INTROGEN THERAPEUTICS INC
Form 10-K
March 16, 2006

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2005.

or

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

For the transition period from to .

Commission file number: 000-21291

Introgen Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**74-2704230**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*
301 Congress Avenue, Suite 1850 Austin, Texas	**78701**
(Address of principal executive offices)	*(Zip Code)*

Registrant s telephone number, including area code:
(512) 708-9310
Securities registered pursuant to Section 12(b) of the Act:
None
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $0.001 par value per share

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the Registrant s knowledge, in definitive proxy or information

statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

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

Large accelerated filer o Accelerated filer þ Non-accelerated filer o

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

The aggregate market value of the voting stock (common stock) held by non-affiliates of the Registrant, as of the last day of the Registrant s second fiscal quarter, was approximately $130.7 million based upon the last sale price reported on the Nasdaq National Market for June 30, 2005. For purposes of this disclosure, shares of common stock held by persons holding more than 5% of the outstanding shares of the Registrant s common stock and shares held by executive officers and directors of the Registrant have been excluded because such persons may be deemed to be affiliates. This determination is not necessarily conclusive.

As of March 13, 2005, the Registrant had 37,180,053 shares of common stock, $0.001 par value per share, issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Items 10, 11, 12, 13 and 14 of Form 10-K is incorporated by reference to the Registrant s proxy statement (2006 Proxy Statement) for the 2006 Annual Stockholders Meeting, which will be filed with the Securities and Exchange Commission within 120 days after the close of the Registrant s fiscal year ended December 31, 2005.

INTROGEN THERAPEUTICS, INC.
ANNUAL REPORT ON FORM 10-K
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PART I

Item 1. *Business*

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). These statements include, among others, statements concerning our future operations, financial condition and prospects, and our business strategies as well as the statements below under Item 1A. Risk Factors. The words believe, expect, anticipate and other similar expressions generally identify forward-looking statements. Investors in our common stock are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements are subject to substantial risks and uncertainties that could cause our future business, financial condition, or results of operations to differ materially from historical results or currently anticipated results. Investors should carefully review the information contained in Item 1A. Risk Factors and elsewhere in, or incorporated by reference into, this Annual Report on Form 10-K.

Access to Company Information

Our Internet website address is www.introgen.com. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act are available free of charge through our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (Commission). Our website and the information contained therein or connected thereto is not intended to be incorporated into this Annual Report on Form 10-K.

Our Corporate Governance Standards, the charters of our Audit Committee, our Compensation Committee and our Nominating and Corporate Governance Committee, as well as our Corporate Code of Ethics for All Employees and Directors and our Corporate Code of Ethics for Financial Officers (which specifically applies to our Chief Executive Officer, Chief Financial Officer and persons performing similar functions) are available on our website under Investor Relations Corporate Governance.

Overview

Introgen Therapeutics, Inc. was incorporated in Delaware in 1993. We are a biopharmaceutical company focused on the discovery, development and commercialization of targeted molecular therapies for the treatment of cancer and other diseases. We are developing product candidates to treat a wide range of cancers using tumor suppressors, cytokines and other targeted molecular therapies. These agents are designed to increase production of normal cancer-fighting proteins that act to overpower cancerous cells, stimulate immune activity and enhance conventional cancer therapies.

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

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

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Key product candidates we are developing, which are further described below under Item 1. Business Product Development Programs, include:

ADVEXIN® therapy

ADVEXIN® therapy, our lead product candidate, combines the p53 tumor suppressor with a non-replicating, non-integrating adenoviral delivery system. Key accomplishments and items of note with respect to our ADVEXIN therapy product development include the following:

We have received Fast Track designation for ADVEXIN therapy from the FDA under its protocol assessment program.

We have submitted a Submission of a Partial Application (SOPA) Request to the FDA Division of Cell and Gene Therapy proposing a rolling Biologics License Application (BLA) for ADVEXIN therapy for the treatment of recurrent head and neck cancer. We have proposed to the FDA that the rolling BLA could be evaluated under the provisions of Subpart H for Accelerated Approval.

We have reviewed historically successful FDA registration strategies for numerous cancer drugs, noting that during the past seven years, approximately 14 cancer drugs were initially approved based upon submissions of Phase 2 clinical data. A number of the Phase 2 trials supporting these approvals employed single-arm studies involving relatively small patient populations. Virtually all of those drugs relied on surrogate endpoints for approval and a substantial number of the products were for orphan drug indications.

Our two ongoing Phase 3 clinical trials of ADVEXIN therapy in patients with recurrent squamous cell cancer of the head and neck are multi-national, multi-site trials. In connection with these trials, the FDA has suggested we consider interim Phase 3 efficacy analyses. We are discussing with the FDA a plan to conduct these analyses in support of the ADVEXIN registration process. In addition, we have requested that the FDA allow us to accelerate the initiation of a previously approved interim safety analysis for one of our ongoing Phase 3 trials.

ADVEXIN therapy for head and neck cancer has been designated an Orphan Drug under the Orphan Drug Act. This designation may give us up to seven years of marketing exclusivity for ADVEXIN therapy for this indication if approved by the FDA.

We have enrolled over 500 patients in ADVEXIN therapy clinical trials, establishing a large safety database that indicates an absence of treatment-limiting side effects frequently associated with many other cancer therapies.

We have tested ADVEXIN therapy used alone and in combination with radiation therapy, chemotherapy, and surgery in various clinical trials.

We have observed that the anti-cancer effects of ADVEXIN therapy are a result of multiple mechanisms of action including induction of tumor cell death, suppression of tumor growth and the inhibition of tumor blood vessels, known as anti-angiogenesis.

Based upon defining prognostic, medical and biological characteristics that represent refined targeting of ADVEXIN therapy, we have identified subpopulations of patients participating in certain of our Phase 2 clinical trials for recurrent squamous cell cancer of the head and neck who may particularly benefit from ADVEXIN therapy. Analysis of the data from these patient subpopulations showed that up to 29% of the patients experienced objective responses with either complete tumor regression or a reduction of tumor size greater than or equal to 50% of the pre-treatment size. We are in the process of filing for patent protection covering certain of these characteristics.

In the combined analysis of the three multi-national, multi-site Phase 2 clinical trials involving 217 patients with recurrent squamous cell carcinoma of the head and neck, 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

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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.

We performed a Phase 2 clinical trial of ADVEXIN therapy combined with neoadjuvant chemotherapy and surgery in women with locally advanced breast cancer. Data from this clinical trial indicated that objective clinical responses were seen following the combined therapy in all of the patients. Complete tumor removal by subsequent surgery was achieved in 100% of the patients. After at least 35 months of follow-up, 92% of the treated patients were alive and 83% had survived without evidence of disease recurrence.

We performed a Phase 2 clinical trial of ADVEXIN therapy administered as a complement to radiation therapy in non-small cell lung cancer. In the 19 patients who participated in the trial, combined ADVEXIN and radiation treatment resulted in 63% biopsy-proven complete responses at three months, which is approximately four times the expected rate using radiotherapy alone.

We performed a Phase 1/early Phase 2 clinical trial of ADVEXIN therapy for the treatment of advanced, unresectable, squamous cell esophageal cancer. Results of this trial in patients with esophageal cancer refractory to chemotherapy and radiation indicate three of the ten patients treated, or 30%, had negative biopsies after receiving ADVEXIN therapy. The median survival of the patients treated with ADVEXIN therapy was approximately twelve months, which compared favorably to historical controls in which a median survival of less than ten months was observed for patients who did not respond to standard treatments. Six patients, or 60%, were still alive one year after beginning ADVEXIN therapy.

Our clinical trials indicate ADVEXIN therapy is well tolerated as a monotherapy and well tolerated when combined with conventional cancer therapies. We have observed that the addition of ADVEXIN therapy to standard chemotherapy, surgery or radiation can increase the activity of these conventional therapies without increasing the severity of side effects normally associated with these standard treatment regimens.

We hold the worldwide rights for the development, manufacturing, marketing and commercialization of ADVEXIN therapy.

We hold or control over 80 issued methods or composition patents related to ADVEXIN therapy and its production.

INGN 241

INGN 241 combines the mda-7 tumor suppressor, also known as interleukin 24 (IL-24), with our adenoviral vector system to kill tumor cells through multiple mechanisms. Our pre-clinical trials have shown the protein produced by INGN 241 suppresses the growth of many cancer cells, including those of the breast, lung, ovary, colon, prostate and central nervous system, while not affecting the growth of normal cells. A Phase 1/early Phase 2 clinical trial indicated that in patients with various solid tumors, INGN 241 is well tolerated, displays minimal toxicity and is biologically active. We are conducting later stage clinical trials using INGN 241 in patients with metastatic melanoma and other cancers.

INGN 225

INGN 225 is an immunotherapy using the p53 tumor suppressor as the basis for a highly specific cancer molecular immunotherapy that stimulates a particular type of immune system cell known as a dendritic cell. Findings during pre-clinical testing suggest a molecular immunotherapy consisting of dendritic cells stimulated by ADVEXIN therapy could have broad utility as a treatment for progression of solid tumors. Introgen academic collaborators are conducting Phase 1 and early stage Phase 2 clinical trials to study INGN 225 in the indications of small cell lung cancer and breast cancer. Interim results from these clinical trials in patients with small cell lung cancer who were previously treated with chemotherapy indicate that greater than 60% of the evaluable patients in the study treated with INGN 225 had objective responses to subsequent chemother-

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apy. Historically, the expected objective response rate in these patients to further chemotherapy is between 5% and 25%.

INGN 234

We are developing INGN 234 for the prevention of oral cancers and the treatment of oral leukoplakia, a pre-malignant condition. We are conducting a Phase 1/early Phase 2 clinical trial in which p53 is being administered in an oral mouthwash formulation to prevent precancerous oral lesions from developing into cancerous lesions. We are conducting pre-clinical work on other topical administrations of tumor suppressors to control or prevent oral or dermal cancers. We are investigating multiple delivery platforms, including both viral and non-viral approaches. We are also investigating delivery with rinses, patches, ointments and enhancing polymers. We believe the opportunity exists to develop safe treatments for pre-malignant and malignant cells that can be effectively exposed to natural biological tumor suppressor and DNA repairing molecules.

INGN 401

INGN 401 is our systemically-delivered nanoparticle therapy that provides the normal FUS-1 tumor suppressor that is frequently altered or missing in the development of many solid tumors. Pre-clinical studies have shown delivery of FUS-1 significantly inhibits the growth of tumors and greatly reduces metastatic spread of lung cancer in animals when delivered to tumor cells using either an adenoviral or non-viral delivery system. INGN 401 is being studied in a Phase 1/2 clinical trial for end-stage, metastatic non-small cell lung cancer patients.

INGN 402

INGN 402 is our systemic, nanoparticle formulation containing the p53 tumor suppressor currently in pre-clinical development. Early studies with INGN 402 have demonstrated a good safety profile and promising anti-cancer activity in murine lung tumor models.

INGN 403

INGN 403 is our systemic, nanoparticle formulation containing the mda-7 tumor suppressor, also known as interleukin 24 (IL-24). Early studies with INGN 403 have demonstrated a good safety profile and promising anti-cancer activity in murine lung tumor models. Data from the INGN 403 pre-clinical mda-7 nanoparticle studies were recently published in *DNA and Cell Biology.*

INGN 007

INGN 007 is a replication-competent viral therapy that over-expresses an adenoviral protein causing rapid disruption of tumor cells in which the adenovirus replicates. Pre-clinical testing indicates this treatment can eradicate human tumors in animal models.

We have an alliance agreement with Colgate-Palmolive Company (Colgate-Palmolive) to develop and potentially market oral healthcare products. See Item 1. Business Business and Collaborative Arrangements Alliance with Colgate-Palmolive Company below for further discussion of this alliance agreement.

Our principal executive offices are located at 301 Congress Avenue, Suite 1850, Austin, Texas 78701. Our telephone number is (512) 708-9310. Our Internet website address is www.introgen.com.

Background

Targeted Therapeutics

A typical living cell in the body contains thousands of different proteins essential to cellular structure, growth and function. The cell produces proteins according to a set of genetic instructions encoded by DNA molecules, which contains all the information necessary to control the cell s biological processes. DNA is

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organized into segments called genes, with each gene molecule containing the information required to produce one or more specific proteins. The production of a protein by a particular gene molecule is known as gene expression or activity. Many of the proteins inside a cell participate in a series of receptor interactions and chemical reactions to form what are known as molecular pathways that enable a cell to perform its various metabolic functions. The improper expression of proteins by one or more genes can alter these pathways and affect a cell s normal function, frequently resulting in disease. The interaction of therapeutic agents with proteins in these pathways is known as targeted therapy. Targeted therapies are believed to provide precision in their action that results in less potential for undesirable side effects.

In recent years, scientists have made significant progress toward understanding the nature of the complete set of human genes, referred to as the human genome, and in evaluating the role that genes and the proteins they express play in both normal and disease states. Academic and governmental initiatives have sequenced a large number of the genes that comprise the human genome. As new genes are discovered and decoded within this sequence, scientists are identifying and understanding their functions and interactions within these pathways. These discoveries provide opportunities to develop targeted therapeutic applications for individual genes and the proteins they express, including treatment and prevention of disease.

Delivery Systems

Targeted molecular therapies are often combined with a delivery system, referred to as a vector, which enables the therapeutic molecule to enter the target cell. The vector must be able to deliver a sufficient dose of the therapeutic molecule to cause a beneficial effect. Among the delivery systems currently in use are modified versions of viruses such as adenoviruses. Scientists often use viruses as delivery systems because viruses have the ability to efficiently infect cells and carry therapeutic molecules into the cells. Scientists can modify these viruses by deleting pieces of the viral genome that are necessary for viral reproduction and replacing the deleted pieces with a therapeutic molecule. The resulting viral vector retains the ability of the virus to efficiently deliver the therapeutic molecule into cells, while losing the ability to reproduce itself and spread to other cells.

While viruses are an efficient means of introducing therapeutic molecules into cells, scientists have also developed synthetic substances such as nanoparticles, which are nanoscale structures that have no viral components. These synthetic or nanoparticle systems can also deliver therapeutic molecules to host cells through systemic administration. Scientists have developed these systems to mimic the characteristics of viral vector systems in order to expand the disease targets that can be treated. We are using both viral and synthetic nanoparticle systems in our clinical trials to deliver therapeutic molecules.

An Overview of Cancer

Cancer is a leading cause of death in the United States. In the United States, approximately 1.4 million people are newly diagnosed with cancer and over 565,000 people die from the disease each year. Although the prevalence of specific cancers varies among different populations, we believe that the overall incidence of cancer worldwide is similar to that experienced in the United States. The National Institutes of Health (NIH) estimate the annual direct cost of treating cancer patients in the United States is approximately $74.0 billion.

Cancer is a group of diseases in which the body s normal self-regulatory mechanisms no longer control the growth of some kinds of cells. Cells are frequently exposed to a variety of agents, from both external and internal sources, which damage DNA. Even minor DNA damage can have profound effects, causing certain genes to become overactive, to undergo partial or complete inactivation, or to function abnormally. Genes control a number of protective pathways in cells that prevent cells from becoming cancerous. For example, pathways that transmit signals for a cell to divide have on-off switches that control cell division. Cells also have mechanisms that allow them to determine if their DNA has been damaged, and they have pathways to repair that damage or eliminate the cell.

