)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee
Common Stock, par value \$.001 per share	\$150,000,000	\$16,050

(1) This Registration Statement registers an indeterminate number of shares of common stock that the Registrant may sell from time to time. The aggregate offering price for all the shares of common stock that the Registrant may sell from time to time pursuant to this Registration Statement will not exceed \$150,000,000.

(2) The registration fee is calculated pursuant to Rule 457(o) under the Securities Act. Pursuant to Rule 415(a)(6)

under the Securities Act, shares of common stock having an aggregate offering price of \$5,685,809.80 from our Registration Statement on Form S-3 (File No. 333-107799) filed August 8, 2003 are included in this Registration Statement. Pursuant to Rule 415(a)(6) and Rule 457(p) of the Securities Act, \$608.38 of the registration fee previously paid by the Registrant in connection with such earlier registration statement is applied to and offset against the registration fee currently due.

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

---

**Table of Contents**

**The information in this prospectus is not complete and may be changed. We may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer, solicitation or sale is not permitted.**

**Subject to completion, dated April 17, 2007**

**PROSPECTUS**

**\$150,000,000**

**Common Stock**

By this prospectus, we may offer and sell from time to time up to an aggregate of \$150,000,000 of our common stock in amounts, at prices and on terms determined at the time of offering. We will provide specific terms of the offerings, including the offering prices, in one or more supplements to this prospectus. The prospectus supplements may also add, update or change information contained in this prospectus. We may sell the common stock directly to you or to or through underwriters, dealers or agents we select. If we use underwriters, dealers or agents to sell the securities, we will name them and describe their compensation in supplements to this prospectus.

Our common stock is traded on the Nasdaq Global Market under the symbol **INGN**. On April 16, 2007, the last reported sale price of our common stock as quoted on the Nasdaq Global Market was \$4.88 per share.

This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement.

**You are urged to carefully read this prospectus, the prospectus supplement relating to any specific offering of common stock and all of the information incorporated by reference herein and therein. Our business, and an investment in our common stock, involves significant risks. These risks are discussed in this prospectus under **Risk Factors** beginning on page 2 and in the documents incorporated by reference into this prospectus.**

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

The date of this prospectus is \_\_\_\_\_, 2007.

**TABLE OF CONTENTS**

	<b>Page</b>
<u>About This Prospectus</u>	1
<u>Summary</u>	1
<u>Risk Factors</u>	3
<u>Disclosure Regarding Forward-Looking Statements</u>	15
<u>Use of Proceeds</u>	16
<u>Plan of Distribution</u>	16
<u>Legal Matters</u>	17
<u>Experts</u>	17
<u>Incorporation of Certain Information by Reference</u>	17
<u>Where You Can Find More Information</u>	18
<u>Disclosure of SEC Position on Indemnification for Securities Act Liabilities</u>	18
<u>Consent of Ernst &amp; Young LLP</u>	

We have not authorized any person to give any information or make any representations in connection with this offering other than those contained or incorporated by reference into this prospectus and any accompanying prospectus supplement in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. You should rely only on the information contained in or incorporated by reference into this prospectus or any applicable prospectus supplement. Neither this prospectus nor any prospectus supplement shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. Neither the delivery of this prospectus or any prospectus supplement nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement is correct as of any date subsequent to the date hereof or of such prospectus supplement.

**ABOUT THIS PROSPECTUS**

This prospectus is part of a registration statement (Registration Statement) that we filed with the Securities and Exchange Commission (SEC) using a shelf registration process. Under this shelf process, we may from time to time sell the securities described in this prospectus in one or more offerings up to a maximum aggregate offering price of \$150,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus.

This prospectus does not contain all of the information included in the Registration Statement. For a more complete understanding of the offering of the securities, you should refer to the Registration Statement, including its exhibits. You should read both this prospectus and any prospectus supplement carefully, including the risks of investing in our common stock discussed under Risk Factors, together with the additional information described under the heading Where You Can Find More Information.

Unless otherwise indicated in this prospectus or any prospectus supplement, or the context otherwise requires, all references to Introgen, the Company, the Registrant, we, us or our mean Introgen Therapeutics, Inc.

**SUMMARY**

**Overview**

Introgen Therapeutics, Inc. was incorporated in Delaware in 1993. We are a biopharmaceutical company focused on the discovery, development and commercialization of targeted molecular therapies for the treatment of cancer and other diseases. We are developing product candidates to treat a wide range of cancers using tumor suppressors, cytokines and other targeted molecular therapies. These agents are designed to increase production of normal

cancer-fighting proteins that act to overpower cancerous cells, stimulate immune activity and enhance conventional cancer therapies.

## Table of Contents

Our primary approach to the treatment of cancers is to deliver targeted molecular therapies that increase production of normal cancer-fighting proteins to induce apoptosis, cell cycle control, cell growth control and gene regulation, including the regulation of angiogenic and immune factors. Our products work by acting as templates for the transient *in vivo* production of proteins that have pharmacological properties. The resultant proteins engage disease-related molecular targets or receptors to produce specific therapeutic effects.

We believe the use of targeted molecular therapies to induce the production of biopharmaceutical proteins represents a new approach for treating many cancers while avoiding the toxic side effects common to traditional therapies. We have developed significant expertise in developing targeted therapies that may be used to treat disease and in using what we believe are safe and effective delivery systems to transport these agents to the cancer cells. We believe we are able to treat a number of cancers in a way that kills cancer cells without harming normal cells.

Our principal executive offices are located at 301 Congress Avenue, Suite 1850, Austin, Texas 78701 and our telephone number is (512) 708-9310. Our website is located at [www.introgen.com](http://www.introgen.com). The information contained on our website is not a part of this prospectus.

### **The Offering**

Securities offered by Introgen Therapeutics, Inc.: Up to \$150,000,000 of common stock in one or more offerings. A prospectus supplement, which we will provide each time we offer common stock, will describe the specific amounts, prices and terms of the common stock.

We may sell the common stock to or through underwriters, dealers or agents or directly to purchasers. We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of common stock. Each prospectus supplement will set forth the names of any underwriter, dealer or agent involved in the sale of common stock described in that prospectus supplement and any applicable fees, commissions or discount arrangements with them.

Use of proceeds: Unless otherwise indicated in any prospectus supplement, the net proceeds from the sale of common stock offered by this prospectus will be used for general corporate purposes and working capital requirements. We may also use a portion of the net proceeds to fund possible investments in and acquisitions of complementary businesses, partnerships, minority investments, products or technologies. Currently, there are no commitments or agreements regarding such acquisitions or investments that are material. Pending their ultimate use, we intend to invest the net proceeds in money market funds, commercial paper and governmental and non-governmental debt securities with maturities of up to five years.

Risk factors: See **Risk Factors** for a discussion of the factors you should carefully consider before deciding to invest in shares of our common stock.

### **RISK FACTORS**

*An investment in our common stock involves a high degree of risk. In addition to the other information contained in this prospectus, you should carefully consider the following risks and uncertainties before purchasing our common stock. Our business, financial condition and operating results could be materially adversely affected by these risks and uncertainties. In that case, the trading price of our common stock could decline and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and*



*uncertainties may also impair our business operations.*

**If we are unable to commercialize ADVEXIN<sup>®</sup> therapy in various markets for multiple indications, particularly for the treatment of recurrent head and neck cancer, our business will be harmed.**

Our ability to achieve and sustain operating profitability depends on our ability to successfully commercialize ADVEXIN therapy in various markets for multiple indications, which depends in large part on our ability to commence, execute and complete clinical programs and obtain regulatory approvals for ADVEXIN therapy and other drug candidates. In particular, our ability to achieve and sustain profitability will depend in large part on our ability to commercialize in the United States ADVEXIN therapy for the treatment of recurrent head and neck cancer. We cannot assure you we will receive approval for ADVEXIN therapy for the treatment of recurrent head and neck cancer or other types of cancer or indications in the United States or in other countries or if approved that we will achieve significant level of sales. If we are unable to do so, our business will be harmed.

