INTROGEN THERAPEUTICS INC
Form 424B3
March 05, 2004

Table of Contents

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement is not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any jurisdiction where such offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(3)
Registration No. 333-107799

PRELIMINARY PROSPECTUS SUPPLEMENT | Subject to completion | March 5, 2004

(To Prospectus dated August 25, 2003)

5,500,000 Shares

Common Stock

We are offering all of the 5,500,000 shares of our common stock offered by this prospectus supplement.

Our common stock is quoted on the Nasdaq National Market under the symbol INGN. On March 3, 2004, the last reported sale price of our common stock on the Nasdaq National Market was $9.43 per share.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock under the heading Risk factors beginning on page S-10 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

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

The underwriters may also purchase from us up to an additional 825,000 shares of common stock from us at the public offering price, less the underwriting discounts and commissions, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

The underwriters are offering shares of common stock as described in Underwriting. Delivery of the shares will be made on or about March , 2004.

Sole Book-Running Manager

UBS Investment Bank

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You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We have not and the underwriters have not authorized anyone to provide information different from that contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. Neither the delivery of this prospectus supplement nor the sale of common stock means that information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is correct after the date of this prospectus supplement. These documents are not an offer to sell or a solicitation of an offer to buy these shares of common stock in any circumstance under which the offer or solicitation is unlawful.

TABLE OF CONTENTS

Prospectus Supplement	Page
Prospectus supplement summary	**S-1**
Risk factors	**S-10**
Forward-looking statements	**S-26**
Use of proceeds	**S-27**
Capitalization	**S-28**
Dilution	**S-29**
Price range of common stock	**S-30**
Dividend policy	**S-30**
Underwriting	**S-31**
Experts	**S-34**
Information incorporated by reference	**S-35**
Legal matters	**S-35**
Summary	**3**
Risk factors	**5**
The Company	**14**
Forward-looking statements	**40**
Use of proceeds	**41**
Plan of distribution	**42**
Legal matters	**42**
Experts	**43**
Incorporation of certain information by reference	**44**
Where you can find more information	**45**
Indemnification of directors and officers	**45**

Table of Contents

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Table of Contents

Prospectus supplement summary

This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including Risk factors, the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision.

Unless the context requires otherwise, the words Introgen, we, company, us and our refer to Introgen Therapeutics, Inc.

BUSINESS OVERVIEW

We are a biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for the treatment of cancer and other diseases. We are developing product candidates to treat a wide range of cancers using non-integrating gene agents. These agents are designed to increase production of normal cancer-fighting proteins that act to overpower cancerous cells. Our lead product candidate, ADVEXIN therapy, combines the p53 gene with a non-replicating, non-integrating adenoviral gene delivery system that we have developed and extensively tested. The p53 gene is one of the most potent members of a group of naturally occurring tumor suppressor genes, which act to kill cancer cells, arrest cancer cell growth and protect cells from becoming cancerous.

We are conducting two multi-national, multi-site Phase 3 clinical trials of ADVEXIN therapy, both by itself and in combination with chemotherapy, in recurrent squamous cell cancer of the head and neck. Earlier multi-national, multi-site Phase 2 clinical trials of ADVEXIN therapy in 217 patients with recurrent squamous cell cancer of the head and neck treated previously with surgery, radiation or chemotherapy indicated that treatment with ADVEXIN therapy provided tumor growth control, including shrinkage and eradication of some tumors, and was well tolerated.

The design of our two Phase 3 clinical trials was agreed to by the Food and Drug Administration, or FDA, under its Special Protocol Assessment program, and we have received Fast Track designation for ADXEVIN therapy from the FDA. By designating ADVEXIN therapy as a Fast Track product, the FDA will take actions to expedite the evaluation and review of the ADVEXIN therapy marketing application. ADVEXIN therapy for head and neck cancer has also been designated as an Orphan Drug under the Orphan Drug Act, which may give us seven years of marketing exclusivity for ADVEXIN therapy for this indication, if approved by the FDA.

We have also completed or are currently conducting numerous Phase 1 and Phase 2 clinical trials of ADVEXIN therapy by itself and in combination with chemotherapy or radiation therapy in a variety of cancers. These trials include a completed Phase 2 clinical trial of ADVEXIN administered as a complement with radiation therapy in non-small cell lung cancer; a Phase 2 clinical trial of ADVEXIN therapy combined with systemic chemotherapy for the treatment of breast cancer; a Phase 1/early Phase 2 clinical trial of ADVEXIN therapy for the treatment of advanced unresectable squamous cell esophageal cancer; a Phase 1 clinical trial of ADVEXIN therapy in prostate cancer; Phase 1 clinical trials of ADVEXIN therapy in bronchoalveolar cancer; and a Phase 1/early Phase 2 clinical trial in which ADVEXIN therapy is being administered to prevent precancerous oral lesions that have a high risk of developing into cancer.

To date, clinical investigators at sites in North America, Europe and Japan have treated over 500 patients with ADVEXIN therapy, establishing a large safety database. We hold the worldwide rights for pre-clinical and clinical development, manufacturing, marketing and commercialization of ADVEXIN therapy.

We are developing our second product candidate, INGN 241, for the treatment of solid tumors and in melanoma, a deadly form of skin cancer. INGN 241 combines the mda-7 gene with our adenoviral gene delivery system to kill tumor cells, including metastatic tumor cells, through multiple mechanisms.

Table of Contents

A Phase 1/early Phase 2 trial indicated that in patients with various solid tumors, INGN 241 is well tolerated, displays minimal toxicity and is biologically active.

ADVEXIN Therapy (p53)

Our primary approach for the treatment of cancers is to deliver genes that increase production of normal cancer-fighting proteins. Rather than acting to repair or replace aberrant or missing genes and thereby creating a long-term or permanent change to the patient s genetic makeup, or genome, our products work in a different manner by acting as templates for the transient in vivo production of proteins that have pharmacologic properties. The resultant proteins engage disease-related molecular targets or receptors to produce a specific therapeutic effect.

Our lead product candidate, ADVEXIN therapy, combines the p53 gene with a non-replicating, non-integrating adenoviral gene delivery system that we have developed and extensively tested. The p53 gene is one of the most potent members of a group of naturally occurring tumor suppressor genes, which act to kill cancer cells, arrest cancer cell growth and protect cells from becoming cancerous. The p53 gene works through multiple mechanisms of action including apoptosis, or programmed cell death, cancer cell growth arrest, and reducing the blood supply to tumors through a process known as anti-angiogenesis. Molecular pathways normally controlled by the p53 gene are abnormal in the vast majority of cancers. Patients may receive multiple doses of ADVEXIN therapy, and some patients have received ongoing ADVEXIN treatments for several years. Physicians typically inject ADVEXIN therapy directly into the tumor. Since the protein produced by the p53 gene is known to be important in controlling growth of most types of solid tumors, we believe that ADVEXIN therapy could be applicable to a broad range of cancers.

Head and neck cancer

In the United States, the annual incidence of squamous cell cancer, a cancer of cells that line the oral cavity, pharynx and larynx, is approximately 40,000. The worldwide annual incidence of head and neck cancer, encompassing squamous cell cancer, as well as cancers of the tongue, mouth, vocal cords and tissues surrounding them, is approximately 400,000 new cases. Head and neck cancer is frequently fatal, with most patients dying from local and regional disease, rather than from metastasis to other organs. Primary treatments for head and neck cancer are generally surgery and radiation therapy. However, these treatments are debilitating and have permanent side effects, including loss of teeth, loss of voice or disfigurement. Moreover, a large number of patients with head and neck cancer experience recurrence. Patients with recurrent cancer do not typically respond well to further therapies, which may typically include chemotherapy, and extended patient survival is rare.