The failure of any of these protective pathways can lead to the development of cancer. Cancer is one of the more suitable initial applications for targeted therapies because molecular targets that will lead to the

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destruction of the cancer cell are understood. The introduction of normal tumor suppressors, such as p53 and mda-7, into cancer cells leads to the destruction of those cancer cells and is a promising approach to treating cancer.

Tumor Suppressors

Tumor suppressors are one class of molecules that play a crucial role in preventing cancer and its spread. This class includes the p53, mda-7, BAK and FUS-1 tumor suppressors, among others.

The best known and most studied of the tumor suppressors is the p53 molecule. The p53 molecule is one of the most potent members of a group of naturally occurring tumor suppressors, which act to kill cancer cells, arrest cancer cell growth and protect cells from becoming cancerous. The p53 tumor suppressor is involved in multiple cellular processes, including control of cell division, DNA repair, cell differentiation, genome integrity, apoptosis, and inhibition of blood vessel growth, or anti-angiogenesis. Angiogenesis refers to the process by which new blood vessels are formed, such as those that supply blood and nutrients to tumors to feed their growth. The p53 tumor suppressor is capable of such wide-ranging effects because it orchestrates the activity of a host of genes and proteins. If a cell suffers DNA damage, p53 responds to the damage by initiating a cascade of protective processes to either repair the DNA damage or to destroy the damaged cell through apoptosis. These p53-mediated processes prevent damaged cells from multiplying and progressing towards cancer.

Current Treatment of Cancer

Conventional therapeutic approaches, including surgery, chemotherapy and radiation therapy, are ineffective or only partially effective in treating many types of cancer. Surgery is inadequate for many patients because the cancer is inaccessible or impossible to remove completely. Surgery, although applicable to over half of all cancer cases, is also inadequate where the cancer has spread, or metastasized. For certain cancers such as head and neck cancer, surgery can be an effective treatment of the cancer, but may result in severe disfigurement and disability for the patient. Radiation therapy and chemotherapy are, by their nature, toxic procedures that damage both normal and cancerous tissue. Physicians must carefully control administration of these therapies to avoid life-threatening side effects, and many patients are unable to withstand the most effective doses due to toxicity. These conventional therapies typically cause debilitating side effects such as bone marrow suppression, nausea, vomiting and hair loss, often requiring additional and costly medications to ameliorate such side effects. Further, the usefulness of certain chemotherapies may be limited in tumors that have developed mechanisms to evade the action of the drugs, a phenomenon known as multi-drug resistance.

Due to the various limitations of most cancer therapies currently utilized, the treatment of cancer remains complex. Physicians refer to the first treatment regimen for a newly-diagnosed cancer, usually surgery if possible, or radiation therapy, as primary treatment. If the primary treatment is not successful, the cancer will re-grow or continue to grow, which is referred to as recurrent disease. In most cases, recurrent cancer is not curable, with secondary treatment regimens, usually chemotherapy, only providing marginal benefits for a limited period of time. Physicians consider recurrent cancer that has proven resistant to a secondary treatment to be refractory. Most new cancer treatments are tested initially in patients with either recurrent or refractory disease because there are no standard therapies likely to provide them with clinical benefit.

Given that established cancer therapies often prove to be incomplete, ineffective or toxic to the patient, there is a need for additional new treatment modalities that either complement established therapies or replace them by offering better therapeutic outcomes. For example, in a limited number of cancers, immunotherapy, which seeks to stimulate a patient s own immune system to kill cancer cells, has rapidly become widely accepted by improving on the shortcomings of existing therapy. However, for a broad range of cancers, additional approaches, especially more specific ones that target specific dysfunctional pathways in the cancer cell, are needed to reduce the toxicity and improve upon marginal benefits common to current cancer treatments. Targeted molecular therapy applications are designed to address the cellular dysfunction that causes cancer, compared with small molecule drugs or immunotherapeutic agents, which may act indirectly.

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The Introgen Approach

Our primary approach for the treatment of cancers is to deliver targeted molecular therapies that increase production of normal cancer-fighting proteins. The resultant proteins engage disease-related molecular targets or receptors to produce specific therapeutic effects. We believe we are able to treat a number of cancers in a way that kills cancer cells without harming normal cells.

Because most cancers are amenable to local treatment and because local cancer treatments are administered far more often than systemic cancer treatments, our locally delivered product candidates, such as ADVEXIN therapy, deposit therapeutic molecules directly into a patient s cancerous tumor by hypodermic syringe. In those cases for which a systemic therapy may be indicated, we use a systemically administered nanoparticle formulation system to deliver tumor suppressors.

We initially focused on advanced cancers lacking effective treatments and in which local tumor growth control, where the tumor stops growing or shrinks, is likely to lead to measurable benefit. We have expanded our focus to include earlier stage cancers and pre-malignancies. We believe our clinical trials have shown that our therapies can be used alone and in combination with conventional treatments such as surgery, radiation therapy and chemotherapy.

The Introgen Strategy

Our objective is to be a leader in the development of targeted molecular tumor suppressor 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, INGN 225 and INGN 241 for Multiple Cancer Indications. We plan to continue our development programs to commercialize our ADVEXIN therapy using the p53 tumor suppressor and our INGN 241 product using the mda-7 tumor suppressor, also know as interleukin 24 (IL-24), in multiple cancer indications.

Develop Our Portfolio of Targeted Molecular Therapies and Other Drug Products. Utilizing our significant research, clinical, regulatory and manufacturing expertise, we are evaluating development of additional molecular therapies for various cancers, such as INGN 225, a highly specific cancer immunotherapy, INGN 234, an oral rinse or mouthwash formulation containing the p53 tumor suppressor, INGN 401, using the FUS-1 tumor suppressor, and INGN 007, a replication-competent viral therapy. 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 vector 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.

Develop a Nanoparticle Systemic Administration Platform. Early pre-clinical and clinical studies with these new nanoparticle drugs have demonstrated a good safety profile and promising anti-cancer activity. In addition to FUS-1, we incorporate the p53 tumor suppressor and the mda-7 tumor suppressor in these nanoparticle formulations.

Develop the Topical Use of Tumor Suppressors. We plan to continue developing topical product candidates for the treatment or prevention of oral and dermal cancers. We believe these treatments are a logical extension of our loco-regional delivery of cancer therapies and represent attractive product candidates since pre-malignant and malignant cells can be exposed to natural, biological tumor suppressors and DNA repairing agents.

Establish Targeted Sales and Marketing Capabilities. The oncology market can be effectively addressed by a small, focused sales force because it is characterized by a concentration of specialists in relatively few major cancer centers. We believe we can address this market by a combination of building a direct sales force as part of the ADVEXIN therapy commercialization process and pursuing

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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 molecular therapy and vector development to pursue targeted molecular 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.

Product Development Programs

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

Product**	**Cancer Indication**	**Development Status**
ADVEXIN Therapy (p53)	Head and Neck (both monotherapy and combined with chemotherapy)	Phase 3
	Non-Small Cell Lung(combined with radiation therapy)	Phase 2
	Breast (combined with chemotherapy)	Phase 1-2
	Perioperative (and surgery)	Phase 1-2
	Esophageal	Phase 1-2
	Prostate	Phase 1*
	Intravenous Administration	Phase 1*
	Ovarian	Phase 1*
	Bladder	Phase 1*
	Bronchoalveolar	Phase 1*
	Brain (glioblastoma)	Phase 1*
INGN 225 (p53 molecular immunotherapy)	Small Cell Lung	Phase 1-2
	Breast	Phase 1-2
INGN 234 (p53 topical)	Oral Cancer Prevention (mouthwash)	Phase 1-2*
INGN 241 (mda-7)	Head and Neck (combined with radiation therapy)	Phase 3
	Melanoma	Phase 1-2
	Other solid tumors	Phase 1-2
	Pancreatic	Pre-clinical
	Breast	Pre-clinical
INGN 401 (FUS-1 program)	Lung	Phase 1
INGN 402 nanoparticle formulation (p53)	Various cancers	Pre-clinical
INGN 403 nanoparticle formulation (mda-7)	Various cancers	Pre-clinical
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.

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ADVEXIN® Therapy (p53)

Our lead product candidate, ADVEXIN® therapy, combines the p53 tumor suppressor with a non-replicating, non-integrating adenoviral delivery system we have developed and extensively tested. The p53 molecule is one of the most potent members of a group of naturally-occurring tumor suppressors, which act to kill cancer cells, arrest cancer cell growth and protect cells from becoming cancerous.

ADVEXIN therapy for head and neck cancer has been designated an Orphan Drug under the Orphan Drug Act. This designation may give us up to seven years of marketing exclusivity for ADVEXIN therapy for this indication if approved by the FDA.

We have two ongoing Phase 3 clinical trials of ADVEXIN therapy in patients with recurrent squamous cell cancer of the head and neck. These trials involve administration of ADVEXIN therapy, both independently and in combination with chemotherapy, in recurrent squamous cell cancer of the head and neck.

We have received Fast Track designation for ADVEXIN therapy from the FDA under its protocol assessment program as a result of the FDA s agreement with the design of our two ongoing Phase 3 clinical trials of ADVEXIN therapy. Under this Fast Track designation, the FDA will take actions to expedite the evaluation and review of the BLA for ADVEXIN therapy. We plan to pursue with the FDA an Accelerated Approval of ADVEXIN therapy, which is one alternative provided under a Fast Track designation.

We have reviewed historically successful FDA registration strategies for numerous cancer drugs, noting that during the past seven years, approximately 14 cancer drugs were initially approved based upon submissions of Phase 2 clinical data. A number of the Phase 2 trials supporting these approvals employed single-arm studies involving relatively small patient populations. Virtually all of those drugs relied on surrogate endpoints for approval and a substantial number of the products were for orphan drug indications. Further, the approval in 2006 of Erbitux® for the treatment of head and neck cancer was based on a Phase 2, uncontrolled study in which 13% of the study patients met an endpoint of partial response.

We have conducted a series of meetings with the FDA to develop and implement the filing strategy for the BLA for ADVEXIN therapy, which is the application for approval to market and sell ADVEXIN therapy in the United States. As a result of these meetings, we are developing and pursuing an initial rolling BLA filing strategy based primarily on data from our Phase 2 clinical trials of ADVEXIN therapy for treatment of recurrent squamous cell cancer of the head and neck. The FDA has concurred that preliminary evaluation of this data suggests a level of efficacy consistent with the standard for the initiation of a rolling BLA (a submission process also known as Submission Of a Partial Application or SOPA). The FDA has also concluded that ADVEXIN therapy continues to show promise with respect to an unmet medical need since there are no approved biological therapies in the United States for recurrent head and neck cancer. The FDA has also concluded that the clinical development program for ADVEXIN therapy for recurrent head and neck cancer continues to meet the criteria for Fast Track designation. In conjunction with the new data, the new analyses, and other newly employed biological techniques, we are hopeful of more specifically targeting recurrent head and neck cancer in patients resulting in even better efficacy than has already been demonstrated.

Accordingly, we have submitted a SOPA Request to the FDA Division of Cell and Gene Therapy proposing a rolling BLA for ADVEXIN therapy for the treatment of recurrent head and neck cancer, based primarily on data from our Phase 2 clinical trials. We have further proposed to the FDA that, since the basis of the proposed rolling BLA is Phase 2 clinical data utilizing surrogate endpoints, the rolling BLA could be evaluated under the provisions of Subpart H for Accelerated Approval. In order to fully explore all of the review and approval possibilities for ADVEXIN therapy, the FDA has requested we submit existing new data and analyses from the Phase 2 ADVEXIN therapy clinical trials for recurrent head and neck cancer and consider conducting interim efficacy analyses on one or both of our ongoing Phase 3 trials. Given that we have two ongoing Phase 3 clinical trials in head and neck cancer as discussed further below, we and the FDA are evaluating the most effective use of the data from these Phase 2 and 3 clinical trials in the review and approval of ADVEXIN therapy. Regulatory approval approaches may allow Accelerated Approval on the basis of Phase 2 clinical data with subsequent confirmatory data being provided by the Phase 3 clinical studies or,

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alternatively, a full approval based on data from Phase 2 and certain Phase 3 clinical trials. We will also be exploring with the FDA whether its recently announced Critical Path Initiative, which permits new product evaluation on the basis of specifically targeted (i.e., by prognostic or biologic parameters) clinical trials and/or patient populations, can be used in the ADVEXIN therapy approval process.

We have proposed to the FDA an acceleration of the initiation of the planned interim safety analysis relative to one of our two ongoing Phase 3 clinical trials of ADVEXIN therapy in patients with recurrent squamous cell cancer of the head and neck. We had anticipated such analysis would have already begun, but the requisite number of survival events (i.e., patient deaths) has not occurred. We believe such safety information will be useful to the FDA as part of our ongoing BLA submission process. We also plan to avail ourselves of suggestions by the FDA that we consider proposing to them an interim efficacy analysis of one or both of the ongoing Phase 3 clinical trials. As with the acceleration of the interim safety analysis, we believe that the interim efficacy results from one or both Phase 3 studies will be useful to the FDA in its review of our BLA.

We have conducted 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. In the combined analysis of these 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 approximately 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. Subpopulations of patients participating in these trials had certain defining prognostic, medical and biological characteristics that represent refined targeting of ADVEXIN therapy. Analysis of the data from these patient subpopulations showed objective response rates of up to 29%. These findings, along with other data, are planned for presentation at future scientific meetings and for future publication in a peer-reviewed medical journal.

We performed a Phase 2 clinical trial of ADVEXIN therapy combined with neoadjuvant chemotherapy and surgery in women with locally advanced breast cancer. After at least 35 months of follow-up, 92% of the treated patients were alive and 83% had survived without evidence of disease recurrence. Objective clinical responses were seen following the combined therapy in all of the patients with a median of 80% reduction in tumor size. Following tumor shrinkage, complete tumor removal by subsequent surgery was achieved in 100% of the patients. The results of the therapy with the addition of ADVEXIN are better than what would be expected from neoadjuvant chemotherapy treatment alone. Neoadjuvant treatments are administered prior to surgery and represent a novel and increasingly applied approach to making surgical tumor resections less invasive, improving outcomes and facilitating breast conservation. These data were announced during the 2005 San Antonio Breast Cancer Symposium.

We completed a Phase 2 clinical trial of ADVEXIN therapy administered as a complement to radiation therapy in non-small cell lung cancer. In the 19 patients who participated in the trial, combined ADVEXIN and radiation treatment resulted in 63% biopsy-proven complete responses at three months, which is approximately four times the expected rate using radiotherapy alone. The results of this study were published in *Clinical Cancer Research.*

We performed a Phase 1/early Phase 2 clinical trial of ADVEXIN therapy for the treatment of advanced, unresectable, squamous cell esophageal cancer. Results of this trial in patients with esophageal cancer refractory to chemotherapy and radiation indicate three of the ten patients treated, or 30%, had negative biopsies after receiving ADVEXIN therapy. The median survival of the patients treated with ADVEXIN therapy was approximately twelve months, which compared favorably to historical controls in which a median survival of less than ten months was observed for patients who did not respond to standard treatments. Six patients, or 60%, were still alive one year after beginning ADVEXIN therapy. This clinical trial was performed at Chiba University in Japan.