**Table of Contents**

**If we fail to comply with FDA or foreign regulatory authority requirements or encounter delays or difficulties in clinical trials for our product candidates we may not obtain regulatory approval of some or all of our product candidates on a timely basis, if at all.**

In order to commercialize our product candidates we must obtain certain regulatory approvals. Satisfaction of regulatory requirements typically takes many years and involves compliance with requirements covering research and development, testing, manufacturing, quality control, labeling and promotion of drugs for human use. To obtain regulatory approvals, we must, among other requirements, complete clinical trials demonstrating our product candidates are safe and effective for a particular cancer type or other disease. Regulatory approval of a new drug is never guaranteed. The FDA and foreign regulatory authorities have substantial discretion in the approval process. Despite the time and experience exerted, failure can occur at any stage, and we could encounter problems causing us to abandon clinical trials.

We have completed or are conducting clinical trials of our lead product candidate, ADVEXIN therapy, for the treatment of various cancers. Current or future clinical trials may demonstrate ADVEXIN therapy is neither safe nor effective.

We have completed or are conducting clinical trials of INGN 241, a product candidate based on the mda-7 tumor suppressor. We will need to continue conducting significant research and animal testing, referred to as pre-clinical testing, to support performing clinical trials for our other product candidates. It will take us many years to complete pre-clinical testing and clinical trials, and failure could occur at any stage of testing. Current or future clinical trials may demonstrate INGN 241 or our other product candidates are neither safe nor effective.

Any delays or difficulties we encounter in our pre-clinical research and clinical trials may delay or preclude regulatory approval. Our product development costs will increase if we experience delays in testing or regulatory approvals or if we need to perform more or larger clinical trials than planned. Any delay or preclusion could also delay or preclude the commercialization of ADVEXIN therapy or any other product candidates. In addition, we, the FDA or foreign regulatory authorities might delay or halt any of our clinical trials of a product candidate at any time for various reasons, including:

- the product candidate is less effective and/or more toxic than current therapies;

- the presence of unforeseen adverse side effects of a product candidate, including its delivery system;

- a longer than expected time required to determine whether or not a product candidate is effective;

- the death of patients during a clinical trial, even if the product candidate did not cause those deaths;

- the failure to enroll a sufficient number of patients in our clinical trials;

- the inability to produce sufficient quantities of a product candidate to complete the trials; or

- the inability to commit the necessary resources to fund the clinical trials.

We cannot be certain the results we observed in our pre-clinical testing will be confirmed in clinical trials or the results of any of our clinical trials will support FDA or other regulatory approval. Pre-clinical and clinical data can be interpreted in many different ways, and FDA or foreign regulatory officials could interpret differently data we consider promising, which could halt or delay our clinical trials or prevent regulatory approval.

Despite the FDA's designation of ADVEXIN therapy as a Fast Track product, we may encounter delays in the regulatory approval process due to additional information requirements from the FDA, unintentional omissions in our BLA for ADVEXIN therapy or other delays in the FDA's review process. Similarly, although we have an agreement with the European Medicines Agency (EMA) to file for marketing approval for ADVEXIN therapy under the EMA's Exceptional Circumstances provisions, we may encounter delays in the regulatory approval process due to additional information requirements from the EMA, unintentional omissions in our Marketing Authorization Application filed with the EMA or other delays in the EMA's review process. We may encounter delays or

rejections in the regulatory approval process because of additional government regulation from future legislation or administrative action or changes in FDA or EMEA policy during the period of product development, clinical trials and FDA and EMEA regulatory review.

## **Table of Contents**

Despite the initiation of the BLA process for ADVEXIN therapy under the FDA's accelerated approval regulations, the FDA could determine that accelerated approval is not warranted and that a traditional BLA filing must be made. Such a determination could delay regulatory approval. Additionally, accelerated approval of an application could be subject to Phase 4 or post-approval studies to validate the surrogate endpoint or confirm the effect on the clinical endpoint. Failure to validate a surrogate endpoint or confirm a clinical benefit during post-marketing studies could cause the product to be withdrawn from the market by the FDA on an expedited basis.

**Even if our products are approved by regulatory authorities, if we fail to comply with ongoing regulatory requirements, or if we experience unanticipated problems with our products, these products could be subject to restrictions or withdrawal from the market.**

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data and promotional activities for such product, will be subject to continual review and periodic inspections by the FDA and other regulatory bodies. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or certain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Later discovery of previously unknown problems with our products, including unanticipated adverse events of unanticipated severity or frequency, manufacturer or manufacturing processes or failure to comply with regulatory requirements, may result in restrictions on such products or manufacturing processes, withdrawal of the products from the market, voluntary or mandatory recall, fines, suspension of regulatory approvals, product seizures or detention, injunctions or the imposition of civil or criminal penalties.

**Failure to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs could prevent us from selling our products in foreign markets, which may adversely affect our operating results and financial conditions.**

For marketing drugs and biologics outside the United States, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country and may require additional testing. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approval on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or to obtain required approvals could impair our ability to develop these markets and could have a material adverse effect on our results of operations and financial condition.

**We have a history of operating losses, expect to incur significant additional operating losses and may never become profitable.**

We have generated operating losses since we began operations in June 1993. As of December 31, 2006, we had an accumulated deficit of approximately \$172.3 million. We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities continue. As we expand our operations and develop systems to support commercialization of our product candidates, these losses, among other things, have had, and are expected to continue to have, an adverse impact on our total assets, stockholders' equity and working capital.

We have no products that have generated any commercial revenue. Presently, we earn minimal revenue from contract services activities, grants, interest income and rent from the lease of a portion of our facilities to M. D. Anderson Cancer Center. We do not expect to generate revenue from the commercial sale of products in the near future, and we may never generate revenue from the commercial sale of products.

**If we continue to incur operating losses for a period longer than we anticipate and fail to obtain the capital necessary to fund our operations we will be unable to advance our development programs and complete our clinical trials.**

Developing a new drug and conducting clinical trials is expensive. Our product development efforts may not lead to commercial products, either because our product candidates fail to be found safe or effective in clinical trials or because we lack the necessary financial or other resources or relationships to pursue our programs through commercialization. Our capital and future revenue may not be sufficient to support the expense of our operations, the

development of commercial infrastructure and the conduct of our clinical trials and pre-clinical research.

**Table of Contents**

We expect we will fund our operations over approximately the next 21 to 24 months with our current working capital, which we accumulated primarily from sales of equity securities, income from contract services and research grants, debt financing of equipment acquisitions, the lease of a portion of our facilities to M. D. Anderson Cancer Center and interest on invested funds. We intend to raise additional capital sooner, however, under various circumstances, including if we experience:

an acceleration of the number, size or complexity of our clinical trials;

slower than expected progress in developing ADVEXIN therapy, INGN 241 or other product candidates;

higher than expected costs to obtain regulatory approvals;

higher than expected costs to pursue our intellectual property strategy;

higher than expected costs to further develop and scale up our manufacturing capability;

higher than expected costs to develop our sales and marketing capability;

faster than expected rate of progress and cost of our research and development and clinical trial activities;

a decrease in the amount and timing of milestone payments we receive from collaborators;

higher than expected costs of preparing an application for FDA or foreign regulatory approval of ADVEXIN therapy;

higher than expected costs of developing the processes and systems to support FDA or foreign regulatory approval of ADVEXIN therapy;

an increase in our timetable and costs for the development of marketing operations and other activities related to the commercialization of ADVEXIN therapy and our other product candidates;

a change in the degree of success in our Phase 3 clinical trial of ADVEXIN therapy and in the clinical trials of our other products;

the emergence of competing technologies and other adverse market developments; or

changes in or terminations of our existing collaboration and licensing arrangements.

We do not know whether additional financing will be available when needed or on terms favorable to us or our stockholders. We may need to raise any necessary funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. To the extent we raise additional capital by issuing equity securities, our stockholders will experience dilution. If we raise funds through debt financings, we may become subject to restrictive covenants. To the extent we raise additional funds through collaboration and licensing arrangements, we may be required to relinquish some rights to our technologies or product candidates or grant licenses on terms not favorable to us. If we are not able to raise additional funds, we may have to delay, reduce or eliminate our clinical trials and our development programs.