We are developing ADVEXIN therapy as a treatment for recurrent squamous cell cancer of the head and neck. Based on clinical results from our Phase 1 and Phase 2 clinical trials, we have commenced patient enrollment in two multi-national, multi-site Phase 3 clinical trials, which we refer to as our 301 and 302 trials. The design of our two Phase 3 clinical trials was agreed to by the FDA under its Special Protocol Assessment program. If these trials are successful, we expect to use the resulting data, along with other data, to apply for regulatory approval.

Clinical trial 301 is a Phase 3 clinical trial that compares the efficacy of ADVEXIN therapy to a standard chemotherapy treatment in patients with recurrent squamous cell cancer of the head and neck in whom standard treatment of surgery and radiation therapy have not been effective. Clinical trial 301 is planned to enroll approximately 240 patients with recurrent disease. Patients in the control group receive weekly treatments of methotrexate, a standard chemotherapy treatment for this condition, while patients in the treatment group receive twice weekly intratumoral injections of ADVEXIN therapy. The clinical trial s primary endpoint is survival.

Clinicial trial 302 is a Phase 3 clinical trial that compares the efficacy of ADVEXIN therapy when it is used in combination with a standard chemotherapy treatment to that of standard chemotherapy treatment used alone in patients with recurrent disease. Clinical trial 302 is planned to enroll

Table of Contents

approximately 255 patients with recurrent squamous cell head and neck cancer. These patients will not have previously been treated with chemotherapy. Patients in the control group receive the chemotherapy drugs cisplatin and 5-fluorouracil, while the patients in the treatment group receive the same drugs plus intratumoral ADVEXIN therapy. Each treatment is repeated every four weeks, which is a standard interval for chemotherapy. The clinical trial s primary endpoint is time to progression of the treated lesions as measured by a patient s tumor growth beyond the patient s baseline, or tumor size at the beginning of the trial. Survival is the secondary endpoint. The 301 and 302 trials are designed to be complementary, with the primary endpoint in each serving as a secondary endpoint, or result that we will evaluate secondarily, in the other. Both of these studies are randomized, and are being conducted at numerous cancer centers in the United States, Canada and Europe.

We conducted three independent, multi-national, multi-site Phase 2 clinical trials of ADVEXIN therapy in 217 patients with recurrent squamous cell head and neck cancers. All of the 217 patients in the Phase 2 head and neck cancer clinical trials had failed initial treatments with surgery, radiation or chemotherapy. Many patients had also been treated with subsequent additional chemotherapy. These patients typically do not respond well to further therapies. The 217 patients were treated with ADVEXIN therapy alone as monotherapy. After treatment with ADVEXIN therapy, many patients received subsequent chemotherapy.

In the combined analysis of the three multi-national, multi-site Phase 2 clinical trials, the overall tumor growth control rate was 59%. Tumor growth control rate represents the percentage of treated tumors where there was disappearance of the tumor, shrinkage of the tumor or the absence of additional tumor growth beyond 25% of pre-treatment measurements. In 10% of the treated lesions, there was either complete tumor regression or a reduction of tumor size greater than or equal to 50% of the pre-treatment size. These clinical findings are consistent with the results of earlier analysis of 112 patients and earlier clinical trials where tumor growth control was observed.

As in all of our previous clinical trials, ADVEXIN therapy was well tolerated without the significant side effects common to conventional cancer treatments.

Non-small cell lung cancer

Lung cancer is the most common cause of cancer-related death in the United States, with an estimated 172,000 new cases diagnosed annually. An estimated 157,000 people die from the disease annually. The five-year survival rate for patients diagnosed with lung cancer is 15%. Non-small cell, or NSC, lung cancer comprises approximately 80% of all lung cancer cases. Surgery can be an effective treatment in the early stages of disease, but only a minority of patients are eligible because early-stage diagnosis is uncommon. Up to 70% of NSC lung cancer patients have disease that is too far advanced for complete surgical resection. These patients typically undergo a combination of surgery, radiation and chemotherapy. This combination treatment is only effective in a small percentage of cases. Clinical data has shown that of patients who have unresectable disease, approximately 80% will again have active cancer cells three months after completing a full course of radiation. Due to the ineffective treatment of NSC lung cancer in many patients, a significant, unmet need for better treatments exists, particularly if it can be combined with existing treatments without increasing the toxicity of those treatments.

We have completed a Phase 2 clinical trial of ADVEXIN therapy in combination with radiotherapy as the primary treatment for patients who had newly-diagnosed, inoperable NSC lung cancer and who could not tolerate chemotherapy. Radiotherapy is the standard treatment for patients in this condition. All patients in this trial received three ADVEXIN therapy injections into their tumors during a five-to-six week course of radiotherapy. These patients were evaluated for the efficacy, safety and side effects of the treatment to ascertain whether the combination of ADVEXIN therapy with radiation was tolerated. Other objectives of this trial were to determine if the addition of ADVEXIN therapy injected directly into the tumor and in combination with standard radiotherapy improved the response rate of

Table of Contents

the injected tumor in patients with inoperable NSC lung cancer, and to evaluate the tolerability of the combination treatment.

We conducted an analysis of 19 patients that the investigators treated and evaluated in the Phase 2 clinical trial of ADVEXIN therapy. This analysis included both radiographs to assess the size of the treated tumor mass supplemented by tumor biopsies to assess for living cancer cells within the tumor at the site of treatment. The patients were then followed without further treatment for clinical evidence of disease progression. The results of this analysis established an acceptable safety profile and showed evidence of local tumor growth control and reductions in tumor size. Twelve of the 19 patients that the investigators treated and evaluated, or 63%, had radiographic evidence of local tumor growth control, including 12 complete or partial responses of the tumor that the investigators injected. Furthermore, the preliminary analysis showed that nine of these 12 patients had no living tumor cells in the biopsy that the investigator took from the site of the injection. This study was published in the January 2003 issue of *Clinical Cancer Research.*

Breast cancer

Physicians diagnose an estimated 213,000 new cases of breast cancer annually in the United States, and approximately 40,000 people are estimated to die from the disease each year. We are conducting a Phase 2 clinical trial using ADVEXIN therapy administered in combination with systemic chemotherapy in women who have newly diagnosed, locally advanced breast cancers. Interim results of this trial were published in June 2003 at the annual meeting of the American Society of Clinical Oncology. Data from this clinical trial indicated that objective clinical responses (complete tumor regression or greater than 50% reduction in tumor size) were documented in 83% of the patients that received ADVEXIN therapy combined with systemic chemotherapy. The resectability rate was 100% at mastectomy. This clinical trial is part of our ADVEXIN therapy development plan, which is to administer ADVEXIN therapy in the setting of primary, multi-modality local therapy of cancer in conjunction with surgery, chemotherapy and radiation therapy.

Other cancers

We are evaluating ADVEXIN therapy in a number of other cancers. All of these programs are in earlier stages of clinical development. We have completed enrollment and treatment in a Phase 1 clinical trial of 30 patients with prostate cancer where investigators injected ADVEXIN therapy into the prostate gland with a subsequent surgical resection of the gland. The patients tolerated the ADVEXIN therapy well. In a preliminary analysis, 27% of the patients showed measurable evidence of tumor shrinkage following ADVEXIN therapy injections.

Together with the National Cancer Institute, or NCI, we are conducting Phase 1 clinical trials using ADVEXIN therapy for the treatment of ovarian, bladder, brain and bronchoalveolar cancers. We and the NCI are also conducting a Phase 1/early Phase 2 clinical trial in which ADVEXIN therapy is administered in the form of an oral rinse or mouthwash. This trial is the first to investigate the effect of ADVEXIN therapy on non-malignant, oral lesions that are at high risk for developing into cancer. In addition, we are conducting a Phase 1/early Phase 2 study of ADVEXIN therapy for the treatment of advanced unresectable squamous cell esophageal cancer. The study protocol was developed and is sponsored by investigators at Chiba University in Japan.