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We are currently conducting additional Phase 1/2 clinical trials of ADVEXIN therapy by itself and in combination with chemotherapy or radiation therapy in a variety of cancers. These additional clinical trials include:

A Phase 2 clinical trial of ADVEXIN therapy in squamous cell carcinoma of the oral cavity, or oropharynx, that can be removed surgically, to assess the feasibility, efficacy and safety of administering ADVEXIN therapy at the time of surgery for suppression of remaining tumor cells, followed by a combination of chemotherapy and radiation therapy.

A Phase 1/early Phase 2 clinical trial in which a mouthwash or oral rinse formulation of ADVEXIN therapy, which has been designated as INGN 234, is administered to prevent precancerous oral lesions from developing into cancerous lesions.

We have completed other clinical trials of Advexin, including Phase 1 studies in prostate cancer and bronchoalveolar carcinoma. 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. Findings from several of our clinical trials have been published in *Clinical Cancer Research* and *Proceedings of the American Society for Clinical Oncology* as well as presented at numerous conferences, including the San Antonio Breast Cancer Conference and various meetings of the American Society of Clinical Oncology, the American Association for Cancer Research and the American Society of Gene Therapy.

A growing body of data suggests ADVEXIN therapy demonstrates clinical activity in a variety of cancer indications. Safety data from our clinical trials suggest this activity may be achieved without the treatment-limiting side effects frequently associated with many other cancer therapies.

Our clinical trials indicate ADVEXIN therapy is well tolerated as a monotherapy. The addition of ADVEXIN therapy to standard chemotherapy, surgery or radiation does not appear to increase the frequency or severity of side effects normally associated with these treatment regimens.

Recent studies provide new insight into the molecular pathways by which the p53 tumor suppressor, the active component of ADVEXIN therapy, kills tumor cells. These studies were undertaken to provide additional molecular data supporting the activity observed during the clinical development of ADVEXIN therapy and to provide additional information regarding the specific pathways that mediate the observed clinical effects of ADVEXIN therapy. The studies were conducted by our collaborators at Okayama University in Japan and at The University of Texas M. D. Anderson Cancer Center and were published in *Molecular Cancer Therapeutics*. Other data suggest the enhanced therapeutic effects of a combination of ADVEXIN and Erbitux therapies in an animal model of human non-small cell lung cancer. Other pre-clinical studies conducted by our collaborators at Wayne State University, the Karmanos Cancer Institute located in Detroit, Michigan and the University of California-Irvine, as published in *The Laryngoscope,* show that the combination of ADVEXIN therapy and docetaxel resulted in increased levels of programmed cell death in head and neck tumor cells. Two lung cancer patients, who were part of our ADVEXIN therapy studies program and who had recently celebrated their five-year survival anniversary, were featured in *Conquest* magazine, a publication of M. D. Anderson Cancer Center. In addition, a patient with recurrent head and neck cancer who achieved a complete tumor remission on ADVEXIN therapy continues to be disease-free over seven years later while receiving repeated ADVEXIN treatments.

We hold the worldwide rights for pre-clinical and clinical development, manufacturing, marketing and commercialization of ADVEXIN therapy.

INGN 241 (mda-7)

INGN 241 uses mda-7, a promising tumor suppressor, 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 tumor suppressor with our adenoviral delivery system to form INGN 241. Our pre-clinical trials have shown 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 the growth of normal cells. Because INGN 241

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kills cancer cells even if other tumor suppressors, including p53, are not functioning properly, it appears 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, the protein produced by mda-7 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 tumor suppressor may act as a cytokine, or immune system modulator, it is also known as interleukin 24, or IL-24. The mda-7 molecule may also work as a radiation sensitizer to make several types of human cancer cells more susceptible to radiation therapy. We have seen evidence of this effect in our pre-clinical work.

We have identified the molecular pathways by which mda-7, the active component of INGN 241, induces growth arrest and programmed cell death or apoptosis in cancer cells. Pre-clinical studies using lung cancer cells have demonstrated the mda-7 protein binds to a critical cellular enzyme known as PKR. The binding of mda-7 to PKR is essential for the anti-cancer activity of INGN 241. The identification of this binding partner demonstrates a significant advancement in understanding how this therapeutic can be effective against cancer. Additional studies have identified bystander killing of pancreatic cancer cells by the mda-7 protein. Bystander killing involves the killing of neighboring tumor cells by the mda-7 protein released from adjacent INGN 241-treated tumor cells.

Pre-clinical data indicate INGN 241 works synergistically with celecoxib, marketed by Pfizer as Celebrex®, to inhibit the growth and increase killing of breast cancer cells. These data demonstrate the potential utility of INGN 241 in combination with celecoxib, a drug approved for treatment of precancerous lesions of the colon as well as arthritis. The combination of celecoxib and INGN 241 showed greater than additive increases in cell death compared with either therapy alone and also resulted in the suppression of tumor cell growth.

In pre-clinical studies, we have observed the expression of mda-7 in ovarian cancer cells potently activates a cell death or apoptotic pathway regulated by the Fas signaling system. This activation resulted in significant increases in apoptosis and inhibition of cancer cell proliferation that were specific to cancer cells. These effects were not observed in normal ovarian tissue, supporting previous data showing a cancer-selective effect of INGN 241.

We have published the results of a pre-clinical study indicating INGN 241 may suppress the growth *in vivo* of non-small cell lung cancer through apoptosis in combination with anti-angiogenesis. The data demonstrate INGN 241 can inhibit production of the VEGF protein, a potent inducer of angiogenesis, within lung cancer cells, which in turn inhibits tumor angiogenesis, a key requirement for tumor growth.

Pre-clinical work has demonstrated administration of INGN 241 results in the development of systemic immune responses against tumor cells and suggests INGN 241 could be used as a novel cancer molecular immunotherapy. In pre-clinical studies, implantation of INGN 241-treated tumor cells into mice resulted in significant inhibition of tumor growth. Significantly, mice immunized with INGN 241-treated cells showed inhibition of tumor growth after a subsequent challenge with additional tumor cells.

We have conducted pre-clinical studies with INGN 241 in breast cancer cell lines as a single agent, as well as in combination with radiation therapy, with chemotherapy (Taxotere or Adriamycin), with the hormone inhibitor Tamoxifen and with Herceptin, a biologic cancer therapy. In all settings, INGN 241 reduced cell growth and increased programmed tumor cell death (apoptosis). This effect was enhanced when combined with drugs currently used to treat breast cancer. In animal models of breast cancer, treatment with INGN 241 alone or in combination with radiation therapy resulted in significant decreases in tumor growth. In particular, our pre-clinical studies have shown treatment with a combination of INGN 241 plus Herceptin induces cell death in Her-2/neu positive breast cancer cells at a rate greater than that seen with either agent alone. In these studies, it was also noted while Herceptin exhibited no activity on Her-2/neu negative cells, INGN 241 did induce cell death in these cells.

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Pre-clinical studies indicate the mda-7 protein released from cells treated with INGN 241 can kill nearby, untreated breast cancer cells resulting in additional therapeutic effect. This bystander effect occurs when the therapeutic protein binds to certain receptors on nearby cancer cells. We believe this bystander effect is significant because it could indicate the number of cancer cells INGN 241 can kill is greater than the number of cells that take up this novel investigational cancer therapy.

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 have initiated later stage clinical trials using INGN 241 in patients with metastatic melanoma and head and neck cancer.

Data from our Phase 1 trial of INGN 241 in patients with solid tumors demonstrate that direct injection of INGN 241 induced programmed cell death in 100% of the tumors treated, even in patients who had failed prior therapy with other anti-cancer drugs. Clinical responses were observed in 44% of the treated lesions, including complete and partial responses (greater than or equal to 50% reduction in tumor size) in two patients with melanoma. Patients treated with INGN 241 had increases in a subset of T-cells that help to destroy cancer cells, which is consistent with the role of the mda-7 protein as a member of the interleukin family of immune stimulating proteins.

Findings and results arising from our development of INGN 241 have been published in the *Journal of Leukocyte Biology, Cancer Gene Therapy, Cancer Research, Molecular Therapy, Oncogene, Surgery,* and *International Immunopharmacolgy*. Data from this work have also been presented at the annual San Antonio Breast Cancer Symposium.

We have an exclusive license to the mda-7 tumor suppressor for our therapeutic applications originally from Corixa Corporation (Corixa), which was acquired by GlaxoSmithKline. Pre-clinical studies regarding the active component of INGN 241 have included research at The University of Texas M. D. Anderson Cancer Center and Columbia University.

INGN 225 (p53 molecular immunotherapy)

We are developing INGN 225 using the p53 tumor suppressor in a different manner to create a molecular immunotherapy for cancer that stimulates a particular type of immune system cell known as a dendritic cell. Research published in *Current Opinion in Drug Discovery & Development* concluded that the p53 tumor suppressor 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 the p53 tumor suppressor, which suggests a molecular immunotherapy consisting of dendritic cells stimulated by p53 could have broad utility as a treatment for progression of solid tumors.

We are conducting a Phase 1/2 clinical trial in collaboration with the Moffitt Cancer Center at the University of South Florida in patients with small cell lung cancer. We are also conducting a Phase 1/2 trial in patients with breast cancer in collaboration with the University of Nebraska. In both trials, INGN 225 is administered after the patients have been treated with standard chemotherapy.

Interim results from the Phase 1/2 trial in patients with extensive small cell lung cancer who were previously treated with chemotherapy indicate that greater than 60% of the evaluable patients in the study treated with INGN 225 had objective responses to subsequent chemotherapy. Historically, the expected objective response rate in similar patients to further chemotherapy is between approximately 5% and 30%. Similar patients with this type of lung cancer have a grave prognosis with a median survival of approximately six months, but treated patients in this study who developed an immune response to p53 had a median survival of approximately twelve months. These findings were published in *Clinical Cancer Research.*

We believe the data indicate INGN 225 may sensitize tumors to the effects of platinum and taxane chemotherapies. Of particular interest, patients with highly aggressive disease (termed platinum resistant) showed improved response rates and increased survival compared to historical controls. These findings are

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consistent with the results observed in lung and breast cancer patients treated with ADVEXIN therapy that increased the expected effects of cisplatin, taxane and doxorubicin chemotherapies. As platinum, taxanes and doxorubicin are among the most common types of cancer chemotherapies, these findings may have important implications for improving the efficacy of these widely utilized cancer treatments.

INGN 234 (p53 topical)

We are developing INGN 234 for the prevention of oral cancers and the treatment of oral leukoplakia. We are conducting a Phase 1/early Phase 2 clinical trial in which p53 is being administered in an oral mouthwash formulation to prevent precancerous oral lesions from developing into cancerous lesions. We are conducting pre-clinical work on other topical administrations of tumor suppressors to control or prevent oral or dermal cancers. We are investigating multiple delivery platforms, including both viral and non-viral approaches. We are also investigating combining delivery of our therapies with rinses, patches, ointments and enhancing polymers. We believe the opportunity exists to develop non-toxic treatments for pre-malignant and malignant cells that can be easily exposed to natural biological tumor suppressor and DNA repairing molecules.

We have entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. See Item 1. Business Business and Collaborative Arrangements Alliance with Colgate-Palmolive Company below for further discussion of this alliance agreement.

INGN 401 (FUS-1)

INGN 401 uses a nanoparticle vector system to deliver the tumor suppressor FUS-1, which we exclusively license from M. D. Anderson Cancer Center. Pre-clinical studies have shown that FUS-1, delivered using an adenoviral or a non-viral delivery system through either intravenous (systemic) administration or direct intratumoral injection, significantly inhibits the growth of tumors and greatly reduces the metastatic spread of lung cancer in animals.

Pre-clinical data suggest that INGN 401 may have utility as a monotherapy in lung cancer. We have observed significant inhibition of tumor growth in lung cancer animal models following INGN 401 monotherapy treatment when compared with untreated animals.

INGN 401 has demonstrated synergistic activity with Gefitinib, a novel class of anti-cancer agents that decrease tumor growth by inhibiting growth factor receptors that promote tumor proliferation. While Gefitinib can produce dramatic responses in a small subset of lung cancer patients, most lung cancers are refractory to its effects. The data indicate nanoparticle delivery of INGN 401 can synergize with Gefitinib in killing lung tumor cells resistant to Gefitinib alone. Furthermore, in Gefitinib-sensitive tumors, INGN 401 delivery significantly enhanced anti-cancer activity.

A Phase 1/early Phase 2 clinical trial is ongoing at M. D. Anderson Cancer Center testing INGN 401 in patients with advanced non-small cell lung cancer who have previously been treated with chemotherapy. Data and findings from our work to develop INGN 401 have been published in *Cancer Gene Therapy* and *Cancer Research.*

INGN 402 and INGN 403 (nanoparticle formulations of p53 and mda-7, respectively)

We are developing two nanoparticle formulations for systemic delivery. INGN 402 contains the p53 tumor suppressor and INGN 403 contains the mda-7 tumor suppressor, also known as interleukin 24 (IL-24). Early studies with these new nanoparticle drug candidates have demonstrated a good safety profile and promising anti-cancer activity in murine lung tumor models. Data from the mda-7 nanoparticle studies was published in *DNA and Cell Biology.*

INGN 007 (replication-competent viral therapy)

We are developing INGN 007, a replication-competent viral therapy in which viruses bind directly to cancer cells, replicate in those cells, and cause those cancer cells to die. Pre-clinical testing in animal models

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indicates INGN 007 over-expresses a molecule that allows the vector to saturate the entire tumor. This testing has demonstrated that INGN 007 has a favorable safety profile and significantly inhibits tumor growth. Findings from this work to develop INGN 007 have been published in *Cancer Research* and were presented at a meeting of the American Society of Clinical Oncology. We are developing this replication-competent viral therapy through our strategic collaboration with VirRx, Inc. (VirRx).

Other Research and Development Programs

We are conducting a number of pre-clinical and research programs involving a variety of targeted therapies for the treatment of cancer. These programs involve molecules that act through diverse mechanisms to inhibit the growth of or kill cancer cells.

We licensed from M. D. Anderson Cancer Center a group of molecules known as the 3p21.3 family. Pre-clinical research performed on these molecules by collaborators at The University of Texas Southwestern Medical Center and M. D. Anderson Cancer Center suggests that the 3p21.3 family plays a critical role in the suppression of tumor growth in lung and other cancers. This family of molecules includes the FUS-1 tumor suppressor we are testing as INGN 401. We are working with M. D. Anderson Cancer Center to further evaluate other 3p21.3 family molecules as clinically relevant therapeutics.