**If we cannot maintain our existing corporate and academic arrangements and enter into new arrangements we may be unable to develop products effectively, or at all.**

Our strategy for the research, development and commercialization of our product candidates may result in our entering into contractual arrangements with corporate collaborators, academic institutions and others. We have entered into sponsored research, license and/or collaborative arrangements with several entities, including M. D. Anderson

Cancer Center, the NCI, Chiba University in Japan, VirRx and Corixa, which was acquired by GlaxoSmithKline, as well as numerous other institutions that conduct clinical trials work or perform pre-clinical research for us. Our success depends upon our collaborative partners performing their responsibilities under these arrangements and complying with the regulations and requirements governing clinical trials. We cannot control the amount and timing of resources our collaborative partners devote to our research and testing programs or product candidates, or their compliance with regulatory requirements which can vary because of factors unrelated to such programs or product

## **Table of Contents**

candidates. These relationships may in some cases be terminated at the discretion of our collaborative partners with only limited notice to us. We may not be able to maintain our existing arrangements, enter into new arrangements or negotiate current or new arrangements on acceptable terms, if at all. Some of our collaborative partners may also be researching competing technologies independently from us to treat the diseases targeted by our collaborative programs.

**If we do not continue to receive grant funding from federal agencies and others we may be unable to continue our research and development programs for certain of our product candidates at current levels or in the manner we have planned for the future.**

We rely on grants from third parties, generally federal agencies, to provide the funding necessary to conduct our research and development programs for some of our technologies and product candidates. Funding of these grants is typically subject to government appropriations. These grants often contain provisions that allow for termination at the convenience of the government. Further, these grants are subject to complex federal guidelines and regulations. If federal agencies or regulatory authorities determine that we, or the programs for which we desire to receive or have received grant funding, do not qualify for funding, our scientific or product development programs could be slowed or stopped and we may suffer financial losses and be unable to successfully commercialize our products.

**If we are not able to create effective collaborative marketing relationships we may be unable to market our products successfully or in a cost-effective manner.**

To effectively market our products, we will need to develop sales, marketing and distribution capabilities. In order to develop or otherwise obtain these capabilities, we may have to enter into marketing, distribution or other similar arrangements with third parties in order to sell, market and distribute our products successfully. To the extent we enter into any such arrangements with third parties, our product revenue is likely to be lower than if we directly marketed and sold our products, and any revenue we receive will depend upon the efforts of such third parties. We have no experience in marketing or selling pharmaceutical products and we currently have no sales, marketing or distribution capability. We may be unable to develop sufficient sales, marketing and distribution capabilities to commercialize our products successfully.

**Serious and unexpected side effects attributable to molecular therapies may result in governmental authorities imposing additional regulatory requirements or a negative public perception of our products.**

ADVEXIN therapy and most of our other product candidates under development could be broadly described as targeted molecular therapies or recombinant DNA therapies. A number of clinical trials are being conducted by other pharmaceutical companies involving related therapies, including compounds similar to, or competitive with, our product candidates. The announcement of adverse results from these clinical trials, such as serious unwanted and unexpected side effects attributable to treatment, or any response by the FDA or foreign regulatory authorities to such clinical trials, may impede the timing of our clinical trials, delay or prevent us from obtaining regulatory approval or negatively influence public perception of our product candidates, which could harm our business and results of operations and depress the value of our stock.

The United States Senate has held hearings concerning the adequacy of regulatory oversight of recombinant DNA therapy clinical trials, as well as the adequacy of research subject education and protection in clinical research in general, and to determine whether additional legislation is required to protect volunteers and patients who participate in such clinical trials. The Recombinant DNA Advisory Committee, which acts as an advisory body to the NIH, has expanded its public role in evaluating important public and ethical issues in recombinant DNA therapy clinical trials. Implementation of any additional review and reporting procedures or other additional regulatory measures could increase the costs of or prolong our product development efforts or clinical trials.

We report to the FDA and other regulatory agencies serious adverse events, including those we believe may be reasonably related to the treatments administered in our clinical trials. Such serious adverse events, whether treatment-related or not, could result in negative public perception of our treatments and require additional regulatory review or measures, which could increase the cost of or prolong our clinical trials.

The FDA has not approved any recombinant DNA therapy products of the types being developed by us for sale in the United States. The commercial success of our products will depend in part on public acceptance of the use of these types of recombinant DNA products, which are a new type of disease treatment for the prevention or treatment of



human diseases. Public attitudes may be influenced by claims that these types of recombinant DNA products are unsafe, and these treatment methodologies may not gain the acceptance of the public or the medical community. Negative public reaction to these types of recombinant DNA products could also

## **Table of Contents**

result in greater government regulation and stricter clinical trial oversight.

**Patient enrollment may be slow and patients may discontinue their participation in clinical studies, which may negatively impact the results of these studies and extend the timeline for completion of our and our collaborators' development programs for our product candidates.**

The time required to complete clinical trials is dependent upon, among other factors, the rate of patient enrollment. Patient enrollment is a function of many factors, including:

the size of the patient population;

the nature of the clinical protocol requirements;

the diversion of patients to other trials or marketed therapies;

the ability to recruit and manage clinical centers and associated trials;

the proximity of patients to clinical sites; and

the patient eligibility criteria for the study.

We are subject to the risk that patients enrolled in our and our collaborators' clinical studies for our product candidates may discontinue their participation at any time during the study as a result of a number of factors, including withdrawing their consent or experiencing adverse clinical events which may or may not be related to our product candidates under evaluation. We are subject to the risk that if a large number of patients in any one of our studies discontinue their participation in the study, the results from that study may not be positive or may not support an NDA for regulatory approval of our product candidates.

**We cannot predict the safety profile of the use of ADVEXIN therapy when used in combination with other therapies.**

Many of our trials involve the use of ADVEXIN therapy in combination with other drugs or therapies. While the data we have evaluated to date suggest ADVEXIN therapy does not increase the adverse effects of other therapies, we cannot predict if this outcome will continue to be true or whether possible adverse side effects not directly attributable to the other drugs will compromise the safety profile of ADVEXIN therapy when used in certain combination therapies.

**If we fail to adequately protect our intellectual property rights our competitors may be able to take advantage of our research and development efforts to develop competing drugs.**

Our commercial success will depend in part on obtaining patent protection for our products and other technologies and successfully defending these patents against third party challenges. Our patent position, like that of other biotechnology and pharmaceutical companies, is highly uncertain. One uncertainty is the United States Patent and Trademark Office, or PTO, or the courts, may deny or significantly narrow claims made under patents issued to us or patent applications we file. This is particularly true for patent applications or patents that concern biotechnology and pharmaceutical technologies, such as ours, since the PTO and the courts often consider these technologies to involve unpredictable sciences. Another uncertainty is any patents that may be issued or licensed to us may not provide any competitive advantage to us because they may not effectively preclude others from developing and marketing products like ours. Also, our patents may be successfully challenged, invalidated or circumvented in the future. In addition, our competitors, many of which have substantial resources and have made significant investments in competing technologies, may seek to apply for and obtain patents that will prevent, limit or interfere with our ability to make, use and sell our potential products either in the United States or in international markets.

Our ability to develop and protect a competitive position based on our biotechnological innovations, innovations involving molecular therapies, recombinant DNA therapeutic agents, viruses for delivering targeted molecular therapies to cells, formulations, delivery systems not involving viruses, and the like, is particularly uncertain. Due to the unpredictability of the biotechnological sciences, the PTO, as well as patent offices in other jurisdictions, has often required patent applications concerning biotechnology-related inventions to be limited or narrowed substantially to

cover only the specific innovations exemplified in the patent application, thereby limiting their scope of protection against competitive challenges. Similarly, courts have invalidated or significantly narrowed many key patents in the biotechnology industry. Thus, even if we are able to obtain patents covering commercially significant

## Table of Contents

innovations, our patents may not be upheld or our patents may be substantially narrowed.