INGN 241 (mda-7)

Our second product candidate, INGN 241, uses the mda-7 gene, a promising tumor suppressor gene that we believe, like p53, has broad potential to induce apoptosis or cell death, in many types of cancer. We have combined the mda-7 gene product with our adenoviral gene delivery system to form INGN 241. Our pre-clinical trials have shown that the protein produced by INGN 241 suppresses the growth of many cancer cells, including those of the breast, lung, ovaries, colon, prostate and the central nervous system, while not affecting growth of normal cells. Because INGN 241 kills cancer

cells, even if other tumor suppressor genes, including p53 or p16, are not functioning properly, it appears that mda-7 functions via a novel mechanism of tumor suppression.

We have conducted pre-clinical work indicating that in addition to its known activity as a tumor suppressor gene, the protein produced by the mda-7 gene may also stimulate the body s immune system to kill metastatic tumor cells and to protect the body against cancer, thereby offering the potential of providing an added advantage in treating various cancers because it may attack cancer using two different mechanisms. Because the mda-7 gene may act as a cytokine, or immune system modulator, it is also known as interleukin-24, or IL-24. The mda-7 gene and the protein it produces may also work as a radiation sensitizer to make several types of human cancer cells more susceptible to radiation therapy, and we have seen evidence of this effect in our pre-clinical work. We have also published the results of a pre-clinical trial indicating INGN 241 may suppress the growth in vivo of non-small cell lung cancer through apoptosis in combination with anti-angiogenesis.

We have completed enrollment of a Phase 1/early Phase 2 clinical trial using INGN 241 to evaluate safety, mechanism of action and efficacy in approximately 25 patients with solid tumors. This trial has indicated that in patients with solid tumors, INGN 241 was well tolerated, was biologically active and displayed minimal toxicity associated with its use. We are planning to initiate a Phase 1/early Phase 2 clinical trial using INGN 241 in melanoma.

We have an exclusive license to the mda-7 gene for our therapeutic applications from Corixa Corporation. Our pre-clinical program with INGN 241 has included research at The University of Texas M. D. Anderson Cancer Center, Columbia University and Corixa Corporation.

INGN 225 (p53 vaccine)

As a supplement to our gene-induced therapeutic protein programs, we are developing INGN 225 using ADVEXIN therapy to create a highly specific therapeutic cancer vaccine that stimulates a particular type of immune system cell known as a dendritic cell. Recently published research in *Current Opinion in Drug Discovery & Development* concluded that ADVEXIN therapy can be used with a patient s isolated dendritic cells as an antigen delivery and immune enhancing therapeutic strategy. Pre-clinical testing has shown that the immune system can recognize and kill tumors after treatment with dendritic cells stimulated by ADVEXIN therapy, which suggests a vaccine consisting of ADVEXIN therapy stimulated dendritic cells (INGN 225) could have broad utility as a treatment for progression of solid tumors. We are conducting a Phase 1/early Phase 2 trial in patients with small-cell lung cancer and are initiating a Phase 1/early Phase 2 trial in patients with breast cancer, both using INGN 225 after treatment with standard chemotherapy.

Table of Contents

PRODUCT DEVELOPMENT PROGRAMS

The following table summarizes the status of our product development programs.

Product (gene)**	Cancer indication	Development status
ADVEXIN Therapy (p53)	Head and Neck	Phase 3
	Non-Small Cell Lung	Phase 2 completed
	Breast	Phase 2
	Perioperative (and surgery)	Phase 1-2
	Esophageal	Phase 1-2
	Prostate	Phase 1 completed
	Intravenous Administration	Phase 1 completed*
	Ovarian	Phase 1 completed*
	Oral Cancer (mouthwash)	Phase 1-2*
	Bladder	Phase 1 completed*
	Bronchoalveolar	Phase 1 completed*
	Brain (glioblastoma)	Phase 1 completed*
	Rheumatoid Arthritis	Pre-clinical
INGN 225 (p53 vaccine)	Small Cell Lung	Phase 1-2
	Breast	Phase 1-2
INGN 241 (mda-7)	Various (solid tumors)	Phase 1-2
	Melanoma	Phase 1-2
	Pancreatic	Pre-clinical
	Breast	Pre-clinical
INGN 401 (FUS-1 program)	Lung	Phase 1
INGN 007 (Replication-competent viral therapy)	Various (solid tumors)	Pre-clinical

* *Conducted in conjunction with the National Cancer Institute.*

** *We hold the worldwide commercial rights to the product candidates related to each of these programs.*

OUR STRATEGY

Our objective is to be the leader in the development of gene-induced protein therapies and other products for the treatment of cancer and other diseases that, like cancer, result from cellular dysfunction and uncontrolled cell growth. To accomplish this objective, we are pursuing the following strategies:

Develop and commercialize ADVEXIN therapy and INGN 241 for multiple cancer indications. We plan to continue developing ADVEXIN therapy using the p53 gene and our INGN 241 product using the mda-7 gene in multiple cancer indications.

Develop our portfolio of gene-induced protein therapy and other drug products. Utilizing our significant research, clinical, and regulatory expertise, we are evaluating development of additional gene-induced protein therapies, such as FUS-1, and other drug products for various cancers. We have established an efficient process for evaluating new drug candidates and advancing them from pre-clinical to clinical development. We have identified and licensed multiple technologies, which we intend to combine with our adenoviral and non-viral gene delivery systems and which we believe are attractive development targets for the treatment of various cancers. We are also evaluating the development of mebendazole (INGN 601), our first small molecule product candidate. We intend to evaluate additional opportunities to in-license or acquire new technologies.

Establish targeted sales and marketing capabilities. Because the oncology market is characterized by a concentration of specialists in relatively few major cancer centers, it can be effectively

Table of Contents

addressed by a small, focused sales force. We believe we can address this market by building a direct sales force as part of the ADVEXIN therapy commercialization process and by pursuing marketing and distribution agreements with corporate partners for ADVEXIN therapy as well as additional products.

Expand our market focus to non-cancer indications. We plan to leverage our scientific, research and process competencies in gene function and vector development to pursue gene-based protein therapies for a variety of other diseases and conditions. We believe these therapies could hold promise for diseases such as cardiovascular disease and rheumatoid arthritis, which, like cancer, result from cellular dysfunction or uncontrolled cell growth.

Table of Contents

The offering

Common stock we are offering	5,500,000 shares
Common stock outstanding immediately following this offering	32,083,274 shares
Nasdaq National Market symbol	INGN
Use of proceeds	We expect to use the net proceeds from the sale of common stock offered by this prospectus supplement to fund regulatory activities relating to our lead product candidate, ADVEXIN therapy, to fund ongoing and planned clinical trials, to continue pre-clinical research and development, and for other 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. See Use of proceeds.

The number of shares of common stock to be outstanding after the offering is based on 26,583,274 shares outstanding as of March 2, 2004 and excludes:

- 4,756,401 shares of common stock underlying options outstanding as of December 31, 2003 at a weighted average exercise price of $2.91 per share;
- 400,000 shares of common stock available for issuance upon the exercise of outstanding warrants as of December 31, 2003 at an exercise price of $7.89 per share;
- 2,343,721 shares of common stock available for issuance upon the conversion of 100,000 shares of Series A non-voting convertible preferred stock as of December 31, 2003; and
- 1,484,113 shares of common stock available for issuance or future grant pursuant to our 2000 Stock Option Plan (includes an increase of 1,326,976 shares on January 1, 2004 pursuant to an automatic reload under the 2000 Stock Option Plan).

Unless we specifically state otherwise, all information contained in this prospectus supplement and the accompanying prospectus assumes that the underwriters do not exercise their over-allotment option to purchase up to an additional 825,000 shares of common stock.