We are evaluating additional molecules, including BAK, which hold promise as therapeutic candidates. BAK is a pro-apoptotic molecule that kills cancer cells. We are working with our collaborators at M. D. Anderson Cancer Center to identify and develop both viral and non-viral vectors containing this therapeutic molecule. We had exclusive rights to use the BAK molecule under a license with LXR Biotechnology, Inc. (LXR), the rights of which were subsequently sold to Tanox, Inc (Tanox).

We are evaluating the development of mebendazole, our first small molecule candidate, which we refer to as INGN 601, for treatment of cancer and other hyperproliferative diseases. The use of the mebendazole compound is approved by the FDA for the oral treatment of parasitic diseases. Pre-clinical work suggests that mebendazole may also be an effective treatment for cancer. The results of pre-clinical investigations involving mebendazole and lung cancer were published in *Clinical Cancer Research* and *Molecular Cancer Therapeutics.*

We believe our research and development expertise gained from our molecular therapies for cancer is also applicable to other diseases that, like cancer, result from cellular dysfunction and uncontrolled cell growth. As a result, we are conducting research in collaboration with medical institutions to understand the safety and effectiveness of our molecular therapy product candidates in the treatment of other diseases.

Introgen Enabling Technologies

We have a portfolio of technologies, referred to as enabling technologies, for administering targeted molecular products to patients and for enhancing the effects of these products, which we plan to exploit to develop additional products to treat cancer and other diseases which, like cancer, result from cellular dysfunction and uncontrolled cell growth.

Nanoscale Viral Delivery Systems

We have demonstrated that ADVEXIN therapy and INGN 241, which use our adenoviral vector system, enter tumor cells and express their proteins despite the body s natural immune response to the adenoviral vector. While the adenoviral vector system used appears to be appropriate for the treatment of cancer by local administration, we have developed a number of additional systems that utilize modified adenoviral vectors for delivery. These systems also may be applicable to indications where activity of the therapeutic molecule for disease treatment is required for longer periods of time or where systemic administration may be necessary.

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Nanoparticle Systemic Delivery Platform

We have in-licensed and are developing a non-viral, nanoparticle delivery platform as a complementary delivery technology for certain types of cancers, or clinical indications, particularly those that require systemic administration. We are currently using this technology in INGN 401, INGN 402 and INGN 403.

Data published in *DNA and Cell Biology* highlight the potential utility of combining our nanoparticle delivery system with the mda-7 tumor suppressor for the treatment of lung cancer. The data reported in this publication demonstrate that combining this innovative delivery system with the mda-7 tumor suppressor results in potent anti-cancer effects and systemic tumor growth inhibition in an animal model of lung cancer. We believe combining potent anti-cancer tumor suppressors, such as mda-7 or p53, with our nanoparticle delivery system could allow development of clinical strategies to attack metastatic cancers.

Replication-Competent Viral Delivery Systems

Through our strategic collaboration with VirRx, we are developing replication-competent viral therapies in which viruses bind directly to cancer cells, replicate in those cells, and cause those cancer cells to die. This technology forms the basis for our INGN 007 product development. We anticipate pursuing clinical confirmation as to whether this self-amplifying delivery system can complement our existing adenoviral delivery system, which is replication disabled, in selected therapeutic scenarios, in applications beyond INGN 007.

Additional Enabling Technologies

Our research and licensing activities include a number of additional technologies that expand our capabilities. These activities include the following:

Multi-Molecule Vector System. This technology is designed to combine multiple therapeutic molecules with a vector. This approach has the potential for use with both viral and non-viral delivery systems to allow the activity of more than one molecular therapy at a time for disease treatment.

Pro-Apoptotic Molecule Delivery System. This technology is designed to allow the activity of pro-apoptotic, or apoptosis-inducing, molecules during treatment only, while temporarily suppressing the ability of the apoptotic molecule to kill producer cells during production. This system could facilitate higher volume production of pro-apoptotic agents.

Tissue-Specific Targeting Systems. This technology is designed to promote the activity of the therapeutic molecule in only those cells which have been affected by the disease being targeted. It is intended to be applied to both viral and non-viral vectors.

Manufacturing and Process Development

Commercialization of a targeted molecular therapy product requires process methodologies, formulations and quality release assays in order to produce high quality materials at a large scale. We believe the expertise we have developed in the areas of manufacturing and process development represents a competitive advantage. We have developed scale-up methodologies for both upstream and downstream production processes, formulations that are safe and stable, and product release assays that support product quality control.

We own and operate state-of-the-art manufacturing facilities, including a commercial-scale, validated manufacturing facility designed to comply with the FDA s Current Good Manufacturing Practice requirements, commonly known as CGMP requirements. We have produced numerous batches of ADVEXIN therapy clinical material for use in our Phase 1, 2 and 3 clinical trials. The design and processes of the facility used for ADVEXIN therapy production have been reviewed with the FDA. We plan to use our facilities for the market launch of ADVEXIN therapy. We also use our facilities to produce INGN 241 and other investigative materials for use in clinical trials of those product candidates. From time to time, as requirements

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for our own products allow, we also manufacture pre-clinical and clinical materials for outside parties for a fee under contract services arrangements.

Business and Collaborative Arrangements

Alliance with Colgate-Palmolive Company

In November 2005, we entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. In connection with the alliance agreement and pursuant to a common stock purchase agreement, Colgate-Palmolive purchased 3,610,760 shares of our common stock at a purchase price of $5.539 per share for a total of approximately $20.0 million. These shares are subject to trading and transfer restrictions for one year from the date of purchase. Under the common stock purchase agreement, Colgate-Palmolive also agreed to vote these shares and any other shares of our capital stock owned by it in favor of corporate actions approved by our Board of Directors. This voting agreement is subject to suspension or termination upon certain events specified in the common stock purchase agreement.

Pursuant to the alliance agreement, we will conduct research and development activities involving specialized formulations of our molecular therapies (such as p53, mda-7 and FUS-1) targeted at precancerous conditions of the oral cavity and at oral cancer. The objective is to market these formulations as oral healthcare products. Excluded from the alliance agreement is our current portfolio of cancer product candidates, including ADVEXIN therapy, INGN 241, INGN 225 and INGN 401.

Under the alliance agreement, Colgate-Palmolive has a first right to negotiate development, manufacturing, marketing and distribution rights with us for specifically designed oral healthcare products for use in the human oral cavity that may result from these research and development activities. In addition, we agreed to use commercially reasonable efforts to develop one or more specialized oral formulations through completion of Phase 2 clinical trials within the seven-year term of the alliance agreement. We can terminate our development efforts earlier under certain circumstances, including if the prospects for these products do not warrant further investment, or if we expend $15.0 million in this effort. In calculating the amount of our expenditures on these efforts, we may include grant funding received by us or our collaborators for work performed by third parties (e.g., universities and other institutions) that is directly related to program activities, as specified in the alliance agreement. The term of the alliance agreement continues to November 2012, unless earlier terminated by the parties as provided in the alliance agreement.

VirRx, Inc.

We are working with VirRx to investigate other vector technologies, specifically replication-competent viral therapies, for delivering products into targeted cells. These technologies form the basis for our INGN 007 product candidate.

We have an agreement with VirRx, which began in 2002, to purchase shares of VirRx s Series A Preferred Stock. From inception of this agreement through December 31, 2005, we have purchased $2,325,000 of this stock for cash, of which we purchased $600,000 per year in 2005, 2004 and 2003. These purchases are recorded as research and development expense. We have agreed to purchase an additional $150,000 of this stock on January 1, 2006, after which time we have no further obligation to make such purchases.

VirRx is required to use the proceeds from these stock sales in accordance with the terms of a collaboration and license agreement between VirRx and us for the development of VirRx s technologies. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice, which would also terminate the requirement for us to make any additional stock purchases.

Provided the collaboration and license agreement remains in place, we are required to make additional milestone stock purchases, either for cash or through the issuance of our common stock, upon the completion of Phase 1, 2 and 3 clinical trials involving technologies licensed under this agreement. We are required to make a $5.0 million cash milestone payment to VirRx, for which we receive no VirRx stock, upon approval by the FDA of a BLA for the first collaboration product based on these technologies. To the extent we have

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already made cash milestone payments, we may receive a credit of 50% of the Phase 2 clinical trial milestone payments and 25% of the Phase 3 clinical trial milestone payments against this $5.0 million cash milestone payment. The additional milestone stock purchases and cash payment are not anticipated to be required in the near future. We have an option to purchase all outstanding shares of VirRx at any time until March 2007.

SR Pharma plc

In July 2005, we purchased approximately 8.3% of the issued share capital of SR Pharma plc (SR Pharma) for approximately $3.0 million. As of December 31, 2005, the shares we purchased had a fair market value of $2.9 million. SR Pharma is a European biotechnology company publicly traded on the Alternative Investment Market of the London Stock Exchange (LSE) that is developing oncology and other products.

Academic and Other Collaborations

Academic collaboration agreements have been a cost-effective way of expanding our intellectual property portfolio, generating data necessary for regulatory submissions, accessing industry expertise and finding new technology in-license candidates, all without building a large internal scientific and administrative infrastructure.

The University of Texas M. D. Anderson Cancer Center

Many of our core technologies were developed by scientists at The University of Texas M. D. Anderson Cancer Center in Houston, Texas, one of the largest academic cancer centers in the world. We sponsor research conducted at M. D. Anderson Cancer Center to further the development of technologies that have potential commercial viability. Through these sponsored research agreements, we have access to M. D. Anderson Cancer Center s resources and expertise for the development of our technology. In addition, we have the right to include certain patentable inventions arising from these sponsored research agreements under our exclusive license with M. D. Anderson Cancer Center.

We entered into a license agreement with The Board of Regents of the University of Texas System and M. D. Anderson Cancer Center in 1994. The license agreement terminates on July 20, 2009 (if no patent rights are applicable) or upon the last to expire of the relevant patents. The agreement is also terminable upon our insolvency, either party s breach or upon our notice on a patent-by-patent basis. The technologies we have licensed from M. D. Anderson Cancer Center under the exclusive license agreement relate to multiple technologies. Under the agreement, we have agreed to pay M. D. Anderson Cancer Center royalties on sales of products utilizing these technologies. We are obligated to reimburse any of M. D. Anderson Cancer Center s costs that may be incurred in connection with obtaining patents related to the licensed technologies. Our strategy for product development is designed to take advantage of the significant multidisciplinary resources available at M. D. Anderson Cancer Center. These efforts have resulted in our becoming a significant corporate sponsor of activities at M. D. Anderson Cancer Center in recent years and have yielded to us exclusive patent and licensing rights to numerous technologies.

National Cancer Institute

We have a cooperative research and development agreement, or CRADA, with the National Cancer Institute (NCI). The CRADA has a flexible duration, but is terminable upon the mutual consent of the parties or upon 30 days notice of either party. Under the CRADA, NCI agreed to sponsor and conduct pre-clinical and human clinical trials to evaluate the effectiveness and potential superiority to other treatments of ADVEXIN therapy against a range of designated cancers, including breast cancer, ovarian cancer, bladder cancer and brain cancer. To date, NCI has conducted or is conducting numerous Phase 1 clinical trials for ADVEXIN therapy. NCI provided most of the funding for these activities. We supplied NCI with ADVEXIN therapy product to be administered in these trials. We have exclusive rights to all pre-clinical and clinical data accumulated under the CRADA.

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Research and License Agreement for the mda-7 Tumor Suppressor

We have a research and license agreement with Corixa, pursuant to which we acquired an exclusive, worldwide license to the mda-7 tumor suppressor for the therapeutic applications we are pursuing. This agreement was originally with Corixa, which subsequently was acquired by GlaxoSmithKline. The agreement is effective until the last to expire of the subject patents. It is terminable upon the breach or insolvency of either party, or upon our notice on a patent-by-patent or product-by-product basis. Under the agreement, we paid Corixa an initial license fee and have agreed to make additional payments upon the achievement of development milestones, as well as royalty payments on product sales. We also made research payments to Corixa in connection with research it performed involving the mda-7 tumor suppressor. Corixa originally licensed the mda-7 tumor suppressor from Columbia University.

The University of South Florida and the Moffitt Cancer Center

We are collaborating with the H. Lee Moffitt Cancer Center and Research Institute to advance our INGN 225 molecular cancer immunotherapy program. Moffitt Cancer Center has conducted pre-clinical research with us, and they are currently treating patients in the ongoing INGN 225 clinical study. We are designing additional studies in collaboration with Moffitt Cancer Center personnel to continue clinical research in the dendritic cell molecular immunotherapy field.

Research and Development Expense

Our research and development expense was $21.4 million, $20.5 million and $15.0 million for the years ended December 31, 2005, 2004 and 2003, respectively.

Marketing and Sales

We are focusing our current product development and commercialization efforts on the oncology market. This market is characterized by its concentration of specialists in relatively few major cancer centers, which we believe can be effectively addressed by a small, focused sales force. As regulatory approval of one or more of our product candidates for commercial sale approaches, we will address the methods of sales and marketing available to us. We will continue to evaluate the merits of building our own direct sales force, pursuing marketing and distribution arrangements with corporate partners or some combination of both.

Patents and Intellectual Property

Our Portfolio

Our success will depend in part on our ability to develop and maintain proprietary aspects of our technology. To this end, we have an intellectual property program directed at developing proprietary rights in technology that we believe may be important to our success. We also rely on a licensing program to ensure continued strong technology development and technology transfer from companies and research institutions with whom we work. We have entered into a number of exclusive license agreements or options with companies and institutions, including M. D. Anderson Cancer Center, Sidney Kimmel Cancer Center, Corixa, which was acquired by GlaxoSmithKline, Aventis Pharmaceutical Products, Inc. (Aventis), which is now Sanofi-Aventis, Columbia University, VirRx and LXR, with the LXR rights being subsequently sold to Tanox. In addition to patents, we rely on trade secrets and proprietary know-how, which we seek to protect, in part, through confidentiality and proprietary information agreements.

We currently own or have an exclusive license to a large number of issued and pending United States and foreign patents and patent applications. If we do not seek a patent term extension, the currently issued United States patents that we own or have exclusively licensed will expire between the years 2010 and 2017. The exclusive licenses that give us rights on the patents, and applications that such licenses cover, will expire no earlier than the life of any patent covered under the license.

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Adenoviral p53 Compositions and Therapies

In developing our patent portfolio, we have focused our efforts in part on seeking protection for our potential products and how they will be used in the clinical trials. Arising out of our work with M. D. Anderson Cancer Center, we currently have an exclusive license to a number of United States and corresponding international patent applications directed to adenoviruses that contain p53, referred to as adenoviral p53, adenoviral p53 pharmaceutical compositions and the use of adenoviral p53 compositions in various cancer therapies and protocols. One of these applications, directed to the clinical use of adenoviral p53 to treat cancer, has issued as a United States patent. Additionally, various other United States patents have issued to which we have licensed exclusive rights, which are directed to adenoviral p53 compositions in general, adenoviral p53 pharmaceutical compositions, therapeutic applications of adenoviral p53, as well as a patent covering the DNA core of adenoviral p53. We have also exclusively licensed from Aventis a patent application directed to adenoviral p53 and its clinical applications. We also have an exclusive license to a United States patent application and corresponding international applications directed to the use of the p53 tumor suppressor in the treatment of cancer patients whose tumors express a normal p53 protein.