Through our exclusive license from The University of Texas System for technology developed at M. D. Anderson Cancer Center, we have obtained and are currently seeking further patent protection for adenoviral p53, including ADVEXIN therapy, and its use in cancer therapy. Further, the PTO issued to us United States patents for our adenovirus production technology and our purified adenoviral compositions. We also control, through licensing arrangements, United States patents for combination therapy involving the p53 tumor suppressor and conventional chemotherapy or radiation, the use of adenoviral p53 in cancer therapy, adenoviral p53 as a product, the core DNA of adenoviral p53, pharmaceutical compositions of adenoviral p53 and clinical applications of such pharmaceutical compositions, as well as patents covering our mda-7 technology. Our competitors may challenge the validity of one or more of our patents in the courts or through an administrative procedure known as an interference, in which the PTO determines the priority of invention where two or more parties are claiming the same invention. The courts or the PTO may not uphold the validity of our patents, we may not prevail in such interference proceedings regarding our patents and none of our patents may give us a competitive advantage. In this regard, we have been notified by the PTO that an unidentified third party is attempting to provoke an interference with one of our patents directed to adenoviral p53 therapy. We do not presently know the identity of this party and cannot assess the likelihood of an interference actually being declared. Should that party prevail in an interference proceeding, a patent may issue to that party that is infringed by, and therefore potentially preclude our commercialization of, products like ADVEXIN therapy that are used for adenoviral p53 therapy.

Schering-Plough filed with the European Patent Office, or EPO, an opposition against our European patent directed to combination therapy with p53 and conventional chemotherapy and/or radiation. An opposition is an administrative proceeding instituted by a third party and conducted by the EPO to determine whether a patent should be maintained or revoked, in part or in whole, based on evidence brought forth by the party opposing the patent. In February 2006, the Technical Board of Appeals of the EPO held a final oral proceeding concerning Schering-Plough's opposition and determined our patent should be maintained as amended. No further appeal by Schering-Plough is possible.

We rely on trade secrets law to protect technology where we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. In addition, we generally require employees, academic collaborators and consultants to enter into confidentiality agreements. Despite these measures, we may not be able to adequately protect our trade secrets or other proprietary information. We are a party to various license agreements that give us rights to use specified technologies in our research and development processes. If we are not able to continue to license this technology on commercially reasonable terms, our product development and research may be delayed. In addition, in the case of technologies that we have licensed, we do not have the ability to make the final decisions on how the patent application process is managed, and accordingly are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology. Our research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be diminished.

### **Third party claims of infringement of intellectual property could require us to spend time and money to address the claims and could limit our intellectual property rights.**

The biotechnology and pharmaceutical industry has been characterized by extensive litigation regarding patents and other intellectual property rights, and companies have employed intellectual property litigation to gain a competitive advantage. We are aware of a number of issued patents and patent applications related to recombinant DNA therapy, the treatment of cancer and the use of the p53 and other tumor suppressors. Schering-Plough, including its subsidiary Canji, controls various United States applications and a European patent and applications, some of which are directed to therapy using p53, and others to adenoviruses containing p53, or adenoviral p53, and to methods for carrying out therapy using adenoviral p53. Adenoviral p53 technology underlies our ADVEXIN therapy product candidate. Furthermore, we are aware of a United States patent directed to replication-deficient recombinant adenoviral vectors apparently controlled by Transgene SA (Transgene). While we believe the claims of the Transgene adenoviral vector patent are invalid or not infringed by our products, Transgene could assert a claim against us.

One of the foregoing patent applications directed to p53 therapy, which we understand is owned by The Johns Hopkins University (Johns Hopkins) and controlled by Schering-Plough, was involved in a PTO interference proceeding with a patent owned by Canji. This Johns Hopkins application was the United States counterpart to the European patent recently revoked in its entirety by the EPO (see below). Priority of invention in that interference was awarded by the PTO to the Johns Hopkins inventors, leading to the issuance of a United States patent, and the Canji patent has been found unpatentable. While it is our belief that the claims of the Johns Hopkins

## **Table of Contents**

patent are invalid and not infringed by our ADVEXIN therapy, Schering-Plough or Johns Hopkins may assert that our ADVEXIN therapy, which uses p53 therapy, infringes the claims of such patent. While we believe we would have both an invalidity and non-infringement defense against such an assertion, in the United States an issued patent enjoys a presumption of validity, which can be overcome only through clear and convincing evidence. We cannot assure such a defense would prevail.

We may also become subject to infringement claims or litigation arising out of other patents and pending applications of our competitors, if they issue, or additional interference proceedings declared by the PTO to determine the priority of inventions. The defense and prosecution of intellectual property suits, PTO interference proceedings and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain. Litigation may be necessary to enforce our issued patents, to protect our trade secrets and know-how or to determine the enforceability, scope and validity of the proprietary rights of others. An adverse determination in litigation or interference proceedings to which we may become a party could subject us to significant liabilities, require us to obtain licenses from third parties, or restrict or prevent us from selling our products in certain markets. Although patent and intellectual property disputes are often settled through licensing or similar arrangements, costs associated with such arrangements may be substantial and could include ongoing royalties. Furthermore, the necessary licenses may not be available to us on satisfactory terms, if at all. In particular, if we were found to infringe a valid claim of the Transgene adenoviral vector United States patent, the Johns Hopkins patent or a patent that may issue from a currently pending application, our business could be materially harmed.

We have recently been involved in patent opposition proceedings before the EPO, in which we have sought to have the EPO revoke three different European patents owned or controlled by Canji/Schering-Plough. These European patents relate to the use of p53, or the use of tumor suppressors, in the preparation of therapeutic products. In one opposition involving a Canji European patent directed to the use of a recombinant tumor suppressor, the EPO revoked the European patent in its entirety in a final, non-appealable decision. In the second opposition, involving a patent that is directed to therapeutic and other applications of the p53 and that is owned by Johns Hopkins and, we understand, controlled by Schering-Plough, the EPO recently revoked the patent in its entirety. The patent owner appealed this decision and the final hearing before the EPO Technical Board of Appeals was held in June 2005, at which time the Technical Board of Appeals confirmed the final revocation of all claims of this patent relevant to clinical therapeutic applications of p53. In a third case involving the use of p53, the European patent at issue was initially upheld, but finally revoked in a hearing held in late April 2004.

**We may be subject to litigation and infringement claims that may be costly, divert management's attention and materially harm our business.**

Extensive litigation regarding patents and other intellectual property rights has been common in the biopharmaceutical industry. Litigation may be necessary to assert infringement claims, enforce patent rights, protect trade secrets or know-how and determine the enforceability, scope and validity of certain proprietary rights. The defense and prosecution of intellectual property lawsuits, PTO interference proceedings, and related legal and administrative proceedings in the United States and internationally involve complex legal and factual questions. As a result, such proceedings are costly and time-consuming to pursue and their outcome is uncertain.

Regardless of merit or outcome, our involvement in any litigation, interference or other administrative proceedings could cause us to incur substantial expense and could significantly divert the efforts of our technical and management personnel. An adverse determination may subject us to the loss of our proprietary position or to significant liabilities, or require us to seek licenses that may include substantial cost and ongoing royalties. Licenses may not be available from third parties, or may not be obtainable on satisfactory terms. An adverse determination or a failure to obtain necessary licenses may restrict or prevent us from manufacturing and selling our products, if any. These outcomes could materially harm our business, financial condition and results of operations.

**If we fail to meet our obligations under license agreements we may lose our rights to key technologies on which our business depends.**

Our business depends in part on patents licensed from third parties. Those third party license agreements impose obligations on us, such as payment obligations and obligations to diligently pursue development of commercial products under the licensed patents. If a licensor believes we have failed to meet our obligations under a license

agreement, the licensor could seek to limit or terminate our license rights, which could lead to costly and time-consuming litigation and, potentially, a loss of the licensed rights. During the period of any such litigation, our ability to carry out the development and commercialization of product candidates could be significantly and negatively affected. If our license rights were restricted or ultimately lost, our ability to continue our business based on the affected technology platform would be severely adversely affected.