Table of Contents

Summary consolidated financial data

The summary consolidated financial data presented below is derived from the audited consolidated financial statements of Introgen Therapeutics, Inc. and our subsidiaries incorporated by reference in this prospectus supplement and the accompanying prospectus, except for the year ended December 31, 2001, which is unaudited. The unaudited consolidated financial statement data includes, in our opinion, all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of our results of operations for this period. The summary consolidated financial data set forth below is qualified in its entirety by, and should be read in conjunction with, the consolidated financial statements and notes thereto and Management s discussion and analysis of financial condition and results of operations incorporated by reference in this prospectus supplement and the accompanying prospectus. The as adjusted balance sheet data gives effect to the issuance and sale by us of 5,500,000 shares of our common stock in this offering at an assumed public offering price of $9.43 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	Year ended December 31,		
Consolidated statement of operations data:	**2001**	**2002**	**2003**
(in thousands, except per share amounts)	**(unaudited)**		
Contract services, grants and other revenue	$ 591	$ 1,173	$ 304
Operating costs and expenses:			
Research and development	19,923	21,512	14,973
General and administrative	6,361	6,722	6,102
Total operating costs and expenses	26,284	28,234	21,075
Loss from operations	(25,693)	(27,061)	(20,771)
Interest income (expense), net	423	(207)	393
Other income	871	1,140	1,052
Net loss	$(24,399)	$(26,128)	$(19,326)
Net loss per share, basic and diluted	$ (1.14)	$ (1.22)	$ (0.84)
Shares used in computing basic and diluted net loss per share	21,440	21,471	22,902

	December 31, 2003	
Consolidated balance sheet data:	**Actual**	**As adjusted**
(in thousands)		
Cash and cash equivalents	$ 36,397	$ 84,750
Working capital	31,091	79,444
Total assets	44,483	92,836
Long-term debt and capital lease obligations, net of current portion	6,714	6,714
Accumulated deficit	(92,969)	(92,969)
Stockholders equity	31,285	79,638

Table of Contents

Risk factors

Investing in our common stock involves a high degree of risk. In addition to the other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, you should carefully consider the risks described below before purchasing our common stock. If any of the following risks actually occur, our business, financial condition and results of operations could materially suffer. As a result, the trading price of our common stock could decline, and you might lose all or part of your investment.

RISKS RELATED TO OUR BUSINESS

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

Our ability to achieve and sustain operating profitability 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 ADVEXIN for the treatment of head and neck cancer in the United States. We cannot assure you that we will receive approval for ADVEXIN for the treatment of 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.

If we fail to comply with FDA 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 that 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 has substantial discretion in the approval process. Despite the time and experience exerted, failure can occur at any stage, and we could encounter problems that could cause us to abandon clinical trials.

We have completed three Phase 2 clinical trials and are conducting two Phase 3 clinical trials of our lead product candidate, ADVEXIN therapy, for the treatment of head and neck cancer. In addition, we have completed a Phase 2 clinical trial of ADVEXIN therapy for the treatment of non-small cell lung cancer and are conducting a Phase 2 clinical trial of ADVEXIN therapy for the treatment of breast cancer. We also are conducting or have conducted several Phase 1 and Phase 2 clinical trials of ADVEXIN therapy for other types of cancer. Current or future clinical trials may demonstrate that ADVEXIN therapy is neither safe nor effective.

While we have completed enrollment in a Phase 1/early Phase 2 clinical trial of INGN 241, a product candidate based on the mda-7 gene, our most significant clinical trial activity and experience has been with ADVEXIN therapy. 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 that 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, in particular the Phase 3 clinical trials of ADVEXIN therapy for the treatment of head and neck cancer, 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 or the FDA 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 that the results we observed in our pre-clinical testing will be confirmed in clinical trials or that the results of any of our clinical trials will support FDA approval. Preclinical and clinical data can be interpreted in many different ways, and FDA officials could interpret data that we consider promising differently, 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 Biologics License Application for ADVEXIN therapy, or other delays in the FDA 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 policy during the period of product development, clinical trials and FDA regulatory review.

Even if our products are approved by regulatory authorities, if we fail to comply with on-going 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 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 problem 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, 2003, we had an accumulated deficit of approximately $93.0 million. We expect to incur substantial additional operating expenses and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities increase. 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 The University of Texas M. D. Anderson Cancer Center. We do not expect to generate revenues from the commercial sale of products in the near future, and we may never generate revenues 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 program 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 revenues may not be sufficient to support the expenses of our operations, the development of commercial infrastructure and the conduct of our clinical trials and pre-clinical research.

We expect that we will fund our operations over approximately the next 18 to 24 months with our current working capital, which we accumulated primarily from sale 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 may need 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;

the rate of progress and cost of our research and development and clinical trial activities;

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

the costs of preparing an application for FDA approval of ADVEXIN therapy;

the costs of developing the processes and systems to support FDA approval of ADVEXIN therapy;

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;

our 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; and

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 that 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 that are 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 National Cancer Institute, Chiba University in Japan, VirRx and Corixa Corporation, as well as numerous other institutions that conduct clinical trials work 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 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 are not able to create effective collaborative marketing relationships, we may be unable to market ADVEXIN therapy 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 that we enter into any such arrangements with third parties, our product revenues are likely to be lower than if we directly marketed and sold our products, and any revenues 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 gene therapy may result in governmental authorities imposing additional regulatory requirements or a negative public perception of our products.

ADVEXIN therapy and our other product candidates under development could be broadly described as gene therapies. A number of clinical trials are being conducted by other pharmaceutical companies involving gene therapy, 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, any response by the FDA 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.

For example, in 2002, the FDA placed a clinical hold on gene therapy clinical trials using retroviral vectors to transduce hematopoietic stem cells after two participants in such a trial for the X-linked form of severe combined immune deficiency disease (X-SCID), being conducted in Europe, developed what appeared to be a leukemia-like illness. This clinical hold requires a case-by-case review of the use of retroviral vectors in these European trials before consideration of the removal of this clinical hold for these trials. We do not use retroviral vectors in our ongoing clinical trials and are not developing products using the production process used in those clinical trials. We have received no communications from the FDA to indicate this clinical hold will affect our clinical trials, and we anticipate no future negative effects on our clinical trials from this event, but we cannot assure you that the FDA or any other regulatory authority will not issue a clinical hold with respect to any of our clinical trials in the future. In accordance with our pharmacovigilance procedures and regulatory requirements, we monitor every patient in our clinical trials for safety and report all side effects to the FDA and the National Institutes of Health.

The United States Senate has held hearings concerning the adequacy of regulatory oversight of gene 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 healthy volunteers and patients who participate in such clinical trials. The Recombinant DNA Advisory Committee, or RAC, which acts as an advisory body to the NIH has expanded its public role in evaluating important public and ethical issues in gene 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 that 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.

To date, the FDA has not approved any gene therapy product or gene-induced product for sale in the United States. The commercial success of our products will depend in part on public acceptance of the use of gene therapy products or gene-induced 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 gene

therapy products or gene-induced products are unsafe, and these treatment methodologies may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy products or gene-induced products could also result in greater government regulation and stricter clinical trial oversight.

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

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 that ADVEXIN therapy does not increase the adverse effects of other therapies, we cannot predict if this 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 that 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 that 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 genes, gene-induced therapeutic protein agents, viruses for delivering the genes to cells, formulations, gene therapy delivery systems that do not involve 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 that patent applications concerning biotechnology-related inventions 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 that cover commercially significant 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 us a United States patent for our adenovirus production technology. We also control, through licensing arrangements, four issued United States patents for combination therapy involving the p53 gene and conventional chemotherapy or radiation, one issued United States patent covering the use of adenoviral p53 in cancer therapy, one issued United States patent covering adenoviral p53 as a product and an issued United States patent covering the core DNA of adenoviral p53. We have recently been notified by the PTO that additional applications relating to our adenoviral p53, purified adenoviral composition and mda-7 technology have been allowed. We cannot assure you these allowed

applications will actually issue as United States patents. 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 recently 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 at present know the identity of this party, and cannot assess the likelihood that an interference will actually be 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 has 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. The EPO held an initial oral proceeding on October 20, 2003 and determined that our patent should be maintained as amended. Schering-Plough can appeal this decision. Resolution of such an appeal, if taken, will require that we expend time, effort and money. If Schering-Plough ultimately prevails in having our European patent revoked on appeal, then the scope of our protection for our product in Europe will be reduced. We would not expect, however, such a result to have a significant impact on our commercialization efforts in Europe.