Combination Therapy with the p53 Tumor Suppressor

Our portfolio development includes seeking protection for clinical therapeutic strategies that combine the use of the p53 tumor suppressor with traditional cancer therapies. In this regard, also arising out of our work with M. D. Anderson Cancer Center, we have an exclusive license to two issued United States patents with corresponding international applications directed to cancer therapy using the p53 tumor suppressor in combination with DNA-damaging agents such as conventional chemotherapy or radiotherapy. This patent and corresponding international applications concern the therapeutic application of the p53 tumor suppressor before, during or after chemotherapy or radiotherapy. We have also exclusively licensed from Aventis a United States patent and corresponding international applications directed to therapy using the p53 tumor suppressor together with taxanes such as Taxol® or Taxotere®. Furthermore, we have exclusively licensed a United States patent application and corresponding international applications directed to the use of the p53 tumor suppressor in combination with surgical intervention in cancer therapy.

Adenovirus Production, Purification and Formulation

Another focus of our research has involved the development of procedures for the commercial-scale production of our potential adenoviral-based products, including that of ADVEXIN therapy. In this regard, we own three issued United States patents as well as a number of pending United States applications and corresponding international applications directed to highly purified adenoviral compositions, commercial-scale processes for producing adenoviral -based compositions having a high level of purity, as well as to storage-stable formulations. These applications include procedures for preparing commercial quantities of recombinant adenovirus products and include procedures applicable to the p53 tumor suppressor, as well as any of our other potential products. We have also licensed from Aventis a United States application and corresponding international applications directed to processes for the production of purified adenoviruses, which are useful for our product applications. With respect to storage-stable formulations, we were issued a United States patent directed to compositions and methods concerning improved, storage-stable adenovirus formulations. This patent is not limited to our ADVEXIN product candidate and may eventually replace formulations currently in use.

Other Tumor Suppressors

We either own or have exclusively licensed rights in a number of other patents and applications directed to the clinical application of various tumor suppressors other than p53, including the mda-7, BAK, the 3p21.3 family (FUS-1) and anti-sense K-ras. We have exclusively licensed or optioned rights in a number of issued United States patents covering the use of the mda-7, BAK and PTEN tumor suppressors.

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Other Therapeutic, Composition and Process Technologies

We own or have exclusively licensed a number of United States and international patent applications on a range of additional technologies. These include various applications and patents relating to p53, combination therapy with 2-methoxyestradiol, anti-proliferative factor technologies, retroviral delivery systems, stimulation of anti-p53, screening and product assurance technologies, as well as second-generation p53 molecules. We have exclusively licensed a number of United States and international applications directed to various improved vector applications employing more than one molecular therapy for disease treatment, as well as applications directed to the delivery of molecular therapies for disease treatment without the use of a vector, or non-viral therapy. For example, a United States patent, exclusively licensed to us, was recently issued that is directed to adenoviruses that exhibit tissue specific replication. We also have exclusive rights in an issued United States patent and corresponding international applications directed to a low toxicity analogue of IL-2, also called F42K.

Benzimidazole Small Molecule Cancer Therapy Program

We also have exclusively licensed a United States and a corresponding international patent application directed to the use of a family of known anti-helminthic benzimidazole molecules, most notably mebendazole, in the treatment of cancer. These applications are directed generally to the use of small molecules of the benzimidazole family to induce apoptosis in cancers, as well as to treat cancer patients, particularly those having p53-related cancers. Both of these therapeutic actions are based on the discovery by our scientists and their collaborators that members of the benzimidazole family will actively induce apoptosis in cancer cells, particularly in conjunction with the action of an endogenous or exogenously added p53 tumor suppressor.

Trade Secrets

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

Government Regulation

The Drug Approval Process

Prescription pharmaceutical products and biologics are subject to extensive pre- and post- marketing regulation by the FDA, including regulations that govern the testing, manufacturing, safety, efficacy, labeling, storage, recordkeeping, advertising and promotion of the products under the Federal Food, Drug, and Cosmetics Act (FDC Act) and the Public Health Services Act, and by comparable regulatory agencies in most foreign countries. The process required by the FDA before a new drug or biologic may be marketed in the United States generally involves:

Completion of preclinical laboratory and animal testing;

Submission of an investigational new drug application, or IND, which must become effective before clinical trials may begin;

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Performance of adequate and well controlled human clinical trials to establish the safety and efficacy of the proposed drug or biologic s intended use; and

In the case of a new drug, approval by the FDA of a New Drug Application (NDA) or of a BLA for a biologic. Our products will be regulated as biologics.

Facilities used to manufacture drugs and biologics are subject to periodic inspection by the FDA and other authorities where applicable, and must comply with the FDA s CGMP regulations. Manufacturers of biologics also must comply with FDA s general biological product standard. Failure to comply with the statutory and regulatory requirements subjects the manufacturer to possible legal or regulatory action, such as suspension of manufacturing, seizure of product or voluntary recall of a product.

Pre-Clinical Testing

Pre-clinical testing includes laboratory evaluation of product chemistry and formulation as well as animal trials to assess the potential safety and effectiveness of the product. Compounds must be adequately manufactured and pre-clinical safety tests must be conducted in compliance with FDA Good Laboratory Practices regulations. The results of the pre-clinical tests are submitted to the FDA as part of an IND application to be reviewed by the FDA prior to the commencement of human clinical trials. Submission of an IND application may not result in FDA authorization to commence clinical trials, but the IND becomes effective if not rejected by the FDA within 30 days. The IND application must indicate: the results of previous testing; how, where and by whom the clinical trials will be conducted; the chemical structure of the compound; the method by which it is believed to work in the human body; any toxic effects of the compound found in the animal trials; and how the compound is manufactured.

Clinical Trials

Clinical trials involve the administration of the drug or biologic to healthy volunteers or to patients, under the supervision of qualified principal investigators. All clinical trials must be conducted in accordance with Good Clinical Practices regulations under protocols that detail the objectives of the trial, the parameters to be used to monitor safety and the effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA for review as part of the IND application prior to commencing the trial. Further, each clinical trial must be conducted under the auspices of an independent review panel termed the Institutional Review Board, or IRB, at the institution at which the trial will be conducted. The IRB will consider, among other things, ethical factors, the safety of human subjects, informed consent and the possible liability of the institution. Progress reports detailing the status of on-going clinical trials must be submitted at least annually to the FDA.

Clinical trials are typically conducted in three sequential phases, but the phases often overlap. In Phase 1, the initial introduction of the drug into healthy volunteers or patients, the drug is tested for safety or adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and clinical pharmacology. Phases 2 and 3 involve clinical trials in patient populations to determine the effectiveness of the drug for specific, targeted indications, determine dosage tolerance and optimal dosage. Phase 3 clinical trials typically contain control groups and are undertaken to further evaluate clinical effectiveness, to further test for safety within an expanded patient population at geographically dispersed clinical trial sites and may be utilized to seek marketing approval by the FDA.

National Institutes of Health

The NIH publishes guidelines concerning recombinant DNA products. The NIH guidelines require that human recombinant DNA protocols subject to the guidelines, and involving a novel product, disease indication, route of administration or other component, be discussed at the quarterly meetings of the NIH Recombinant DNA Advisory Committee. Companies involved in clinical trials as sponsors generally are expected to report all serious adverse events to the NIH.

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We report to the FDA and the NIH serious adverse events and deaths, whether treatment-related or not, that occur in our clinical trials. Clinical trials we conduct include cancer patients who have failed all conventional treatments available to them, and who therefore have short life expectancies and who sometimes die before completion of their full course of treatment in our clinical trials.

Marketing Applications

If the clinical data indicate that the drug is safe and effective, a BLA or an NDA is filed with the FDA for approval of the marketing and commercial shipment of the drug. This marketing application must contain all of the information on the drug gathered to that date, including data from the clinical trials. It is often over 100,000 pages in length.

The FDA reviews all marketing applications submitted to it before it accepts them for filing and may request additional information, rather than accepting the application for filing. In such event, the application must be re-submitted with the additional information and the application is again subject to review before filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the BLA or NDA. Under the FDC Act, the FDA has 180 days in which to review it and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification of information already provided in the submission. The FDA may refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. However, the FDA is not bound by the recommendation of an advisory committee. If the FDA evaluations of the marketing application and the manufacturing facilities are favorable, the FDA may issue either an approval letter or an approvable letter. An approvable letter usually contains a number of conditions that must be met in order to secure final approval of the application. When, and if, those conditions have been met to the FDA s satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. Approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. If the FDA s evaluation of the submission or manufacturing facilities is not favorable, the FDA may refuse to approve the BLA or NDA or issue a not-approvable letter.

If the FDA approves the BLA or NDA, the drug becomes available for physicians to prescribe. Periodic reports must be submitted to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional trials, referred to as Phase 4 clinical trials, to evaluate long-term effects. Phase 4 clinical trials and post-marketing trials may also be conducted to explore new indications and to broaden the application and use of the drug and its acceptance in the medical community.

Satisfaction of FDA premarket approval requirements for new drugs and biologics typically takes several years and the actual time required may vary substantially based upon the type, complexity and novelties of the product or disease. Government regulation may delay or present marketing of potential products for a considerable period of time and impose costly procedures upon our activities. Success in early stage clinical trials and on prior versions of the products does not assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval.

Orphan Drug Act

We have received Orphan Drug designation for ADVEXIN therapy for the treatment of head and neck cancer under the Orphan Drug Act. This act provides incentives to manufacturers to develop and market drugs for rare diseases and conditions affecting fewer than 200,000 people in the United States. The first developer to receive FDA marketing approval for an Orphan Drug is entitled to a seven-year exclusive marketing period in the United States following FDA approval of that product. However, the FDA will allow the sale of a drug clinically superior to or different from another approved Orphan Drug, although for the same indication, during the seven-year exclusive marketing period.

We may pursue Orphan Drug designation for other products we are developing. We cannot be sure that any of those potential products will ultimately receive Orphan Drug designation, or that the benefits currently

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provided by such a designation will not subsequently be amended or eliminated. The Orphan Drug Act has been controversial, and legislative proposals have from time to time been introduced in Congress to modify various aspects of the Orphan Drug Act, particularly the market exclusivity provisions. New legislation may be introduced in the future that could adversely affect the availability or attractiveness of Orphan Drug status for our potential products. Orphan Drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Off-Label Use

Physicians may prescribe drugs for uses that are not described in the product s labeling that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties and may constitute the best treatment for many patients in various circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers communications on the subject of off-label use. Companies cannot actively promote FDA-approved drugs for off-label uses. However, new regulations, if followed, provide a safe harbor from FDA enforcement action that would allow us to disseminate to physicians articles published in peer-reviewed journals, such as the *New England Journal of Medicine,* that discuss off-label uses of approved products. We cannot disseminate articles concerning drugs that have not been approved for any indication.

Fast Track Products

Fast Track Designation. The FDA s Fast Track program is intended to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and that demonstrates the potential to address unmet medical needs for their condition. Under the Fast Track program, the sponsor of a new drug may request the FDA to designate the drug for a specific indication as a Fast Track product at any time during the clinical development of the product. The FDA must determine if the product qualifies for Fast Track designation within 60 days of receipt of the sponsor s request.

If Fast Track designation is obtained, the FDA may initiate review of sections of an NDA or BLA before the applicant is complete. This rolling review is available if the applicant provides a schedule for the submission of the remaining information and pays applicable user fees. However, the time period specified in the Prescription Drug User Fees Act, which governs the time period goals the FDA has committed to reviewing an application, does not begin until the complete application is submitted. Additionally, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

In some cases, a Fast Track designated product may also qualify for one or more of the following programs:

Priority Review. Under FDA policies, a product is eligible for priority review, or review within a six-month time frame from the time an NDA or BLA is accepted for filing, if the product provides a significant improvement compared to marketed products in the treatment, diagnosis, or prevention of a disease. A Fast Track designated product would ordinarily meet the FDA s criteria for priority review. We cannot guarantee any of our products will receive a priority review designation, or if a priority designation is received, that review or approval will be faster than conventional FDA procedures.

Accelerated Approval. Under the FDA s Accelerated Approval regulations, the FDA is authorized to approve products that have been studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments based upon either a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than patient survival. In clinical trials, surrogate endpoints are alternative measurements of the symptoms of a disease or condition that are substituted for measurements of observable clinical symptoms. Accelerated Approval of an application will be subject to Phase 4 or post-approval studies to validate the surrogate endpoint or confirm the effect on the clinical endpoint. Failure to validate a surrogate endpoint or confirm a clinical benefit during post-

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marketing studies will allow the product to be withdrawn from the market by the FDA on an expedited basis. All promotional materials for drugs approved under accelerated regulations are subject to prior review by the FDA.

Although we have obtained a Fast Track designation for ADVEXIN therapy from the FDA, we cannot guarantee a faster development process, review process or approval compared to conventional FDA procedures. We also may elect not to seek or we may be prevented from seeking approval under the Accelerated Approval process for any of our products.

When appropriate, we also intend to seek Fast Track designation for our other products. We cannot predict the ultimate impact, if any, of the Fast Track process on the timing or likelihood of FDA approval of any of our other potential products.

ADVEXIN therapy is designated as a Fast Track product by the FDA for its effect on prolonging survival and the time to loco-regional disease progression in patients with recurrent, unresectable squamous cell carcinoma of the head and neck. By designating ADVEXIN therapy as a Fast Track product, the FDA will take actions to expedite the evaluation and review of the application for approval of ADVEXIN therapy.

We will continue to seek Fast Track designation to secure expedited review of additional appropriate products. It is uncertain whether we will obtain Fast Track designation. We cannot predict the ultimate effect, if any, of the new Fast Track process on the timing or likelihood of FDA approval of any of our potential products.

International

Steps similar to those in the United States must be undertaken in virtually every other country comprising the market for our products before any such product can be commercialized in those countries. The approval procedure and the time required for approval vary from country to country and may involve additional testing. We cannot be sure that approvals will be granted on a timely basis, or at all. In addition, regulatory approval of prices is required in most countries, other than the United States. There can be no assurance that the resulting prices would be sufficient to generate an acceptable return to us.

Competition

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may arise from other drug development technologies, methods of preventing or reducing the incidence of disease, including molecular immunotherapies, and new small molecule or other classes of therapeutic agents. Developments by others may render our product candidates or technologies obsolete or non-competitive.