**Table of Contents**

**Competition and technological change may make our product candidates and technologies less attractive or obsolete.**

We compete with pharmaceutical and biotechnology companies, including Canji and Genvec, which are pursuing forms of treatment similar to ours for the diseases ADVEXIN therapy and our other product candidates target. We are aware that Canji, with its parent Schering-Plough, has in the past been involved in research and/or development of adenoviral p53 products and has numerous patents and patent applications relating to adenoviral p53 therapy. We understand Schering-Plough has stopped its adenoviral p53 clinical trials, and it is unknown whether these parties are continuing their adenoviral p53 research and/or development efforts. We are also aware that a Chinese pharmaceutical company, SiBiono GeneTech, has recently announced it has received regulatory approval from the Chinese drug regulatory agency to market an adenoviral p53 product only in China. We control an issued Chinese patent covering adenoviral p53, and a number of pending Chinese applications directed to p53 therapy and adenoviral production. We understand enforcement of patents in China is unpredictable and we do not know if monetary damages could be recovered from SiBiono GeneTech if its product infringes our patent or patent applications. Patent enforcement and respect of international patent standards, rules and laws have not historically been a key characteristic of the Chinese government and patent system. Further, geopolitical developments, including trade and tariff disputes between the government of China and the United States Department of Commerce could add additional uncertainty to any effort to enforce patents, recover damages, if any, or engage in the sales and marketing of patented or non-patented products in China. We are aware that ImClone and Bristol Myers Squibb have obtained marketing approval for a monoclonal antibody product (Erbix) for the treatment of certain kinds of recurrent head and neck cancer. We also may face competition from companies that may develop internally or acquire competing technology from universities and other research institutions. As these companies develop or acquire their technologies, they may develop competitive positions that may prevent or limit our product commercialization efforts.

Some of our competitors are established companies with greater financial and other resources than ours. Other companies may succeed in developing products earlier than we do, obtaining FDA or foreign regulatory authority approval for products before we do or developing products that are more effective than our product candidates. While we will seek to expand our technological capabilities to remain competitive, research and development by others may render our technology or product candidates obsolete or non-competitive or result in treatments or cures superior to any therapy developed by us.

**Even if we receive regulatory approval to market our ADVEXIN therapy, INGN 241, INGN 225 or other product candidates we may not be able to commercialize them profitably.**

Our profitability will depend on the market's acceptance of ADVEXIN therapy, INGN 241, INGN 225 and our other product candidates, if approved. The commercial success of our product candidates will depend on whether:

they are more effective than alternative treatments;

their side effects are acceptable to patients and doctors;

insurers and other third party healthcare payers will provide adequate reimbursement for them;

we produce and sell them at a profit; and

we market ADVEXIN therapy, INGN 241, INGN 225 and our other product candidates effectively.

**We must achieve significant market share and obtain high per-patient prices for our products to achieve profitability.**

ADVEXIN therapy, our lead product candidate, will, if approved, initially be targeted for the treatment of recurrent head and neck cancer, a disease with an annual incidence of approximately 40,000 patients in the United States. As a result, our per-patient prices must be sufficiently high in order to recover our development costs and achieve profitability. Until additional disease targets with larger potential markets are approved, we believe we will need to market worldwide to achieve significant market penetration. If we are unable to obtain sufficient market share for our drug products at a high enough price, or obtain expanded approvals for larger markets, we may not achieve



profitability or be able to independently continue our product development efforts.

**If we are unable to manufacture our products in sufficient quantities or obtain regulatory approvals for our manufacturing facilities, or if our manufacturing process is found to infringe a valid patented process or processes of another company, then we may be unable to meet demand for our products and lose potential revenue.**

**Table of Contents**

To complete our clinical trials and commercialize our product candidates, if approved, we will need access to, or to develop, facilities to manufacture a sufficient supply of our product candidates. We have used manufacturing facilities we constructed in Houston, Texas to manufacture ADVEXIN therapy, INGN 241 and other product candidates for currently planned clinical trials. We anticipate our facilities are suitable for the initial commercial launch of ADVEXIN therapy. We have no experience manufacturing ADVEXIN therapy, INGN 241 or any other product candidates in the volumes necessary to support commercial sales. If we are unable to manufacture our product candidates in clinical or, when necessary, commercial quantities, then we will need to rely on third party manufacturers to produce our products for clinical and commercial purposes. These third party manufacturers must receive FDA approval before they can produce clinical material or commercial product. Our products may be in competition with other products for access to these facilities and may be subject to delays in manufacturing if third parties give other products greater priority than ours. In addition, we may not be able to enter into any necessary third party manufacturing arrangements on acceptable terms. There are a limited number of contract manufacturers who currently have the capability to produce ADVEXIN therapy, INGN 241 and our other product candidates, and the inability of any of these contract manufacturers to deliver our required quantities of product candidates timely and at commercially reasonable prices would negatively affect our operations.

Before we can begin commercially manufacturing ADVEXIN therapy, INGN 241 or any other product candidate we must obtain regulatory approval of our manufacturing facilities and process. Manufacturing of our product candidates for clinical and commercial purposes must comply with the FDA's current good manufacturing practice (CGMP) requirements and foreign regulatory requirements. The CGMP requirements govern quality control and documentation policies and procedures. In complying with CGMP and foreign regulatory requirements we will be obligated to expend time, money and effort in production, record keeping and quality control to assure the product meets applicable specifications and other requirements. We must also pass a FDA inspection prior to FDA approval.

Our current manufacturing facilities have not yet been subject to a Pre-Approval Inspection by the FDA or foreign regulatory authorities. Failure to pass Pre-Approval Inspections may significantly delay approval of our products. If we fail to comply with these requirements, we would be subject to possible regulatory action and may be limited in the jurisdictions in which we are permitted to sell our products. Further, the FDA and foreign regulatory authorities have the authority to perform unannounced periodic inspections of our manufacturing facilities to ensure compliance with CGMP and foreign regulatory requirements. Our facilities in Houston, Texas are our only manufacturing facilities. If these facilities were to incur significant damage or destruction, then our ability to manufacture ADVEXIN therapy, INGN 241 or any other product candidates would be significantly hampered and our pre-clinical testing, clinical trials and commercialization efforts would be delayed.

In order to produce our products in the quantities we believe will be required to meet anticipated market demand if our products are approved, we will need to increase, or scale-up, our production process. If we are unable to do so, or if the cost of this scale-up is not economically viable to us, we may not be able to produce our products in a sufficient quantity to meet the requirements of future demand.

Canji controls a United States patent and the corresponding international applications, including a European counterpart, relating to the purification of viral or adenoviral compositions. While we believe our manufacturing process does not infringe this patent, Canji could still assert a claim against us. We may also become subject to infringement claims or litigation if our manufacturing process infringes other patents. The defense and prosecution of intellectual property suits and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

**We rely on a limited number of suppliers for some of our manufacturing materials. Any problems experienced by such suppliers could negatively affect our operations.**

We rely on third party suppliers for most of the equipment, materials and supplies used in the manufacturing of ADVEXIN therapy, INGN 241 and our other product candidates. Some items critical to the manufacturing of these product candidates are available from a limited number of suppliers or vendors. We do not have supply agreements with these key suppliers. To mitigate the related supply risk, we maintain inventories of these items. Any significant problem experienced by one or more of these limited number of suppliers could result in a delay or interruption in the supply of materials to us until the supplier cures the problem or until we locate an alternative source of supply. Such

problems would likely lead to a delay or interruption in our manufacturing operations or could require a significant modification to our manufacturing process, which could impair our ability to manufacture our product candidates in a timely manner and negatively affect our operations.

**If product liability lawsuits are successfully brought against us we may incur substantial damages and demand for our product candidates may be reduced.**

**Table of Contents**

The testing and marketing of medical products is subject to an inherent risk of product liability claims. Regardless of their merit or eventual outcome, product liability claims may result in:

decreased demand for our product candidates;

injury to our reputation and significant media attention;

withdrawal of clinical trial volunteers;

substantial delay in FDA or foreign regulatory authority approval;

costs of litigation; and

substantial monetary awards to plaintiffs.

We currently maintain product liability insurance with coverage of \$5.0 million per occurrence with a \$10.0 million annual aggregate limit. This coverage may not be sufficient to protect us fully against product liability claims. We intend to expand our product liability insurance coverage beyond clinical trials to include the sale of commercial products if we obtain marketing approval for any of our product candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against product liability claims could prevent or limit the commercialization of our products.