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 that relate to gene therapy, the treatment of cancer and the use of the p53 and other tumor suppressor genes. Schering-Plough Corporation, including its subsidiary Canji, Inc., controls various United States patent applications and a European patent and applications, some of which are directed to therapy using the p53 gene, and others to adenoviruses that contain the p53 gene, or adenoviral p53, and to methods for carrying out therapy using adenoviral p53. Adenoviral p53 technology underlies our ADVEXIN therapy product candidate. In addition, Canji controls an issued United States patent and its international counterparts, including a European patent, involving a method of treating mammalian cancer cells lacking normal p53 protein by introducing a p53 gene into the cancer cell. Furthermore, we are aware of a United States patent directed to replication-deficient recombinant adenoviral vectors apparently controlled by Transgene SA. While we believe that the claims of the Canji p53 patents or the Transgene adenoviral vector patent are invalid or not infringed by our products, Transgene, Canji or Schering-Plough 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 and controlled by Schering-Plough, is involved in a PTO interference proceeding with a patent owned by Canji. We further understand that this Johns Hopkins application is the United States counterpart to the European patent that was recently revoked in its entirety by the EPO (see below). We have now learned that priority of invention in this interference has been awarded by the PTO to the Johns Hopkins application, and the Canji patent has been found unpatentable. We cannot at present assess whether any patent might ultimately issue on the Johns Hopkins application or the potential impact, if any, of this PTO ruling on our business. If this application issues as a patent, Schering-Plough or Johns Hopkins may assert that our ADVEXIN therapy, which uses p53 therapy, infringes the claims of such patent. While we believe that we would have an invalidity 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 you that 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, Canji p53 issued United States patent or a claim that may issue from a currently pending application, such as the Johns Hopkins application discussed above or other patents that might issue with similar claims, our business could be materially harmed.

We are currently involved in opposing three European patents in proceedings before the EPO, in which we are seeking to have the EPO revoke three different European patents owned or controlled by Canji/ Schering-Plough. These European patents relate to the use of a p53 gene, or the use of tumor suppressor genes, in the preparation of therapeutic products. In one opposition involving a European patent directed to the use of a tumor suppressor gene, the EPO revoked the European patent in its entirety. Canji has appealed this revocation. A hearing to determine the outcome of this appeal is scheduled for late April 2004. In the second opposition, involving a patent that is directed to therapeutic and other applications of the p53 gene 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 has appealed this decision. In a third case involving the use of a p53 gene, the European patent at issue was upheld following an initial hearing. A second hearing to determine whether this patent should be revoked will be held in late April 2004. If we do not ultimately prevail in one or more of these oppositions, our competitors could seek to assert by means of litigation any patent surviving opposition against European commercial activities involving our potential products. If our competitors are successful in any such litigation, it could have a significant detrimental effect on our ability to commercialize our potential commercial products in Europe.

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 that 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 products 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.

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

We compete with pharmaceutical and biotechnology companies, including Canji, Inc. and Genvec, Inc., 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 Corporation, 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 that 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, Inc., has recently announced that it has received regulatory approval from the Chinese drug regulatory agency to market an adenoviral p53 product 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 do not at present know whether SiBioNo s adenoviral p53 product is covered by patent protection or whether it infringes our Chinese patent or pending applications. We understand that 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 that are currently ongoing 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 products in China. 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 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 approval for products more rapidly than 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.

Table of Contents

Even if we receive regulatory approval to market 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, if approved, and our other product candidates. 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 other product candidates effectively.

Because the target patient populations for the primary indication of ADVEXIN therapy, our lead product candidate, are small, we must achieve significant market share and obtain high per-patient prices for our products to achieve profitability.

ADVEXIN therapy, our lead product candidate for the treatment of recurrent squamous cell cancer of the head and neck, targets diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development costs and achieve profitability. We estimate that the annual incidence for squamous cell cancer of the head and neck is 40,000 patients in the United States. We believe that we will need to market worldwide to achieve significant market penetration. In addition, we are developing other drug candidates to treat cancers with small patient populations. Due to the expected costs of treatment for ADVEXIN therapy, we may be unable to obtain sufficient market share for our drug products at a price high enough to justify our product development efforts.

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

To complete our clinical trials and commercialize our product candidates, if approved, we will need access to, or development of, facilities to manufacture a sufficient supply of our product candidates. We have used a manufacturing facility in Houston, Texas, which we constructed and own, to manufacture ADVEXIN therapy, INGN 241 and other product candidates for currently planned clinical trials. We anticipate that this facility is 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 that would be 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 manufacture 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 very limited contract manufacturers who currently have the capability to produce ADVEXIN therapy, INGN 241 or 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 facility and process.

Table of Contents

Manufacturing of our product candidates for clinical and commercial purposes must comply with the FDA s current Good Manufacturing Practices requirements, commonly known as 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 that the product meets applicable specifications and other requirements. We must also pass a pre-approval inspection prior to FDA approval.

Our current manufacturing facilities have not yet been subject to an FDA or other regulatory dossier-related inspection. Failure to pass a pre-approval inspection may significantly delay FDA 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 facility in Houston, Texas is our only manufacturing facility. If this facility 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 that 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 for 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 that 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 upon 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 only one supplier for some of our manufacturing materials. Any problems experienced by any such supplier 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 manufacture of these product candidates are available from only one supplier or vendor. 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 that one of our sole source suppliers experiences could result in a delay or interruption in the supply of materials to us until that 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.

Table of Contents

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

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 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 $15.0 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, and any claims relating to improper handling, storage or disposal of these materials could 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 an improper or unauthorized release of, or exposure of individuals to, hazardous materials, we could be subject to civil damages 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 prevent us from conducting our business.

Our stock price may fluctuate substantially.

The market price for our common stock will 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.

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.

Any acquisition we might make may be costly and difficult to integrate, may 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 that 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 expenses; 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.

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 this prospectus supplement. 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.

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 and other personnel. The development of new therapeutic products requires expertise from a number of different disciplines, some of which are 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 requirements and for the advancement of our product candidates toward FDA approval. The quality and reputation of our scientific, clinical and regulatory 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 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.

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., a health care investment firm which 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 that 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 the Company s affairs. EJ Financial is also involved in the management of health care 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.

We are in negotiations with Dr. Robert Sobol, our Senior Vice President, Medical and Scientific Affairs, to acquire a company of which he is the sole shareholder. The terms of the proposed transaction have not been determined, but the purchase price is likely to be between $1 million and $2 million and to be paid in shares of our common stock. We believe the technology which is owned by Dr. Sobol s company will be a valuable addition to our intellectual property portfolio. We have endeavored to conduct the negotiations at arms length, and any transaction would be subject to the approval of the independent members of our Board of Directors.

In addition, we have relationships with Jack A. Roth, M.D., and The University of Texas 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 the notes to our consolidated financial statements.

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

RISKS RELATED TO THE OFFERING

Market volatility may affect our stock price, and the value of your investment in our common stock may be subject to sudden decreases.

The trading price for our common stock has been, and we expect it to continue to be, volatile. The price at which our common stock trades depends on number of factors, including the following, many of which are beyond our control:

- our historical and anticipated operating results, including fluctuations in our financial and operating results;
- pre-clinical and clinical trial results;
- market perception of the prospects for biotechnology companies as an industry sector;
- general market and economic conditions;
- changes in government regulations affecting product approvals, reimbursement or other aspects of our or our competitors businesses;
- FDA review of our product development activities;

announcements of technological innovations or new commercial products by us or our competitors;

developments concerning our key personnel and intellectual property rights;

announcements regarding significant collaborations or strategic alliances; and

publicity regarding actual or potential performance of products under development by us or our competitors.