We are aware that the Chinese pharmaceutical companies SiBiono GeneTech, Inc. (SiBiono GeneTech) and Shanghai Sunway Biotech Co. Ltd. have announced they have received regulatory approval from the Chinese drug regulatory authorities to market an adenoviral p53 product and an oncolytic virus product, respectively, both only in China. We are also aware of other pharmaceutical and biotechnology companies, including Canji, Inc. (Canji), Genvec, Inc. (Genvec) and ImClone Systems, Inc., which are pursuing forms of treatment for the diseases ADVEXIN therapy and our other product candidates target. We are aware that ImClone and Bristol Myers Squibb have obtained marketing approval based on a supplemental application to the FDA for a monoclonal antibody product (Erbitux) for the treatment of certain kinds of head and neck cancer. Erbitux was approved for two stages of treatment of the cancer, one for an early, as yet untreated form, and a second for refractory head and neck cancer already treated with chemotherapy. We are also aware that Canji, with its parent Schering-Plough Corporation (Schering-Plough), has in the past been involved in research and/or development of adenoviral p53 products and owns or controls patents and patent applications directed to adenoviral p53 therapy. We understand that Canji/ Schering-Plough has stopped its adenoviral p53 clinical trials, and it is unknown whether these parties are continuing their adenoviral p53 research and/or

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development efforts. There are many other companies, both publicly and privately held, including well-known pharmaceutical companies, engaged in developing products for human therapeutic applications. We also compete with universities and other research institutions in the development of products, technologies and processes. In many instances, we compete with other commercial entities in acquiring products or technologies from universities and other research institutions.

We expect that competition among products approved for sale will be based, among other things, on product efficacy, safety, reliability, availability, price, patent position and sales, marketing and distribution capabilities. Our competitive position also depends upon our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes, and secure sufficient capital resources for the often substantial period between technological conception and commercial sales.

Human Resources

As of March 15, 2006, we had approximately 80 employees and contracted personnel engaged in research and development, regulatory affairs, clinical affairs, manufacturing and quality, finance and corporate development activities. Our employees include eight holders of a Ph.D. or M.D. degree. Many of our employees have extensive experience in pharmaceutical and biotechnology industries.

Scientific Advisory Board

We receive guidance on a broad range of scientific, clinical and technical issues from our Scientific Advisory Board. Members of our Scientific Advisory Board are recognized experts in their respective fields of research and clinical medicine related to molecular oncology. The members of the Scientific Advisory Board are:

Jack A. Roth, M.D., Chairman of the Scientific Advisory Board, is Chairman of the Department of Thoracic and Cardiovascular Surgery and Director of the W.M. Keck Center for Cancer Gene Therapy at M.D. Anderson Cancer Center where he holds the Bud Johnson Clinical Distinguished Chair. Dr. Roth was one of our founders and is our Chief Medical Advisor. Dr. Roth is a widely-recognized pioneer in the application of targeted molecular therapies to the treatment of cancer. He is the primary inventor of the technology supporting our tumor suppressor products. He received his M.D. from The Johns Hopkins University School of Medicine.

Carol L. Prives, Ph.D., is a professor of biology at Columbia University. She is the Chair of the NIH Experimental Virology Trial Section, a member of the NCI Intramural Scientific Advisory Board and a member of the Advisory Board of the Dana-Farber Cancer Center in Boston. Dr. Prives is an editor of the Journal of Virology and serves on the editorial boards of three other prominent journals. She received her Ph.D. in biochemistry from McGill University.

Daniel D. Von Hoff, M.D., is the Director of the Arizona Cancer Center in Tucson, Arizona, and a professor of medicine in the Department of Medicine of the University of Arizona. Dr. Von Hoff is a past President of the American Association for Cancer Research. Dr. Von Hoff is certified in medical oncology by the American Board of Internal Medicine. He received his M.D. from The Columbia College of Physicians and Surgeons.

Elizabeth Grimm, Ph.D., is a professor of experimental therapeutics at M. D. Anderson Cancer Center. Dr. Grimm has served as Cancer Expert, Surgical Branch of the NCI. She received her Ph.D. in microbiology from the University of California, Los Angeles School of Medicine.

Michael J. Imperiale, Ph.D., is the Director of Cancer Biology Training Programs at the University of Michigan Cancer Center and holds a concurrent position in the Department of Microbiology and Immunology at the University of Michigan. Dr. Imperiale earned his Ph.D. degree in biological sciences from Columbia University and received postdoctoral training at the Rockefeller University Laboratory of Molecular Cell Biology, where he studied the regulation of adenoviruses.

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Item 1A. ***Risk Factors***

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 on our ability to successfully commercialize ADVEXIN therapy in various markets for multiple indications, which depends in large part on our ability to commence, execute and complete clinical programs and obtain regulatory approvals for ADVEXIN therapy and other drug candidates. In particular, our ability to achieve and sustain profitability will depend in large part on our ability to commercialize ADVEXIN therapy for the treatment of head and neck cancer in the United States. We cannot assure you we will receive approval for ADVEXIN therapy 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 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 causing 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 ADVEXIN therapy is neither safe nor effective.

While we have completed enrollment of patients in a Phase 1/early Phase 2 clinical trial of INGN 241, a product candidate based on the mda-7 tumor suppressor, and have initiated a follow-on Phase 2 clinical trial of INGN 241 for patients with metastatic melanoma, 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 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;

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

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

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

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

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

Despite the FDA s designation of ADVEXIN therapy as a Fast Track product, we may encounter delays in the regulatory approval process due to additional information requirements from the FDA, unintentional omissions in our BLA for ADVEXIN therapy, or other delays in the FDA s review process. 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.

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

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

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

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

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

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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, 2005, we had an accumulated deficit of approximately $143.5 million. We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities 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 M. D. Anderson Cancer Center. We do not expect to generate revenue from the commercial sale of products in the near future, and we may never generate revenue from the commercial sale of products.

If we continue to incur operating losses for a period longer than we anticipate and fail to obtain the capital necessary to fund our operations, we will be unable to advance our development 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 revenue may not be sufficient to support the expense of our operations, the development of commercial infrastructure and the conduct of our clinical trials and pre-clinical research.

We expect 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;
- faster than expected rate of progress and cost of our research and development and clinical trial activities;
- a decrease in the amount and timing of milestone payments we receive from collaborators;
- higher than expected costs of preparing an application for FDA approval of ADVEXIN therapy;
- higher than expected costs of developing the processes and systems to support FDA approval of ADVEXIN therapy;
- an increase in our timetable and costs for the development of marketing operations and other activities related to the commercialization of ADVEXIN therapy and our other product candidates;

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

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

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

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

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

Our strategy for the research, development and commercialization of our product candidates may result in our entering into contractual arrangements with corporate collaborators, academic institutions and others. We have entered into sponsored research, license and/or collaborative arrangements with several entities, including M. D. Anderson Cancer Center, the NCI, Chiba University in Japan, VirRx and Corixa, which was acquired by GlaxoSmithKline, as well as numerous other institutions that conduct clinical trials work or perform pre-clinical research for us. Our success depends upon our collaborative partners performing their responsibilities under these arrangements and complying with the regulations and requirements governing clinical trials. We cannot control the amount and timing of resources our collaborative partners devote to our research and testing programs or product candidates, or their compliance with regulatory requirements which can vary because of factors unrelated to such programs or product candidates. These relationships may in some cases be terminated at the discretion of our collaborative partners with only limited notice to us. We may not be able to maintain our existing arrangements, enter into new arrangements or negotiate current or new arrangements on acceptable terms, if at all. Some of our collaborative partners may also be researching competing technologies independently from us to treat the diseases targeted by our collaborative programs.

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

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

If we are not able to create effective collaborative marketing relationships, we may be unable to market 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 we enter into any such arrangements with third parties, our product revenue are likely to be lower than if we directly marketed and sold our products, and any revenue we receive will depend upon the efforts of such third parties. We have no experience in marketing or selling pharmaceutical products and we currently have no sales, marketing or distribution capability. We may be unable to develop sufficient sales, marketing and distribution capabilities to commercialize our products successfully.

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

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

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

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

The FDA has not approved any recombinant DNA therapy products of the types being developed by Introgen for sale in the United States. The commercial success of our products will depend in part on public acceptance of the use of these types of recombinant DNA products, which are a new type of disease treatment for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that these types of recombinant DNA products are unsafe, and these treatment methodologies may not gain the acceptance of the public or the medical community. Negative public reaction to these types of recombinant DNA products could also result in greater government regulation and stricter clinical trial oversight.

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

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

the size of the patient population;

the nature of the clinical protocol requirements;

the diversion of patients to other trials or marketed therapies;

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

the proximity of patients to clinical sites; and

the patient eligibility criteria for the study.

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

studies discontinue their participation in the study, the results from that study may not be positive or may not support an NDA for regulatory approval of our product candidates.

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

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

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

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

Our ability to develop and protect a competitive position based on our biotechnological innovations, innovations involving molecular therapies, recombinant DNA therapeutic agents, viruses for delivering targeted molecular therapies to cells, formulations, delivery systems not involving viruses, and the like, is particularly uncertain. Due to the unpredictability of the biotechnological sciences, the PTO, as well as patent offices in other jurisdictions, has often required patent applications concerning biotechnology-related inventions to be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting their scope of protection against competitive challenges. Similarly, courts have invalidated or significantly narrowed many key patents in the biotechnology industry. Thus, even if we are able to obtain patents covering commercially significant 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 as well as a related patent for purified adenoviral compositions. We also control, through licensing arrangements, five issued United States patents for combination therapy involving the p53 tumor suppressor and conventional chemotherapy or radiation, two issued United States patents covering the use of adenoviral p53 in cancer therapy, one issued United States patent covering adenoviral p53 as a product, one issued United States patent covering the core DNA of adenoviral p53, one issued patent covering pharmaceutical compositions of adenoviral p53 and clinical applications of such pharmaceutical compositions, as well as three patents covering our mda-7 technology. Our competitors may challenge the validity of one or more of our patents in the courts or through an administrative procedure known as an interference, in which the PTO determines the priority of invention where two or more parties are claiming the same invention. The courts or the PTO may not uphold the validity of our patents, we may not prevail in such interference proceedings regarding our patents and none of our patents may give us a competitive advantage. In this regard, we have been notified by the PTO that an unidentified third party is attempting to provoke an interference with one of our patents directed to adenoviral p53 therapy. We do not at present know the identity of this party and cannot assess the likelihood of an interference actually being declared. Should that party prevail in an interference proceeding, a patent may issue to that party that is

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infringed by, and therefore potentially preclude our commercialization of, products like ADVEXIN therapy that are used for adenoviral p53 therapy.

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

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

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

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

One of the foregoing patent applications directed to p53 therapy, which we understand is owned by The Johns Hopkins University and controlled by Schering-Plough, was involved in a PTO interference proceeding with a patent owned by Canji. This Johns Hopkins application was the United States counterpart to the European patent recently revoked in its entirety by the EPO (see below). Priority of invention in that interference was awarded by the PTO to the Johns Hopkins inventors, leading to the issuance of a United States patent, and the Canji patent has been found unpatentable. While it is our belief that the claims of the Johns Hopkins patent are invalid and not infringed by our ADVEXIN therapy, Schering-Plough or Johns Hopkins may assert that our ADVEXIN therapy, which uses p53 therapy, infringes the claims of such patent. While we believe we would have both an invalidity and non-infringement defense against such an assertion, in the United States an issued patent enjoys a presumption of validity, which can be overcome only through clear and convincing evidence. We cannot assure such a defense would prevail.

We may also become subject to infringement claims or litigation arising out of other patents and pending applications of our competitors, if they issue, or additional interference proceedings declared by the PTO to determine the priority of inventions. The defense and prosecution of intellectual property suits, PTO

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

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

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

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

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

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

Our business depends in part on patents licensed from third parties. Those third-party license agreements impose obligations on us, such as payment obligations and obligations to diligently pursue development of commercial products under the licensed patents. If a licensor believes we have failed to meet our obligations under a license agreement, the licensor could seek to limit or terminate our license rights, which could lead to costly and time-consuming litigation and, potentially, a loss of the licensed rights. During the period of any such litigation, our ability to carry out the development and commercialization of product candidates could be

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

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

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

Our profitability will depend on the market s acceptance of ADVEXIN therapy, INGN 241, INGN 225, 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.

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

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

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

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 manufacturing facilities we constructed in Houston, Texas to manufacture ADVEXIN therapy, INGN 241 and other product candidates for currently planned clinical trials. We anticipate our facilities are suitable for the initial commercial launch of ADVEXIN therapy. We have no experience manufacturing ADVEXIN therapy, INGN 241 or any other product candidates in the volumes necessary to support commercial sales. If we are unable to manufacture our product candidates in clinical or, when necessary, commercial quantities, then we will need to rely on third-party manufacturers to produce our products for clinical and commercial purposes. These third-party manufacturers must receive FDA approval before they can produce clinical material or commercial product. Our products may be in competition with other products for access to these facilities and may be subject to delays in 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 a limited number of 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 facilities and process. Manufacturing of our product candidates for clinical and commercial purposes must comply with the FDA s CGMP requirements, and foreign regulatory requirements. The CGMP requirements govern quality control and documentation policies and procedures. In complying with CGMP and foreign regulatory requirements, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure the product meets applicable specifications and other requirements. We must also pass a FDA inspection prior to FDA approval.

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

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

Canji controls a United States patent and the corresponding international applications, including a European counterpart, relating to the purification of viral or adenoviral compositions. While we believe our manufacturing process does not infringe this patent, Canji could still assert a claim against us. We may also become subject to infringement claims or litigation if our manufacturing process infringes 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 a limited number of suppliers for some of our manufacturing materials. Any problems experienced by such suppliers could negatively affect our operations.

We rely on third-party suppliers for most of the equipment, materials and supplies used in the manufacturing of ADVEXIN therapy, INGN 241 and our other product candidates. Some items critical to the manufacture of these product candidates are available from only a limited number of suppliers or vendors. We do not have supply agreements with these key suppliers. To mitigate the related supply risk, we maintain inventories of these items. Any significant problem experienced by one or more of this limited number of suppliers could result in a delay or interruption in the supply of materials to us until the supplier cures the problem or until we locate an alternative source of supply. Such problems would likely lead to a delay or interruption in our manufacturing operations or could require a significant modification to our manufacturing process, which could impair our ability to manufacture our product candidates in a timely manner and negatively affect our operations.

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

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

We use hazardous materials in our business, 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

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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.

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 Annual Report on Form 10-K. Our estimates are based on present facts and a variety of assumptions. Many of the underlying assumptions are outside of our control. If milestones are not achieved when we expect them to be, investors could be disappointed, and our stock price may decrease.

Any acquisition we might make may be costly and difficult to integrate, 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 we undertake will be accompanied by the risks commonly encountered in business acquisitions. These risks include, among other things:

potential exposure to unknown liabilities of acquired companies;

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

diversion of management time and attention and other resources;

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

the incurrence of amortization expense; and

possible dilution to our stockholders.

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

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

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

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

A change in accounting standards or practices or a change in existing taxation rules or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and taxation rules and varying interpretations of accounting pronouncements and taxation practice have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business. For example, Statement of Financial Accounting Standards No. 123 (revised 2004), Share-Based Payment, (SFAS No. 123R) is effective for us beginning the first quarter of fiscal year 2006. This statement requires that employee share-based compensation be measured based on its fair-value on the grant date and treated as an expense that is reflected in the financial statements over the related service period. While we are currently evaluating the impact on our Consolidated Financial Statements of the adoption of SFAS No. 123R, we anticipate that our adoption of SFAS No. 123R will have a significant impact on our results of operations for 2006 and subsequent periods.