**We use hazardous materials in our business. Any claims relating to improper handling, storage, use or disposal of these materials could significantly harm our business.**

Our business involves the use of a broad range of hazardous chemicals and materials. Environmental laws impose stringent civil and criminal penalties for improper handling, disposal and storage of these materials. In addition, in the event of the improper or unauthorized release of, or the exposure of individuals to, hazardous materials we could be subject to civil liability due to personal injury or property damage caused by the release or exposure. A failure to comply with environmental laws could result in fines and the revocation of environmental permits, which could significantly harm our business.

**Our stock price may fluctuate substantially.**

The market price for our common stock may be affected by a number of factors, including:

progress and results of our pre-clinical and clinical trials;

announcement of technological innovations by us or our competitors;

developments concerning proprietary rights, including patent and litigation matters;

publicity regarding actual or potential results with respect to products under development by us or by our competitors;

regulatory developments;

the announcement of new products by us or our competitors;

quarterly variations in our or our competitors' results of operations;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

developments in our industry; and

general market conditions and other factors.

## **Table of Contents**

In addition, stock prices for many companies in the technology and emerging growth sectors have experienced wide fluctuations that have often been unrelated to the operating performance of such companies.

### **If we do not progress in our programs as anticipated our stock price could decrease.**

For planning purposes, we estimate the timing of a variety of clinical, regulatory and other milestones, such as when a certain product candidate will enter clinical development, when a clinical trial will be completed or when an application for regulatory approval will be filed. Some of our estimates are included in our Annual Report on Form 10-K for the year ended December 31, 2006, filed with the SEC on March 8, 2007. Our estimates are based on present facts and a variety of assumptions. Many of the underlying assumptions are outside of our control. If milestones are not achieved when we expect them to be investors could be disappointed and our stock price may decrease.

### **Any acquisition we might make may be costly and difficult to integrate, divert management resources or dilute stockholder value.**

As part of our business strategy, we may acquire assets or businesses principally relating to or complementary to our current operations, and we have in the past evaluated and discussed such opportunities with interested parties. Any acquisitions we undertake will be accompanied by the risks commonly encountered in business acquisitions. These risks include, among other things:

potential exposure to unknown liabilities of acquired companies;

the difficulty and expense of assimilating the operations and personnel of acquired businesses;

diversion of management time and attention and other resources;

loss of key employees and customers as a result of changes in management;

the incurrence of amortization expense; and

possible dilution to our stockholders.

In addition, geographic distances may make the integration of businesses more difficult. We may not be successful in overcoming these risks or any other problems encountered in connection with any acquisitions.

### **Due to the potential value of our strategic investments we could be determined to be an investment company, and if such a determination were made we would become subject to significant regulation that would adversely affect our business.**

We may be deemed to be an investment company under the Investment Company Act of 1940 (Investment Company Act) if, among other things, we own investment securities with a value exceeding 40% of the value of our total assets, unless a particular exemption or safe harbor is applicable. We invest certain of our assets in short-term, investment grade securities, some of which may qualify as investment securities under the Investment Company Act. Additionally, from time to time we may make strategic investments in businesses that we do not operate or control, which investments may also qualify as investment securities under the Investment Company Act. Our non-controlling position in SR Pharma, along with investments of our available cash resources in certain types of fixed-income securities, could be considered investment securities under the Investment Company Act. Investment companies are subject to registration under the Investment Company Act and compliance with a variety of restrictions and requirements imposed by the Investment Company Act. If we were to be deemed an investment company we would become subject to these restrictions and requirements, and the consequences of having been an investment company without registering under the Investment Company Act could have a material adverse effect on our business, financial condition and results of operations, as well as restrict our ability to sell and issue securities, borrow funds, engage in various transactions or other activities and make certain investment decisions. In addition, we may incur significant costs to avoid investment company status if an exemption from the Investment Company Act were to be considered unavailable to us at a time when the value of our investment securities exceeds 40% of the value of our total assets. We believe that we are primarily engaged in the research, development and commercialization of biological cancer therapies and that any investment securities are ancillary to our primary business. We believe we are generally otherwise exempted from the definition of an investment company and the registration requirements of the Investment

Company Act, but, absent an exemptive order from the SEC, this result cannot be assured. Nevertheless, to address any uncertainty in this regard, we generally invest a significant portion of our portfolio in money market funds and U.S. government securities and limit the level of

**Table of Contents**

investment in corporate bonds and other instruments that could be considered investment securities.

At December 31, 2006, the value of our investment securities exceeded 40% of the value of our total assets due primarily to our non-controlling position in SR Pharma. In addition, certain other exemptions under the Investment Company Act upon which we may normally rely were not available to us. Accordingly, our Board of Directors elected to take advantage of the Rule 3a-2 exemption for transient investment companies as of such date, which allows us to avoid being deemed an investment company for up to one year as long as we have a bona fide intent to be engaged primarily, as soon as is reasonably possible, in a business other than that of investing, reinvesting, holding or trading in securities. In connection with such election, our Board of Directors directed management to take appropriate actions to regain compliance with the prima facie provisions of the Investment Company Act, including, among other things, liquidating certain investment securities. Accordingly, among other things, we intend over time to reduce the level of our investment securities by periodic sales or other dispositions of such investment securities. These dispositions may be effected under unfavorable market conditions. The lower rates of return realized after the reinvestment of our investment portfolio, and any required dispositions of non-controlling investments, could adversely affect our future reported results.

**If we lose key personnel or are unable to attract and retain additional, highly skilled personnel required to develop our products or obtain new collaborations our business will suffer.**

We depend, to a significant extent, on the efforts of our key employees, including senior management and senior scientific, clinical, regulatory, manufacturing and other personnel. The development of new therapeutic products requires expertise from a number of different disciplines, some of which is not widely available. We depend upon our scientific staff to discover new product candidates and to develop and conduct pre-clinical studies of those new potential products. Our clinical and regulatory staff is responsible for the design and execution of clinical trials in accordance with FDA and foreign regulatory authority requirements and for the advancement of our product candidates toward FDA and foreign regulatory authority approval. Our manufacturing staff is responsible for designing and conducting our manufacturing processes in accordance with the FDA's CGMP requirements. The quality and reputation of our scientific, clinical, regulatory and manufacturing staff, especially the senior staff, and their success in performing their responsibilities, are a basis on which we attract potential funding sources and collaborators. In addition, our Chief Executive Officer and other executive officers are involved in a broad range of critical activities, including providing strategic and operational guidance. The loss of these individuals, or our inability to retain or recruit other key management and scientific, clinical, regulatory, manufacturing and other personnel, may delay or prevent us from achieving our business objectives. We face intense competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

**Future changes in financial accounting standards or practices or existing taxation rules or practices may cause adverse unexpected financial reporting fluctuations and affect our reported results of operations.**

A change in accounting standards or practices or a change in existing taxation rules or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and taxation rules and varying interpretations of accounting pronouncements and taxation practice have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business. For example, Statement of Financial Accounting Standards (SFAS) No. 123R, Share-Based Payment, became effective for us on January 1, 2006. This statement requires that employee share-based compensation be measured based on its fair value on the grant date and treated as an expense that is reflected in the financial statements over the related service period. SFAS No. 123R has had a significant impact on our results of operations for the year ended December 31, 2006. Using the Black-Scholes option pricing model to compute share-based compensation expense as we do requires extensive use of accounting judgment and financial estimates. Items requiring estimation include the expected term optionholders will retain their vested stock options before exercising them, the estimated volatility of our common stock price over the expected term of a stock option and the number of stock options that will be forfeited prior to the completion of their vesting requirements. Application of alternative assumptions could result in significantly different share-based compensation amounts being recorded in our financial statements. We anticipate that SFAS No. 123R will continue to have a significant impact on our results of operations.



**Our corporate governance structure, including provisions in our certificate of incorporation and by-laws, and Delaware law may prevent a change in control or management that stockholders may consider desirable.**

Section 203 of the Delaware General Corporation Law and our certificate of incorporation and by-laws contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company. These provisions include the inability of stockholders to act by written consent or to call special meetings, the ability of our

**Table of Contents**

board of directors to designate the terms of and issue new series of preferred stock without stockholder approval and the fact that our board of directors is divided into three classes serving staggered three year terms.

These provisions could have the effect of delaying, deferring or preventing a change in control of us or a change in our management that stockholders may consider favorable or beneficial. These provisions could also discourage proxy contests and make it more difficult for stockholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock or our other securities.