In addition, the stock market has from time to time experienced extreme price and volume fluctuations. These broad market fluctuations may lower the market price of our common stock and affect the volume of trading in our stock. The high and low sale prices per share of our common stock on the Nasdaq National Market were $9.43 and $2.01, respectively, from January 1, 2003 through March 3, 2004. During this period, the average daily trading volume of our common stock on the Nasdaq National Market was approximately 300,000 shares. During periods of stock market price volatility, share prices of many biotechnology companies have often fluctuated in a manner not necessarily related to their individual operating performance. Accordingly, our common stock may be subject to greater price volatility than the stock market as a whole.

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

Provisions of our certificate of incorporation and bylaws will make it more difficult for a third party to acquire us on terms not approved by our board of directors and may have the effect of deterring hostile takeover attempts. For example, our certificate of incorporation authorizes our board of directors to issue up to 5,000,000 shares of preferred stock, of which 100,000 shares have been designated as Series A Non-Voting Convertible Preferred Stock, and to fix the price, rights, preferences, privileges and restrictions, including voting rights, of those shares without any further vote or action by the stockholders.

In connection with the restructuring of the Aventis collaboration and pursuant to a stock purchase agreement with Aventis executed on June 30, 2001, we issued and sold to Aventis 100,000 shares of Series A Non-Voting Convertible Preferred Stock, $0.001 par value per share. The shares of Series A Non-Voting Convertible Preferred Stock are not subject to repurchase or redemption, and are convertible at any time, at our option or the option of Aventis, into 2,343,721 shares of our common stock. Under a voting agreement, Aventis must vote these shares of common stock in the same manner as the shares voted by a majority of the other stockholders on any corporate action put to a vote of our stockholders. This voting requirement terminates at the earliest of the tenth anniversary of the voting agreement, registration of these shares with the Securities and Exchange Commission or the sale of these shares to an Aventis non-affiliate, as defined in the voting agreement. A registration rights agreement grants the holder of a majority of the common stock issuable upon conversion of the Series A Non-Voting Convertible Preferred Stock three demand registrations and three piggyback registrations.

The rights of the holders of our common stock will be subject to, and may be harmed by, the rights of the holders of any preferred stock that may be issued in the future. The issuance of preferred stock could reduce the voting power of the holders of our common stock and the likelihood that common stockholders will receive payments upon liquidation.

In addition, our certificate of incorporation divides our board of directors into three classes having staggered terms. This may delay any attempt to replace our board of directors. These and other impediments to a third-party acquisition or change of control could limit the price investors are willing to pay in the future for shares of our common stock.

We are also subject to provisions of Delaware law that could have the effect of delaying, deferring or preventing a change in control of our company. One of these provisions prevents us from engaging in a business combination with any interested stockholder for a period of three years from the date the person becomes an interested stockholder, unless specified conditions are satisfied.

If registration rights that we have previously granted are exercised, then our stock price may be negatively affected.

We have granted registration rights in connection with the issuance of our securities to a number of our stockholders and warrant holders. In the aggregate, as of December 31, 2003, these registration rights covered approximately 8,665,940 shares of our common stock which were then outstanding. If these registration rights, or similar registration rights that may apply to securities we may issue in the future, are exercised by the holders, it could result in additional sales of our common stock in the market, which may have an adverse effect on our stock price. We currently have in effect a registration statement relating to up to 2,400,000 shares held by various stockholders pursuant to which these stockholders may freely resell these 2,000,000 shares, as well as an additional 400,000 shares upon the exercise of warrants, into the public market at any time or from time to time.

Our issuance of shares pursuant to future collaborations or other agreements or under our shelf registration statement will dilute the equity ownership of our existing stockholders.

We may enter into certain other agreements involving our issuance of additional shares of common stock. In connection with any such collaboration or any other similar agreement that we may enter into in the future, we may issue additional shares of common stock or other equity securities, and the value of the securities issued may be substantial.

In addition, we may sell up to an additional $30.0 million of our common stock under our outstanding shelf registration statement. Future sales under our shelf registration statement will depend primarily on the market price of our common stock, the interest in our company by institutional investors and our cash needs. In addition, we may register additional shares with the SEC for sale in the future.

We do not intend to pay cash dividends on our common stock in the foreseeable future.

We do not anticipate paying cash dividends on our common stock in the foreseeable future. Any payment of cash dividends will depend upon our financial condition, results of operations, capital requirements and other factors and will be at the discretion of our board of directors. Furthermore, we may become subject to contractual restrictions or prohibitions on the payment of dividends.

Table of Contents

Forward-looking statements

Certain statements in this prospectus supplement and the accompanying 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, and Section 21E of the Securities and Exchange Act of 1934, as amended, 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 concernin opportunity or 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 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 this prospectus supplement and the accompanying 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.

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

Table of Contents

Use of proceeds

We estimate that the net proceeds to us from this offering will be approximately $48.2 million, or $55.5 million if the underwriters over-allotment option is exercised in full, assuming a public offering price of $9.43 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Unless otherwise indicated in the prospectus supplement, we intend to use the net proceeds from the sale of common stock offered by this prospectus supplement to fund regulatory activities relating to our lead product candidate, ADVEXIN therapy, to fund ongoing and planned clinical trials, to continue pre-clinical research and development, and for other 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 in amount. The amounts and timing of the expenditures will depend on numerous factors, such as the timing and progress of our clinical trials and research and development efforts, technological advances and the competitive environment for our drug candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, we will retain broad discretion over the use of these proceeds.

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.

Table of Contents

Capitalization

The following table shows our cash and cash equivalents and capitalization as of December 31, 2003:

- on an actual basis; and
- as adjusted to give effect to the sale by us of 5,500,000 shares of our common stock in this offering at an assumed public offering price of $9.43 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

This table should be read with Management s discussion and analysis of financial condition and results of operations and our financial statements and the related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of December 31, 2003	
	Actual	As adjusted
	(in thousands, except per share data)	
Cash and cash equivalents	$ 36,397	$ 84,750
Long term debt and capital lease obligation, net of current portion	6,714	6,714
Stockholders equity:		
Series A non-voting, convertible preferred stock, $0.001 par value per share; 100 shares authorized, issued and outstanding, actual and as adjusted	1	1
Common stock, $0.001 par value per share; 50,000 shares authorized; 26,539 shares issued and outstanding, actual; 32,040 shares issued and outstanding, as adjusted	27	32
Additional paid-in capital	124,270	172,618
Deferred compensation	(44)	(44)
Accumulated deficit	(92,969)	(92,969)
Total stockholders equity	$ 31,285	$ 79,638
Total capitalization	37,999	86,352

The number of shares of common stock outstanding is based on the number of shares outstanding as of December 31, 2003 and excludes:

- 4,756,401 shares of common stock underlying options outstanding as of December 31, 2003 at a weighted average exercise price of $2.91 per share;
- 400,000 shares of common stock available for issuance upon the exercise of outstanding warrants at an exercise price of $7.89 per share;
- 2,343,721 shares of common stock available for issuance upon the conversion of 100,000 shares of Series A non-voting convertible preferred stock; and
- 1,484,113 shares of common stock available for issuance or future grant pursuant to our 2000 Stock Option Plan (includes an increase of 1,326,976 shares on January 1, 2004 pursuant to an automatic reload under the 2000 Stock Option Plan).

Table of Contents

Dilution

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

Our net tangible book value at December 31, 2003 was approximately $31.3 million, or $1.18 per share of common stock. Net tangible book value per share is equal to our total tangible assets minus total liabilities, all divided by the number of shares of common stock outstanding as of December 31, 2003. After giving effect to the sale by us of the 5,500,000 shares of common stock we are offering and deducting underwriting discounts and commissions and our estimated offering expenses, our as adjusted net tangible book value would have been approximately $79.6 million, or $2.49 per share of common stock. This represents an immediate increase in net tangible book value of $1.31 per share to existing stockholders and an immediate dilution of $6.94 per share to new investors. The following table illustrates this calculation on a per share basis:

Assumed public offering price per share		$9.43
Net tangible book value per share as of December 31, 2003	$1.18	
Increase per share attributable to the offering	1.31	
As adjusted net tangible book value per share after this offering		$2.49
Dilution per share to new investors		$6.94

If the underwriters exercise their over-allotment option in full, the as adjusted net tangible book value as of December 31, 2003 would have been $2.65 per share, representing an increase to existing stockholders of $1.47 per share, and there will be an immediate dilution of $6.78 per share to new investors.