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

Section 203 of the Delaware General Corporation Law and our certificate of incorporation and by-laws contain provisions that might enable our management to resist a takeover of our company or discourage a third party from attempting to take over our company. These provisions include the inability of stockholders to act by written consent or to call special meetings, the ability of our board of directors to designate the terms of and issue new series of preferred stock without stockholder approval and the fact that our board of directors is divided into three classes serving staggered thee-year terms.

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

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

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

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

In October 2004, we acquired all of the outstanding capital stock of Magnum Therapeutics Corporation (Magnum), a company owned at the time of this acquisition by one of our executive officers. We paid approximately $1.75 million for the Magnum stock by (1) issuing approximately 252,000 shares of our common stock valued at approximately $1.48 million at the acquisition date and (2) assuming liabilities of approximately $272,000. With respect to the common stock we issued for the acquisition, 50% of the shares were held by an independent escrow agent for a period of approximately one year subsequent to the acquisition date to satisfy the indemnification obligations of the selling shareholder under terms of the purchase agreement. Such shares have since been released from escrow. Magnum s primary asset is the funding it receives under a research grant from the NIH, which supplements our ongoing research and development programs. During the year ended December 31, 2005, we earned $1.0 million of revenue under this grant. In the event certain of Magnum s technologies result in commercial products, we may be obligated to pay royalties related to the sales of those products to certain third parties.

We have relationships with Jack A. Roth, M.D., and M. D. Anderson Cancer Center, both of whom are affiliated with The Board of Regents of the University of Texas System, one of our stockholders. For more information concerning these relationships, see our Notes to Consolidated Financial Statements beginning on page F-7 of this Annual Report on Form 10-K.

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

Item 1B. ***Unresolved Staff Comments***

Not applicable.

Item 2. ***Properties***

Our primary operations are conducted from facilities in Houston, Texas, totaling approximately 42,000 square feet in two buildings. These buildings consist of a 12,000 square foot CGMP production facility designed to support an ADVEXIN therapy product launch and a 30,000 square foot building containing our research and development laboratories and administrative offices. We own these facilities through TMX Realty Corporation (TMX), our wholly-owned subsidiary. Our corporate offices are located in Austin, Texas. We expect our current facilities to satisfy our requirements for the foreseeable future.

TMX leases the land under our Houston facilities from a third party. The buildings are financed and pledged as collateral under a mortgage note payable. Certain equipment in the buildings is financed and pledged as collateral under notes payable. See the discussion below under Item 7. Management s Discussion

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and Analysis of Financial Condition and Results of Operations Liquidity and Capital Resources for a summary of our obligations under notes payable and leases.

We sublease to M. D. Anderson Cancer Center approximately 10,000 square feet in the facilities described above. This lease provides for rent payments at prevailing market rates and has an initial term expiring in 2009.

In addition to the facilities described above, we lease other space in Houston, Texas in which we constructed and operate a second production facility. We use that facility to produce investigative material for INGN 241 and other product candidates in an environment separate from that used for production of ADVEXIN therapy.

Item 3. ***Legal Proceedings***

We are involved from time to time in legal proceedings relating to claims arising out of our operation in the ordinary course of business, including actions relating to intellectual property rights.

We do not believe that the outcome of any present, or all litigation in the aggregate, will have a material effect on our business. You can read the discussion of our opposition of the patents under Item 1A. Risk Factors above.

Item 4. ***Submission of Matters to a Vote of Security Holders***

No matter was submitted to a vote of security holders during the fourth quarter of the fiscal year covered by this Annual Report on Form 10-K.

PART II

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

Market and Equityholder Information

Our common stock has been quoted on the Nasdaq National Market under the symbol INGN since our initial public offering in October 2000. Prior to October 2000, there was no established public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low sale prices reported on the Nasdaq National Market.

	High	Low
Fiscal Year Ended December 31, 2004:		
First Fiscal Quarter	$ 10.37	$ 7.29
Second Fiscal Quarter	9.20	4.20
Third Fiscal Quarter	7.10	2.96
Fourth Fiscal Quarter	9.81	5.00
Fiscal Year Ended December 31, 2005:		
First Fiscal Quarter	$ 8.60	$ 6.35
Second Fiscal Quarter	8.10	6.07
Third Fiscal Quarter	7.40	4.90
Fourth Fiscal Quarter	6.60	4.54

At December 31, 2005, there were 37,147,351 shares of our common stock issued and outstanding held by approximately 152 stockholders of record. A substantially greater number of holders of our common stock are street name or beneficial holders, whose shares are held of record by banks, brokers and other financial institutions.

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Dividend Policy

We have never declared or paid any dividends on our capital stock. We currently expect to retain all of our future earnings, if any, to support the development of our business. We do not anticipate paying any cash dividends in the foreseeable future.

Stock Repurchases

We did not repurchase any shares of capital stock during the fourth quarter of the fiscal year covered by this Annual Report on Form 10-K.

Item 6. ***Selected Financial Data***

The selected consolidated financial data set forth below is qualified in its entirety by, and should be read in conjunction with, our Consolidated Financial Statements and notes thereto and Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this Annual Report on Form 10-K.

	Year Ended June 30,	Six Months Ended	Year Ended December 31,				
	2001(b)	December 31, 2001(b)	2001(c)	2002(b)	2003(a)	2004(a)	2005(a)
			(Unaudited) (In thousands except per share amounts)				
Statement of Operations Data:							
Contract services, grants and other revenue	$ 684	$ 298	$ 591	$ 1,173	$ 304	$ 1,808	$ 1,867
Collaborative research and development revenue from affiliate	3,016						
Product sales to affiliate	1,500						
Cost of product sales	2,488						
Gross margin on product sales	(988)						
Operating costs and expense:							
Research and development	15,014	10,063	19,923	21,512	14,973	20,474	21,400
General and administrative	4,875	3,526	6,361	6,722	6,102	6,597	7,834
Total operating costs and expense	19,889	13,589	26,284	28,234	21,075	27,071	29,234

Loss from operations	(17,177)	(13,291)	(25,693)	(27,061)	(20,771)	(25,263)	(27,367)
Interest income (expense), net	381	445	423	(207)	393	(191)	166
Other income	354	518	871	1,140	1,052	1,067	1,098
Net loss	$ (16,442)	$ (12,328)	$ (24,399)	$ (26,128)	$ (19,326)	$ (24,387)	$ (26,103)
Net loss per share, basic and diluted	$ (1.02)	$ (0.58)	$ (1.14)	$ (1.22)	$ (0.84)	$ (0.91)	$ (0.80)
Shares used in computing basic and diluted net loss per share	16,163	21,440	21,440	21,471	22,902	26,943	32,780

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	December 31,				
	2001(b)	2002(b)	2003(b)	2004(a)	2005(a)
Balance Sheet Data:					
Cash, cash equivalents, and short-term investments	$ 48,825	$ 23,467	$ 36,397	$ 38,180	$ 33,122
Working capital	43,175	18,852	31,091	31,981	29,529
Total assets	60,424	33,316	44,483	48,057	42,981
Notes payable, net of current portion	9,037	7,435	6,714	7,901	7,784
Deferred revenue, long-term	361	619	876	1,132	1,404
Accumulated deficit	(47,515)	(73,643)	(92,969)	(117,356)	(143,459)
Stockholders equity	44,566	19,835	31,285	32,166	27,011

(a) The selected Consolidated Statement of Operations data for the years ended December 31, 2005, 2004 and 2003 and the Consolidated Balance Sheet data as of December 31, 2005 and 2004, are derived from our and our subsidiaries audited Consolidated Financial Statements, which appear in Part IV of this Annual Report on Form 10-K.

(b) The selected Consolidated Statement of Operations data for the year ended June 30, 2001, the six months ended December 31, 2001, the year ended December 31, 2002, and the Consolidated Balance Sheet data as of December 31, 2003, 2002 and 2001, are derived from our and our subsidiaries audited Consolidated Financial Statements included in our Annual Reports on Form 10-K filed with the Commission on March 15, 2005 and March 5, 2004.

(c) The selected Consolidated Statement of Operations data for the year ended December 31, 2001 are derived from our and our subsidiaries unaudited Consolidated Financial Statements.

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

The following discussion and analysis should be read in conjunction with our Condensed Consolidated Financial Statements and the related notes thereto included in this Annual Report on Form 10-K. The discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. These statements include the statements under Item 1A. Risk Factors. These forward-looking statements are based on our current expectations and entail various risks and uncertainties. Our actual results could differ materially from those projected in the forward-looking statements as a result of various factors, including those set forth under Item 1A. Risk Factors.

Overview

Introgen Therapeutics, Inc. was incorporated in Delaware in 1993. 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 tumor suppressors, cytokines and other targeted molecular therapies. These agents are designed to increase production of normal cancer-fighting proteins that act to overpower cancerous cells, stimulate immune activity and enhance conventional cancer therapies. See Item 1. Business Overview above for a more complete discussion of our business.

Since our inception in 1993, we have used our resources primarily to conduct research and development activities for ADVEXIN therapy and, to a lesser extent, for other product candidates. At December 31, 2005, we had an accumulated deficit of $143.5 million. We anticipate we will incur losses in the future that may be greater than losses incurred in prior periods. At December 31, 2005, we had cash, cash equivalents and short-term investments of

$33.1 million. During the year ended December 31, 2005, we used $21.7 million of cash and cash equivalents for operating activities. In addition, we used $509,000 for purchases of property and equipment and $707,000 for principal payments on notes payable to support those activities. These uses of cash were offset by the receipt of $772,000 under notes payable primarily to finance equipment acquisitions,

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$19.6 million net of related fees and expense from the sale of common stock to Colgate-Palmolive and $615,000 from sales of common stock resulting from stock option exercises. We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities continue and as we evolve our operations and systems to support commercialization of our product candidates. These losses, among other things, have caused and may cause our total assets, stockholders equity and working capital to decrease. Currently, we earn revenue or income from federal research grants, contract services and process development activities, the lease of a portion of our facilities to M. D. Anderson Cancer Center and interest income on cash placed in short-term, investment grade securities. In order to fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders.

In June 2003, we sold 2.0 million shares of our common stock for an aggregate purchase price of $11.5 million to selected institutional investors through a private placement pursuant to Regulation D promulgated under the Securities Act. Our net proceeds from this transaction, after related fees and expense, were $10.8 million. In connection with this sale, we issued warrants to purchase 400,000 shares of our common stock at $7.89 per share. These warrants are exercisable at any time by the warrant holders through June 2008. We may force the exercise of these warrants if the average closing market price of our common stock during any 20 consecutive trading days is greater than $15.78 per share. The resale of the shares of common stock issued and issuable upon the exercise of the warrants issued in this transaction was registered pursuant to a registration statement on Form S-3, effective August 7, 2003 (Commission File No. 333-107028).

In December 2003, we sold approximately 2.9 million shares of our common stock in a direct equity offering pursuant to a shelf registration for an aggregate purchase price of approximately $20.0 million. Our net proceeds from this transaction, after related fees and expense, were approximately $18.5 million. The issuance of the shares of common stock in this transaction was registered pursuant to a registration statement on Form S-3, effective August 25, 2003 (Commission File No. 333-107799) registering the issuance of shares of our common stock with an aggregate offering price of $100.0 million. We may sell additional shares of our common stock pursuant to this registration statement in the future.

In December 2004, we sold approximately 3.5 million shares of our common stock in a direct equity offering pursuant to a shelf registration statement for an aggregate purchase price of approximately $24.3 million. Our net proceeds from this transaction, after related fees and expense, were approximately $22.9 million. The shares of common stock issued in this transaction were registered pursuant to a registration statement on Form S-3, effective August 25, 2003 (Commission File No. 333-107799) registering shares of our common stock with an aggregate offering price of $100.0 million. We may sell additional shares of our common stock pursuant to this registration statement in the future. In connection with this transaction, we have issued or will issue warrants to the placement agents representing us in this stock sale to purchase up to 225,238 shares of our common stock at a price of $6.65 per share and to purchase up to 88,707 shares of our common stock at a price of $8.00 per share. These warrants are exercisable beginning in December 2005 and expire in December 2009.

In November 2005, we sold approximately 3.6 million shares of our common stock in a direct equity sale to Colgate-Palmolive pursuant to a shelf registration statement for an aggregate purchase price of approximately $20.0 million. Our net proceeds from this transaction, after related fees and expense, were approximately $19.6 million. See Item 1. Business Business and Collaborative Arrangements Alliance with Colgate-Palmolive Company above for further discussion of our agreement with Colgate-Palmolive.

Mortgage Note Payable

In May 2004, we amended the mortgage note payable related to our facilities. The original $6.0 million principal balance of our note payable was increased to $7.8 million. The proceeds from this increase were used to pay in full the principal and interest outstanding on another note payable with an original principal balance of approximately $3.3 million, which resulted in that other note being retired. In addition to this note

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retirement, the proceeds from this loan amendment were used to pay $96,000 of costs related to this transaction and to add $668,000 to our cash and cash equivalents. The amended mortgage note payable bears interest at 6.25%. The note is payable in monthly installments of $56,400 until May 2006. At that time, we may extend the note to a November 2009 maturity date. Upon such extension, the interest rate is modified to the lesser of (a) 2.5% above the five-year U.S. Treasury Bond Note rate or (b) 8.5%, and principal and interest on the note become payable in equal monthly installments based on a 225-month amortization period. The principal balance outstanding on the note s extended maturity date is payable in full at that time.

Acquisition of Magnum Therapeutics Corporation

In October 2004, we acquired all of the outstanding capital stock of Magnum, a company owned at the time of this acquisition by one of our executive officers. We paid approximately $1.75 million for the Magnum stock by (1) issuing approximately 252,000 shares of our common stock valued at approximately $1.48 million at the acquisition date and (2) assuming liabilities of approximately $272,000. With respect to the common stock we issued pursuant to the acquisition, 50% of the shares were held by an independent escrow agent for a period of approximately one year subsequent to the acquisition date to satisfy the indemnification obligations of the selling shareholder under terms of the purchase agreement. Such shares have since been released from escrow.

Magnum s primary asset is the funding it receives under a research grant from the NIH, which supplements our ongoing research and development programs. During the years ended December 31, 2005 and 2004, we earned revenue of $1.0 million and $1.1 million, respectively, under this grant. In the event certain of Magnum s technologies result in commercial products, we may be obligated to pay royalties related to the sales of those products to certain third parties.

The results of Magnum s operations have been included with ours for the period subsequent to the October 2004 acquisition date. Since Magnum was a development stage company at the time we acquired it, this acquisition has been accounted for as an asset acquisition and not a business combination.

The total purchase consideration has been allocated to the assets acquired based on their respective fair values at the date of acquisition. The fair value of the net assets acquired is as follows (in thousands):

Cash and cash equivalents	$ 9
Acquired grant rights	$ 1,741

Conversion of Preferred Stock to Common Stock

In June 2005, the 100,000 issued and outstanding shares of our Series A Non-Voting Convertible Preferred Stock held by Aventis were converted into 2,343,721 shares of our common stock. The shares of preferred stock were cancelled and replaced by newly issued shares of our common stock. The preferred shares cancelled are no longer issuable. We received no cash or other consideration in connection with this conversion.