**Some of our insiders are parties to transactions with us that may cause conflicting obligations.**

Dr. John N. Kapoor, the Chairman of our Board of Directors, is also associated with EJ Financial Enterprises, Inc. (EJ Financial), a healthcare investment firm that is wholly owned by him, and therefore may have conflicts of interest in allocating his time among us and his other business activities, and he may have legal obligations to multiple entities. We have entered into a consulting agreement with EJ Financial. The consulting agreement provides we will pay EJ Financial \$175,000 per year for certain management consulting services, which is based on anticipated time spent by EJ Financial personnel on our affairs. EJ Financial is also involved in the management of healthcare companies in various fields, and Dr. Kapoor is involved in various capacities with the management and operation of these companies. In addition, EJ Financial is involved with other companies in the cancer field. Although these companies are pursuing different therapeutic approaches for the treatment of cancer, discoveries made by one or more of these companies could render our products less competitive or obsolete.

David Parker, Ph.D., J.D., our Vice President, Intellectual Property, is a partner with the law firm Fulbright & Jaworski LLP, which provides legal services to us as our primary outside counsel for intellectual property matters.

In October 2004, we acquired all of the outstanding capital stock of Magnum Therapeutics Corporation (Magnum), a company owned at the time of this acquisition by one of our executive officers. We paid approximately \$1.75 million for the Magnum stock by issuing approximately 252,000 shares of our common stock valued at approximately \$1.48 million at the acquisition date and assuming liabilities of approximately \$272,000. With respect to the common stock we issued for the acquisition, 50% of the shares were held by an independent escrow agent for a period of approximately one year subsequent to the acquisition date to satisfy the indemnification obligations of the selling shareholder under terms of the purchase agreement. Such shares have since been released from escrow. Magnum's primary asset is the funding it receives under a research grant from the NIH, which supplements our ongoing research and development programs. During the year ended December 31, 2006, we earned \$163,000 of revenue under this grant, which completed the funding available to us under this grant. In the event certain of Magnum's technologies result in commercial products, we may be obligated to pay royalties related to the sales of those products to certain third parties.

We have relationships with Jack A. Roth, M.D., and M. D. Anderson Cancer Center, both of whom are affiliated with The Board of Regents of the University of Texas System, one of our stockholders. For more information concerning these relationships, see our Notes to Consolidated Financial Statements beginning on page F-22 of our Annual Report on Form 10-K for the year ended December 31, 2006, filed with the SEC on March 8, 2007.

Subsequent to December 31, 2006, we became an owner of 49% of the outstanding stock of Introgen Research Institute (IRI). The other 51% of IRI is owned by our corporate Secretary, who is also an Introgen shareholder. We transferred to IRI an NIH grant originally awarded to us. IRI will be responsible for the remaining research contemplated by that grant and will receive future funding, if any, from the NIH under that grant. We have contractual relationships with IRI under which we may perform research and development services for them in the future.

We believe the foregoing transactions with insiders were and are in our best interests and the best interests of our stockholders. However, the transactions may cause conflicts of interest with respect to those insiders.

**DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS**

Certain statements in this prospectus and the documents incorporated herein by reference are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Securities and Exchange Act of 1934, as amended (Exchange Act), that involve risks and uncertainties. Any statements contained herein (including without limitation statements to the effect that we estimate, expect, anticipate, plan, believe, project, continue, may, or will or statements concerning potential

variations thereof or comparable terminology or the negative thereof) that are not statements of historical fact should be construed as forward-looking statements. These statements are not

## **Table of Contents**

guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Actual results could differ materially and adversely from those anticipated in such forward-looking statements as a result of certain factors, including those described in the prospectus under Risk Factors. Because of these and other factors that may affect our operating results, past performance should not be considered an indicator of future performance and investors should not use historical results to anticipate results or trends in future periods. We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements. Readers should carefully review the risk factors described in other documents we file from time to time with the SEC including our annual reports on Form 10-K and our quarterly reports on Form 10-Q.

We have not authorized any person to give any information or to make any representation other than those contained in this prospectus in connection with this offering. You should not rely on such information or representation. Neither the delivery of this prospectus nor any sale made pursuant to this prospectus shall create any implication that the information contained in this prospectus is correct as of any time subsequent to the date hereof. This prospectus does not constitute an offer to sell or solicitation of an offer to buy any security other than the common stock covered by this prospectus.

### **USE OF PROCEEDS**

Unless otherwise indicated in any prospectus supplement, the net proceeds from the sale of common stock offered by this prospectus will be used for general corporate purposes and working capital requirements. We may also use a portion of the net proceeds to fund possible investments in and acquisitions of complimentary businesses, partnerships, minority investments, products or technologies. Currently, there are no commitments or agreements regarding such acquisitions or investments that are material. Pending their ultimate use, we intend to invest the net proceeds in money market funds, commercial paper and governmental and non-governmental debt securities with maturities of up to five years.

### **PLAN OF DISTRIBUTION**

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

ordinary brokerage transactions and transactions in which underwriters, dealers or agents solicit purchasers;

block trades in which underwriters, dealers or agents will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by an underwriter, dealer or agent as principal and resale by the underwriter, dealer or agent for its account pursuant to its prospectus;

an over-the-counter distribution in accordance with the rules of the Nasdaq Global Market;

privately negotiated transactions;

underwriters, dealers or agents may agree to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

We will describe the method of distribution of common stock in the applicable prospectus supplement.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions, in amounts to be negotiated, from us (or, if any underwriter, dealer or agent acts as agent for the purchaser of shares, from the purchaser) in connection with the sale of common stock. These underwriters, dealers and agents may qualify

as underwriters within the meaning of the Securities Act. As a result, discounts, commissions or profits on resales received by underwriters, dealers and agents may be treated as underwriting discounts and commissions. Each prospectus supplement will identify any underwriter, dealer or agent and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

**Table of Contents**

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers and agents under agreements between us and the underwriters, dealers and agents.

We may grant underwriters who participate in the distribution of common stock the option to purchase additional securities to cover over-allotments, if any, in connection with the distribution.

In connection with the offering of common stock, certain persons participating in such offering may engage in transactions that stabilize, maintain or otherwise affect the market prices of such common stock, including stabilizing transactions, syndicate covering transactions and the imposition of penalty bids. Specifically, such persons may over-allot in connection with the offering and may bid for and purchase the common stock in the open market. We will describe any of these activities known to us in the applicable prospectus supplement.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

To the extent required, this prospectus may be amended and supplemented from time to time to describe a specific plan of distribution.

**LEGAL MATTERS**

The validity of the common stock being registered hereby is being passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Austin, Texas.

**EXPERTS**

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2006, filed with the SEC on March 8, 2007, and management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006, as set forth in their reports, which are incorporated by reference into this prospectus and elsewhere in the Registration Statement. Our financial statements and management's assessment are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

**INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

The SEC allows us to incorporate by reference the information we file with them, which means that we can disclose important information to you by referring you to documents that we have previously filed with the SEC or documents that we will file with the SEC in the future. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference into this prospectus any filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus until the termination of this offering (except for information contained in any such filing where we indicate that such information is being furnished and not filed under the Exchange Act), as well as the following documents:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2006, filed with the SEC on March 8, 2007;
- our Definitive Proxy Statement, filed with the SEC on April 10, 2007;
- our Current Report on Form 8-K filed with the SEC on March 27, 2007; and
- the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on September 8, 2000, and any further amendment or report filed hereafter for the purpose of updating such description.

This prospectus may contain information that updates, modifies or is contrary to information in one or more of the documents incorporated by reference into this prospectus. Reports we file with the SEC after the date of this prospectus may also contain information that updates, modifies or is contrary to information in this prospectus or in documents incorporated by reference into this prospectus. Investors should review these reports as they may disclose a change in our business, prospects, financial condition or other

**Table of Contents**

affairs after the date of this prospectus.

You may request a copy of any of these filings, at no cost to you, by writing or telephoning us at the following address and telephone number: Introgen Therapeutics, Inc., 301 Congress Avenue, Suite 1850, Austin, Texas 78701; telephone number (512) 708-9310. These filings are also available from the SEC's website and Public Reference Room described under the heading "Where You Can Find More Information."