The foregoing table does not take into effect further dilution to new investors that could occur upon the exercise of outstanding options having a per share exercise price less than the offering price per share in this offering. As of December 31, 2003, there were:

4,756,401 shares of common stock underlying options outstanding at a weighted average exercise price of $2.91 per share;

400,000 shares of common stock available for issuance upon the exercise of outstanding warrants at an exercise price of $7.89 per share;

2,343,721 shares of common stock reserved for issuance upon the conversion of 100,000 shares of Series A non-voting convertible preferred stock; and

1,484,113 shares of common stock available for issuance or future grant pursuant to our 2000 Stock Option Plan (includes an increase of 1,326,976 shares on January 1, 2004 pursuant to an automatic reload under the 2000 Stock Option Plan).

Table of Contents

Price range of common stock

Our common stock is quoted on the Nasdaq National Market under the symbol INGN. The following table sets forth, for the periods indicated, the high and low reported sale prices of our common stock as reported on the Nasdaq National Market:

	High	Low
Year ended December 31, 2002		
First quarter	$ 5.59	$3.56
Second quarter	4.97	1.80
Third quarter	2.80	1.35
Fourth quarter	2.58	1.48
Year ended December 31, 2003		
First quarter	$ 3.36	$1.97
Second quarter	10.16	1.98
Third quarter	11.24	5.26
Fourth quarter	10.20	6.95
Year ending December 31, 2004		
First quarter (through March 2, 2004)	$10.37	$8.07

As of March 3, 2004, there were 156 holders of record of our common stock. On March 3, 2004, the last sale price reported on the Nasdaq National Market for our common stock was $9.43 per share.

Dividend policy

We have never paid our stockholders dividends, and we do not anticipate paying any cash dividends in the foreseeable future as we intend to retain any earnings for use in our business. The payment of any future cash dividends on our common stock will depend upon our earnings and financial needs and will be subject to applicable legal and contractual restrictions.

Table of Contents

Underwriting

We are offering the shares of our common stock described in this prospectus supplement through the underwriters named below. UBS Securities LLC, SG Cowen Securities Corporation and Leerink Swann & Co. are the representatives of the underwriters. UBS Securities LLC is the sole book-running manager of this offering.

We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, each of the underwriters has severally agreed to purchase the number of shares of common stock listed next to its name in the following table:

Underwriters	Number of shares
UBS Securities LLC	
SG Cowen Securities Corporation	
Leerink Swann & Co.	
Total	5,500,000

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

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

- receipt and acceptance of our common stock by the underwriters; and
- the underwriters right to reject orders in whole or in part.

In connection with this offering, certain of the underwriters and securities dealers may distribute prospectus supplements and the accompanying prospectuses electronically.

Sales of shares made outside of the United States may be made by affiliates of the underwriters.

OVER-ALLOTMENT OPTION

We have granted the underwriters an option to buy up to an aggregate of 825,000 additional shares of our common stock. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with this offering. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If the underwriters exercise the option, they will each purchase additional shares approximately in proportion to the amounts specified in the table above.

COMMISSIONS AND DISCOUNTS

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

Table of Contents

Underwriting

The following table shows the per share and total underwriting discounts and commissions we will pay to the underwriters assuming both no exercise and full exercise of the underwriters option to purchase up to an additional 825,000 shares.

Paid by the Company	No exercise	Full exercise
Per share	$	$
Total	$	$

We estimate that the total expenses of the offering payable by us, not including underwriting discounts and commissions, will be approximately $400,000.

NO SALES OF SIMILAR SECURITIES

We and our executive officers and directors have entered into lock-up agreements with the underwriters. Under these agreements, we and each of these persons generally may not, without the prior written approval of UBS Securities LLC, subject to certain permitted exceptions, offer, sell, contract to sell or otherwise dispose of or hedge our common stock or securities convertible into or exercisable or exchangeable for our common stock. These restrictions will be in effect for a period of 90 days after the date of this prospectus supplement. At any time and without public notice, UBS Securities LLC may, in its sole discretion, release all or some of the securities from these lock-up agreements.

INDEMNIFICATION AND CONTRIBUTION

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

NASDAQ NATIONAL MARKET QUOTATION

Our common stock is quoted on the Nasdaq National Market under the symbol INGN.

PRICE STABILIZATION, SHORT POSITIONS, PASSIVE MARKET MAKING

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

- stabilizing transactions;
- short sales;
- purchases to cover positions created by short sales;
- imposition of penalty bids; and
- syndicate covering transactions.

Stabilizing transactions consist of bids or purchases made for the purpose of preventing or retarding a decline in the market price of our common stock while this offering is in progress. These transactions may also include making short sales of our common stock, which involves the sale by the underwriters of a greater number of shares than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered short sales, which are short positions in an amount not greater than the underwriters over allotment option referred to above, or may be naked short sales, which are short positions in excess of that amount.

Table of Contents

Underwriting

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

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

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

In addition, in connection with this offering, certain of the underwriters (and selling group members) may engage in passive market making transactions in the common stock on the Nasdaq National Market prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq National Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of such transactions. If passive market making is commenced, it may be discontinued at any time.

AFFILIATIONS

Certain of the underwriters and their affiliates have in the past provided, and may from time to time provide, other services to us, including investment banking and financial advisory services, for which they were and will be entitled to receive separate compensation. The underwriters and their affiliates may from time to time in the future engage in transactions with us and perform services for us in the ordinary course of their business.

Table of Contents

Experts

Our consolidated financial statements for the years ended December 31, 2003 and 2002, incorporated by reference in this prospectus supplement and the accompanying prospectus have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon (the 2001 and 2000 financial statements were audited by other auditors who have ceased operations and for which Ernst & Young LLP has expressed no opinion or other form of assurance on the 2001 and 2000 financial statements taken as a whole) incorporated by reference herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Additionally, our audited consolidated financial statements incorporated by reference in this prospectus supplement and the accompanying prospectus to the extent and for the periods indicated in their reports have been audited with respect to our and our subsidiaries consolidated balance sheet as of December 31, 2001 and June 30, 2001 and 2000, and the related consolidated statements of operations, stockholders equity and cash flows for the six months ended December 31, 2001 and the years ended June 30, 2001 and 2000, by Arthur Andersen LLP, independent public accountants. These reports are incorporated by reference in this prospectus supplement and the accompanying prospectus in reliance upon the authority of these accounting firms as experts in giving these reports.

We have been unable to obtain, after reasonable efforts, the written consent of Arthur Andersen LLP to our naming it as an expert and as having audited the consolidated financial statements for the six months ended December 31, 2001 and the two years ended June 30, 2001 and 2000 and including its audit report in this prospectus supplement and the accompanying prospectus. Under these circumstances, Rule 437(a) of the Securities Act of 1933, as amended, permits this prospectus supplement to be filed without the consent of Arthur Andersen LLP. This lack of consent may limit your ability to recover damages from Arthur Andersen LLP under Section 11 of the Securities Act for any untrue statements of material fact contained in the financial statements audited by Arthur Andersen LLP or any omissions to state a material fact required to be stated therein or necessary to make the statements therein not misleading.

We changed certifying accountants from Arthur Andersen LLP to Ernst & Young LLP effective March 6, 2002. Arthur Andersen LLP s report on the financial statements for the six months ended December 31, 2001 and the years ended June 30, 2001 and 2000 did not contain an adverse opinion or disclaimer of opinion and was not qualified or modified as to uncertainty, audit scope or accounting principles. The decision to change accountants was approved by our Board of Directors. During each of the two years ended June 30, 2000 and 2001 and for the six-month transition period ended December 31, 2001, and through March 20, 2002, there were no disagreements with Arthur Andersen LLP on any matter of accounting principles or practices, financial statement disclosure, or auditing scope or procedures, which disagreements, if not resolved to the satisfaction of Arthur Andersen LLP, would have caused it to make reference to the subject matter of the disagreement in connection with its report. During each of the two years ended June 30, 2000 and 2001 and for the six-month transition period ended December 31, 2001, and through March 20, 2002, Arthur Andersen LLP did not advise us of any reportable events as described in Item 304(a)(1)(v) of Regulation S-K under the Securities Act of 1933, as amended. We have requested and received from Arthur Andersen LLP the letter required by Item 304(a)(3) of Regulation S-K (and filed the same as Exhibit 16 to our report on Form 8-K filed on March 12, 2002), and we state that Arthur Andersen LLP agrees with the statements made by us in this prospectus supplement and the accompanying prospectus in response to Item 304(a)(1) of Regulation S-K.

Table of Contents

Information incorporated 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 supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference into this prospectus supplement 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 supplement until the termination of this offering, as well as the following documents:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2003, filed with the SEC on March 5, 2004;
- our Proxy Statement, filed with the SEC on April 30, 2003, as amended on May 8, 2003; 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 incorporated by reference from Description of Capital Stock set forth in our Registration Statement on Form S-1, originally filed with the SEC on February 17, 2000 (File No. 333-30582) and all amendments thereto.

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.

Additionally, we make these filings available, free of charge, on *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 supplement and is not incorporated by reference into this document.

Legal matters

The validity of the common stock being offered hereby is being passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Austin, Texas. Dewey Ballantine LLP, New York, New York, is counsel for the underwriters in connection with this offering.

Table of Contents

PROSPECTUS

$100,000,000

By this prospectus, we may offer shares of our common stock from time to time. We will provide specific terms of the common stock in supplements to this prospectus. You should read this prospectus and any supplement carefully before you purchase any of our common stock.

Our common stock is traded on the Nasdaq National Market under the symbol INGN. On August 20, 2003, the last reported sale price for the common stock on the Nasdaq National Market was $7.00 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 the Risk Factors section beginning on page 5 of this prospectus, which describes the specific risks and certain other information associated with an investment in our common stock.

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.

We may offer the common stock in amounts at prices and on terms determined at the time of offering. We may sell the common stock directly to you, through agents we select, or through underwriters and dealers we select. If we use agents, underwriters or dealers to sell the securities, we will name them and describe their compensation in a prospectus supplement.

The date of this prospectus is August 25, 2003

Table of Contents

TABLE OF CONTENTS

Summary	**3**
Risk Factors	**5**
The Company	**14**
Forward-Looking Statements	**40**
Use of Proceeds	**41**
Plan of Distribution	**42**
Legal Matters	**42**
Experts	**43**
Incorporation of Certain Information by Reference	**44**
Where You Can Find More Information	**45**
Indemnification of Directors and Officers	**45**

No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in 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. 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.

Table of Contents

Summary

This prospectus is part of a registration statement that we filed with the Commission, 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 total dollar amount of $100,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. 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. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement, including the risk factors, together with the additional information described under the heading Where You Can Find Information. All references to Introgen, the Company, the Registrant, we, u our mean Introgen Therapeutics, Inc.

Table of Contents

The offering

Securities offered by Introgen Therapeutics, Inc.:	Up to $100,000,000 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 underwriters, dealers or agents involved in the sale of common stock described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.
Use of proceeds:	Unless otherwise indicated in the 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.

Table of Contents

Risk factors

We may encounter delays or difficulties in clinical trials for our product candidates, which may delay or preclude regulatory approval of some or all of our product candidates.

In order to commercialize our product candidates, we must obtain 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 that our product candidates are safe and effective for a particular cancer type or other disease.

We are conducting Phase 3 clinical trials of our lead product candidate, ADVEXIN therapy, for the treatment of head and neck cancer, have completed a Phase 2 clinical trial of ADVEXIN therapy for the treatment of non-small cell lung cancer, are conducting a Phase 2 clinical trial of ADVEXIN therapy for the treatment of breast cancer and either have conducted or are conducting several Phase 1 and Phase 2 clinical trials of ADVEXIN therapy for other cancer types. Current or future clinical trials may demonstrate that ADVEXIN therapy is neither safe nor effective.

While we are conducting a Phase 1-2 clinical trial of INGN 241, a product candidate based on the mda-7 gene, our most significant clinical trial activity and experience has been with ADVEXIN therapy. 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 that 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, in particular the Phase 3 clinical trials of ADVEXIN therapy for the treatment of head and neck cancer, 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 or the United States Food and Drug Administration (FDA) might delay or halt any of our clinical trials of a product candidate at any time for various reasons, including:

- the failure of the product candidate to be more effective 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 though the product candidate may not have caused 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 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 policy during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution,

civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our product candidates or us.

Outside the United States, our ability to market a product is contingent upon receiving clearances from the appropriate regulatory authorities. This foreign regulatory approval process includes all of the risks associated with FDA clearance described above.

We have a history of operating losses and expect to incur significant additional operating losses.

We have generated operating losses since we began operations in June 1993. As of March 31, 2003, we had an accumulated deficit of approximately $79.1 million. We expect to incur substantial additional operating expenses and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities increase. 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 The University of Texas M. D. Anderson Cancer Center. Prior to December 31, 2000, we earned revenue from Aventis Pharmaceuticals, Inc. under collaborative agreements for research and development and sales of ADVEXIN therapy for use in Aventis clinical trials, which are revenues we no longer receive. We do not expect to generate revenues from the commercial sale of products in the foreseeable future, and we may never generate revenues 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 program and complete our clinical trials.

Developing a new drug and conducting clinical trials for multiple disease indications is expensive. We expect that we will fund our operations over the approximately the next 18 to 24 months with our current working capital, resulting primarily from the net proceeds from our initial public offering in October 2000, the sale of Series A Non-Voting Convertible Preferred Stock to Aventis in June 2001, net proceeds from the sale of common stock and warrants to purchase common stock in a private placement to selected institutional investors in June 2003, 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 may need to raise additional capital sooner, however, due to a number of factors, including:

- 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 our manufacturing capability;
- higher than expected costs to develop our sales and marketing capability; and
- slower than expected progress in reducing our operating costs.

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 that 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 that are not favorable to us.

If we cannot maintain our corporate and academic arrangements and enter into new arrangements, product development could be delayed.

Our strategy for the research, development and commercialization of our product candidates may require us to enter into contractual arrangements with corporate collaborators, academic institutions and others. We have entered into sponsored research and/or collaborative arrangements with several entities, including M. D. Anderson Cancer Center, the National Cancer Institute, Chiba University in Japan, VirRx and Corixa Corporation, as well as numerous other institutions who conduct clinical trials work for us. Our success depends upon our collaborative partners performing their responsibilities under these arrangements. We cannot control the amount and timing of resources our collaborative partners devote to our research and testing programs or product candidates, which can vary because of factors unrelated to such programs or product 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 are not able to create effective collaborative marketing relationships, we may be unable to market ADVEXIN therapy 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 successfully sell, market and distribute our products. To the extent that we enter into any such arrangements with third parties, our product revenues are likely to be lower than if we directly marketed and sold our products, and any revenues 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 successfully commercialize our products.

Serious unwanted side effects attributable to gene therapy may result in governmental authorities imposing additional regulatory requirements or a negative public perception of our products.

Serious unwanted side effects attributable to treatment, which physicians classify as treatment-related adverse events, occurring in the field of gene therapy may result in greater governmental regulation and negative public perception of our product candidates, as well as potential regulatory delays relating to the testing or approval of our product candidates. The FDA recently placed a clinical hold on gene therapy clinical trials using retroviral vectors to transduce hematopoietic stem cells after two participants in