Additionally, we make these filings available, free of charge, on our website at [www.introgen.com](http://www.introgen.com) as soon as reasonably practicable after we electronically file such materials with, or furnish them to, the SEC. The information on the website listed above, other than these filings, is not, and should not be, considered part of this prospectus and is not incorporated by reference into this document.

**WHERE YOU CAN FIND MORE INFORMATION**

We file annual, quarterly and periodic reports, proxy statements and other information with the SEC. You may inspect these documents without charge at the principal office of the SEC located at 100 F Street, N.E., Washington, D.C. 20549, and you may obtain copies of these documents from the SEC's Public Reference Room at its principal office. Information regarding the operation of the Public Reference Room may be obtained by calling 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC's website is [www.sec.gov](http://www.sec.gov).

**DISCLOSURE OF SEC POSITION ON INDEMNIFICATION  
FOR SECURITIES ACT LIABILITIES**

We are organized under the laws of the State of Delaware. Our Certificate of Incorporation, as amended, and bylaws, as amended, eliminate the personal liability of our directors to the fullest extent permitted by the Delaware General Corporation Law. In addition, our Certificate of Incorporation, as amended, and bylaws, as amended, provide indemnity for our current or former officers and directors against all liabilities and costs of defending an action or suit in which they were involved by reason of their positions with us. However, we cannot indemnify any person if a court finds that the person did not act in good faith. Our bylaws, as amended, also provide that we may purchase insurance to protect any director, officer, employee or agent against any liability. We have entered into separate indemnification agreements with each of our directors and executive officers, whereby we have agreed, among other things, to indemnify them to the fullest extent permitted by the Delaware General Corporation Law, subject to specified limitations, against certain liabilities actually incurred by them in any proceeding in which they are a party that may arise by reason of their status as directors, officers, employees or agents or may arise by reason of their serving as such at our request for another entity and to advance their expenses incurred as a result of any proceeding against them as to which they could be indemnified. We intend to enter into similar separate indemnification agreements with any directors or officers who may join us in the future. There is no pending litigation or proceeding involving any of our directors, officers, employees or other agents as to which indemnification is being sought nor are we aware of any pending or threatened litigation that may result in claims for indemnification.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or controlling persons pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act, and is therefore unenforceable.

18

---

**PART II  
INFORMATION NOT REQUIRED IN PROSPECTUS  
ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION**

The following table sets forth the costs and expenses, other than underwriting discounts, commissions and concessions, payable by the Registrant in connection with the sale of common stock being registered hereby. All amounts are estimates except the SEC registration fee.

**Amount to Be Paid  
by**

	<b>Registrant(1)</b>
SEC registration fee	\$ 16,050
Legal fees and expenses	\$ 150,000
Accounting fees and expenses	\$ 50,000
Printing and engraving expenses	\$ 50,000
Transfer agent and registrar expenses	\$ 25,000
Miscellaneous expenses	\$ 50,000
<b>Total</b>	<b>\$ 341,050</b>

- (1) Each of the amounts set forth above, other than the SEC registration fee, is an estimate.

#### **ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS**

We are organized under the laws of the State of Delaware. Our Certificate of Incorporation, as amended, and bylaws, as amended, eliminate the personal liability of our directors to the fullest extent permitted by the Delaware General Corporation Law. In addition, our Certificate of Incorporation, as amended, and bylaws, as amended, provide indemnity for our current or former officers and directors against all liabilities and costs of defending an action or suit in which they were involved by reason of their positions with us. However, we cannot indemnify any person if a court finds that the person did not act in good faith. Our bylaws, as amended, also provide that we may purchase insurance to protect any director, officer, employee or agent against any liability. We have entered into separate indemnification agreements with each of our directors and executive officers, whereby we have agreed, among other things, to indemnify them to the fullest extent permitted by the Delaware General Corporation Law, subject to specified limitations, against certain liabilities actually incurred by them in any proceeding in which they are a party that may arise by reason of their status as directors, officers, employees or agents or may arise by reason of their serving as such at our request for another entity and to advance their expenses incurred as a result of any proceeding against them as to which they could be indemnified. We intend to enter into similar separate indemnification agreements with any directors or officers who may join us in the future. There is no pending litigation or proceeding involving any of our directors, officers, employees or other agents as to which indemnification is being sought nor are we aware of any pending or threatened litigation that may result in claims for indemnification.

#### **ITEM 16. EXHIBITS**

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
1.1(1)	Form of Underwriting Agreement
4.1(1)	Specimen Common Stock Certificate
4.2(1)	Certificate of Incorporation as currently in effect
4.3(1)	Amendment to Certificate of Incorporation, effective as of December 21, 2001
4.4(1)	Amendment to Certificate of Incorporation, effective as of August 6, 2004
4.5(1)	Bylaws of Introgen as currently in effect



Edgar Filing: INTROGEN THERAPEUTICS INC - Form S-3/A

5.1(1)	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation
23.1(2)	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation
23.2	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm

---

II-1

**Table of Contents**

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
24.1(1)	Power of Attorney
(1)	Previously filed with our Registration Statement on Form S-3 (File No. 333-140424), filed with the SEC on February 2, 2007.
(2)	Included in Exhibit 5.1.

**ITEM 17. UNDERTAKINGS**

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective Registration Statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement; *provided, however*, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) of this section do not apply if the Registration Statement is on Form S-3 or Form F-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the Registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new Registration Statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the Registration Statement as of the date the filed prospectus was deemed part of and included in the Registration Statement; and

(ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a Registration Statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act shall be deemed to be part of and

included in the Registration Statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the Registration Statement relating to the securities in the Registration Statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. *Provided, however,* that no statement made in a Registration Statement or prospectus that is part of the Registration Statement or made in a document incorporated or deemed incorporated by reference into the Registration Statement or prospectus that is part of the Registration Statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the Registration Statement or prospectus that was part of the Registration Statement or made in any such document immediately prior to such effective date.

II-2

---

**Table of Contents**

(5) That, for the purpose of determining liability of the Registrant under the Securities Act to any purchaser in the initial distribution of the securities:

The undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this Registration Statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new Registration Statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions described under Item 15 above, or otherwise, the Registrant has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(d) The undersigned Registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective; and

(2) For purposes of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new Registration Statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

**Table of Contents****SIGNATURES**

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to Registration Statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Austin, State of Texas, on April 17, 2007.

**INTROGEN THERAPEUTICS, INC.**

By: /s/ David G. Nance  
David G. Nance  
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act, this Amendment No. 1 to Registration Statement on Form S-3 has been signed by the following persons in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ David G. Nance (David G. Nance)	President, Chief Executive Officer and Director (Principal Executive Officer)	April 17, 2007
/s/ James W. Albrecht, Jr. (James W. Albrecht, Jr.)	Chief Financial Officer (Principal Financial and Accounting Officer)	April 17, 2007
* (John N. Kapoor, Ph.D.)	Chairman of the Board and Director	April 17, 2007
* (William H. Cunningham, Ph.D.)	Director	April 17, 2007
* (Charles E. Long)	Director	April 17, 2007
* (S. Malcolm Gillis, Ph.D.)	Director	April 17, 2007
* (Peter Barton Hutt)	Director	April 17, 2007
* By: /s/ James W. Albrecht, Jr. James W. Albrecht, Jr., Attorney-in-Fact		



**Table of Contents**

**INDEX TO EXHIBITS**

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
1.1(1)	Form of Underwriting Agreement
4.1(1)	Specimen Common Stock Certificate
4.2(1)	Certificate of Incorporation as currently in effect
4.3(1)	Amendment to Certificate of Incorporation, effective as of December 21, 2001
4.4(1)	Amendment to Certificate of Incorporation, effective as of August 6, 2004
4.5(1)	Bylaws of Introgen as currently in effect
5.1(1)	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation
23.1(2)	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation
23.2	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm
24.1(1)	Power of Attorney

(1) Previously filed with our Registration Statement on Form S-3 (File No. 333-140424), filed with the SEC on February 2, 2007.

(2) Included in Exhibit 5.1.