Under a voting agreement related to these shares, Aventis must vote these shares 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 June 2011 or the sale of these shares pursuant to an effective registration statement, on the open market or to an Aventis non-affiliate, as defined in the voting agreement. Pursuant to a demand registration made by Aventis in accordance with the terms of a registration rights agreement related to these shares, in November 2005 we filed a Registration Statement on Form S-3 (File No. 333-129687) registering for sale a total of 4,322,369 shares held by Aventis, which includes the converted shares.

After this conversion, we have 5.0 million shares of authorized and unissued preferred shares, of which 100,000 shares have been cancelled and 4.9 million shares are undesignated and issuable.

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Investment in SR Pharma plc

In July 2005, we purchased approximately 8.3% of the issued share capital of SR Pharma for approximately $3.0 million. As of December 31, 2005, the shares we purchased had a fair market value of $2.9 million. SR Pharma is a European biotechnology company publicly traded on the Alternative Investment Market of the LSE that is developing oncology and other products.

London Stock Exchange

We are evaluating the feasibility of listing our common stock on the LSE, which would be in addition to the listing of our common stock on the NASDAQ National Market System in the United States. We believe an LSE listing may allow us to better leverage our assets on a global basis and, specifically, in Europe and Asia.

Research Grants

We have a grant from the National Cancer Institute to support our Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma. We received grant funding and earned grant revenue under this grant of $148,000, $650,000 and $230,000 during the years ended December 31, 2003, 2004 and 2005, respectively.

Magnum, our wholly-owned subsidiary, has a grant from the NIH for the development of complementary adenoviral vectors for the treatment of cancer. Magnum received grant funding and earned grant revenue under this grant of zero, $1.1 million and $1.0 million during the years ended December 31, 2003, 2004 and 2005, respectively.

The amount of grant funding, if any, available to us to perform research and development is dependent upon many factors, including the availability of grants from government agencies, our performing the work and incurring the costs contemplated by the grants we currently have, our success in obtaining additional grants in the future and our compliance with statutes and regulations governing such grants.

Critical Accounting Policies

Use of Estimates. The preparation of financial statements in conformity with generally accepted accounting principles in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expense during the reporting period. Actual results could differ from those estimates.

Cash, Cash Equivalents and Short-term Investments. Our cash, cash equivalents and short-term investments include investments in short-term, investment grade securities, which currently consist primarily of United States federal government obligations. These investments are classified as held-to-maturity and are carried at amortized cost. At any point in time, amortized costs may be greater or less than fair value. If investments are sold prior to maturity, we could incur a realized gain or loss based on the fair market value of the investments at the date of sale. We could incur future losses on investments if the investment issuer becomes impaired or the investment is downgraded.

Marketable Securities. Our marketable securities consist of issued share capital of other public companies and are classified as available-for-sale. Unrealized gains and losses are computed using the published share price of the applicable stock exchange at the close of business on the last day of the reporting period and are reported as a separate component of accumulated other comprehensive income (loss) in shareholders equity until realized.

Intangible Assets. Grant rights acquired, which are presented as an intangible asset on our balance sheet, resulted from our asset acquisition related to the Magnum purchase in October 2004. We amortize that asset to expense on a straight-line basis over the estimated remaining life of that asset. We review purchased intangible assets for impairment whenever changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Such evaluations compare the carrying amount of an asset to future

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undiscounted net cash flows expected to be generated by the asset over its expected useful life. If the asset is considered to be impaired, we record an impairment charge equal to the amount by which the carrying value of the asset exceeds its fair value determined by utilizing a discounted cash flow technique.

Revenue Recognition. Contract services revenue is recognized when the related services are completed and delivered to the customer. Deferred revenue is recorded for cash received for which the related expense had not been incurred. Grant revenue is recognized as research expense relating to a grant is incurred and the work contemplated under the grant has been performed. Rental income from the sublease of laboratory space to third parties under leases that have variable monthly rent amounts over the term of the lease is recognized on a straight-line basis over the term of the lease. Any cash payments received in excess of rental income recognized is recorded as deferred revenue. Rental income is included in other income in the accompanying Consolidated Statement of Operations.

Research and Development Costs. In conducting our clinical trials of ADVEXIN therapy and other product candidates, we procure services from numerous third-party vendors. The cost of these services constitutes a significant portion of the cost of these trials and of our research and development expense in general. These vendors do not necessarily provide us billings for their services on a regular basis and, accordingly, are often not a timely source of information to determine the costs we have incurred relative to their services for any given accounting period. As a result, we make significant accounting estimates as to the amount of costs we have incurred relative to these vendors in each accounting period. These estimates are based on numerous factors, including, among others, costs set forth in our contracts with these vendors, the period of time over which the vendor will render the services and the rate of enrollment of patients in our clinical trials. Using these estimates, we record expenses and accrued liabilities in each accounting period that we believe fairly represent our obligations to these vendors. Actual results could differ from these estimates, resulting in increases or decreases in the amount of expense recorded and the related accrual. We have consistently applied these estimation procedures in the past and plan to continue applying such procedures in the same manner during the foreseeable future. Our experience has been that our estimates have reasonably reflected the expense we actually incur.

Recently Issued Accounting Pronouncements

In December 2004, SFAS No. 123R, Share-Based Payment, was issued. This statement establishes standards for the accounting for transactions in which an entity exchanges its equity investments for goods and services. It also addresses transactions in which an entity incurs liabilities in exchange for goods or services that are based on the fair value of the entity s equity instruments or that may be settled by the issuance of those equity instruments. The statement does not change the accounting guidance for share-based payments with parties other than employees. The statement requires measurement of the cost of employee service received in exchange for an award of equity instruments based on the grant date fair value of the award, with limited exceptions. That cost is to be recognized over the period during which an employee is required to provide service in exchange for the award, which is usually the vesting period of the award. A public entity will initially measure the cost of employee services received in exchange for an award of a liability instrument based on the instrument s current fair value. The fair value of that award will be remeasured subsequently at each reporting date through the settlement date. Changes in fair value during the requisite service period will be recognized as compensation over that period. The grant date fair value of employee share options and similar instruments will be estimated using option pricing models adjusted for the unique characteristics of these instruments.

We will be required to comply with SFAS No. 123R for the annual reporting period beginning January 1, 2006. We have not yet determined which fair-value method and transitional provision we will follow. We expect the adoption of SFAS No. 123R will have a significant impact on our results of operations. We do not expect such adoption to significantly impact our financial position or liquidity. See Share-Based Compensation in Note 2 to our Consolidated Financial Statements for the pro forma impact on net loss and net loss per share from calculating share-based compensation costs under the fair value alternative of SFAS No. 123. The calculation of compensation cost for share-based payment transactions after the effective date of

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SFAS No. 123R may be different from the calculation of compensation cost under SFAS No. 123, but such differences have not yet been quantified.

Results of Operations

Our operations consist primarily of the research and development of our product candidates and technologies described in Item 1. Business Product Development Programs above. Our research and development expense includes, but is not limited to, expense related to personnel, facilities and equipment, pre-clinical research, clinical trials, manufacturing of materials for use in clinical trials, conducting data analysis and conducting regulatory documentation submissions to the FDA. Our research and development expense can be divided between programs in the pre-clinical stage and programs in the clinical stage, and general research and development expense attributable to all programs. We manage our business by tracking research and development expense in these categories in lieu of tracking research and development expense on a project-by-project basis. Tables setting forth the amount of research and development expense we have incurred in each of these categories are presented below under Comparison of the Years Ended December 31, 2005 and December 31, 2004 and Comparison of the Years Ended December 31, 2004 and December 31, 2003.

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 pre-clinical research, clinical trials, manufacturing, quality control, labeling and promotion of drugs for human use. To obtain regulatory approvals, we must, among other requirements, complete clinical trials and other work demonstrating our product candidates are safe and effective for a particular cancer type or other disease. The FDA and other similar agencies throughout the world have substantial discretion over the work we must perform to obtain regulatory approval.

The likelihood that a product candidate will be commercially successful may be affected by a variety of factors, including, among others, the quality of the product candidate, the validity of the target and disease indication, early clinical data, competition, manufacturing capability and commercial viability. Because of the discretion of the FDA and similar agencies throughout the world, as well as the foregoing factors, we cannot predict with reasonable accuracy (1) the future expense we will incur developing these product candidates, (2) when we will complete our work in developing these product candidates or (3) when, if ever, we will earn significant revenue from approved products that might result from these product development programs.

For a discussion of the risks and uncertainties associated with developing our products, as well as the risks and uncertainties associated with potential commercialization of our product candidates, see Item 1A. Risk Factors, and particularly the risk factors entitled:

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 ;

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 ;

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

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 ;

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 ;

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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 ;

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 ; and

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

Comparison of Years Ended December 31, 2005 and 2004

In the following comparison of years ended December 31, 2005, and December 31, 2004, references to the 2005 period refer to the year ended December 31, 2005, and references to the 2004 period refer to the year ended December 31, 2004.

Revenue

Contract Services, Grant and Other Revenue. For the 2005 period, we earned revenue from (a) research grants from U.S. Government agencies and (b) third parties under agreements to provide manufacturing process development and product production services for them. In the 2004 period, we earned revenue from (a) research grants from U.S. Government agencies and (b) contract research services provided to Aventis, one of our stockholders, under an agreement through which Aventis provided funding for the conduct of a Phase 2 clinical trial of ADVEXIN therapy in breast cancer. Total contract services, grant and other revenue was $1.9 million for the 2005 period compared to $1.8 million for the 2004 period, an increase of 6%. This increase was primarily due to increased contract services revenue from third parties under agreements to provide manufacturing process development and product production services for them partially offset by a decrease in revenue earned from research grants from U.S. Government agencies.

Costs and Expense

Research and Development. Research and development expense consisted of the following (in thousands):

	Year Ended December 31,	
	2004	**2005**
Pre-clinical stage programs expense	$ 2,632	$ 2,644
Clinical stage programs expense	14,822	15,713
General research and development expense	3,020	3,043
Total research and development expense	$ 20,474	$ 21,400

Research and development expense included share-based payments expense of $396,000 in the 2005 period and $48,000 in the 2004 period.

The 5% increase in research and development expense in the 2005 period compared to the 2004 period was a result of (1) increased amortization related to the amortization of grant rights acquired in the purchase of Magnum, (2) increased share-based compensation expense for the reasons discussed below under Share-Based Compensation Expense, (3) increased manufacturing and process development costs in the 2005 period compared to the 2004 period resulting from ongoing development of production processes for our product candidates and (4) increased manufacturing process development and product production services for third parties. These increases were offset by lower costs in the 2005 period compared to the 2004 period related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA since significant portions of that initial work were completed in 2004.

General and Administrative. General and administrative expense was $7.8 million for the 2005 period compared to $6.6 million for the 2004 period. This expense included share-based compensation expense of

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$936,000 in the 2005 period and $205,000 in the 2004 period. This 18% increase in general and administrative expense was due to (1) higher share-based compensation expense, which increased for the reasons discussed below under Share-Based Compensation Expense, (2) increased consulting and professional fees related to the pursuit of foreign capital offset by (3) decreased costs related to securities offerings not pursued to completion in the 2004 period that were not repeated in the 2005 period.

Share-Based Compensation Expense. Share-based compensation expense was $1.3 million for the 2005 period compared to $253,000 for the 2004 period. The 514% increase in this expense was primarily due to the grant of shares of our common stock to certain of our officers in the 2005 period as a result of the expiration of certain of their stock options during that period and for which there was no similar transaction during the 2004 period.

During the 2005 period, options to purchase an aggregate of 191,200 shares of our common stock held by certain of our officers reached the end of their stated contractual ten year life, resulting in the expiration of the right to exercise those options. To provide those officers with an economic equivalent to those expired options, we granted them an aggregate of 178,362 shares of our common stock during the 2005 period, of which 113,349 shares were issued to those officers and 65,013 shares were withheld by us in consideration for our payment on their behalf of approximately $411,000 of federal income taxes. We recorded compensation expense of approximately $1.1 million in connection with these share issuances.

Our insider trading policy restricts sales of our common stock by our officers and employees. Accordingly, the expiring options described above could not be exercised pursuant to a cashless exercise program prior to their respective expiration dates due to these insider trading restrictions.

See Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations Recently Issued Accounting Pronouncements above for a discussion of our application of Statement of Financial Accounting Standards (SFAS) No. 123, Accounting for Stock-Based Compensation and the expected future effects of our adoption of SFAS No. 123R, Share-Based Payment.

Interest Income, Interest Expense and Other Income

Interest income was $787,000 for the 2005 period compared to $309,000 for the 2004 period, an increase of 155%. This increase was primarily due to (1) a higher overall average balance of cash, cash equivalents and short-term investments in the 2005 period compared to the 2004 period and (2) higher interest rates earned on our invested funds during the 2005 period compared to the 2004 period.

Interest expense was $621,000 for the 2005 period compared to $500,000 for the 2004 period, an increase of 24%. This increase was primarily due to (1) additional borrowings in the 2005 period to finance equipment acquisitions and (2) higher interest rates charged on borrowings originating in the 2005 period compared to borrowings originating in earlier periods.

Other income was $1.1 million for both the 2005 period and the 2004 period. This income is earned primarily from our sublease of space to M. D. Anderson Cancer Center for which there were no substantial change between periods in the business activity related to that lease.

Comparison of Years Ended December 31, 2004 and 2003

In the following comparison of years ended December 31, 2004, and December 31, 2003, references to the 2004 period refer to the year ended December 31, 2004, and references to the 2003 period refer to the year ended December 31, 2003.

Revenue

Contract Services, Grant and Other Revenue. For the 2003 and 2004 periods, we earned revenue from (a) research grants from U.S. Government agencies and (b) contract research services provided to Aventis, one of our stockholders, under an agreement through which Aventis provided funding for the conduct of a Phase 2 clinical trial of ADVEXIN therapy in breast cancer. In the 2003 period, we also earned revenue from

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third parties under agreements to provide manufacturing process development and product production services for them. Total contract services, grant and other revenue was $1.8 million for the 2004 period and $304,000 for the 2003 period, an increase of 492%. This increase was primarily due to increased grant funding earned under (1) our grant from the National Cancer Institute to support our Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma as a result of our increased activity related to that research and (2) the grant from the NIH held by Magnum, our wholly-owned subsidiary, as a result of our acquisition of Magnum in October 2004. During 2004, we earned $1.1 million under the grant held by Magnum.

Costs and Expense

Research and Development. Research and development expense consisted of the following (in thousands):

	Year Ended December 31,	
	2003	**2004**
Pre-clinical stage programs expense	$ 2,775	$ 2,632
Clinical stage programs expense	9,820	14,822
General research and development expense	2,378	3,020
Total research and development expense	$ 14,973	$ 20,474

Research and development expense was $20.5 million for the 2004 period, compared to $15.0 million for the 2003 period. This expense included share-based payments expense of $48,000 for the 2004 period and $242,000 for the 2003 period. This 37% increase in research and development expense was a result of increased activity related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work.

General and Administrative. General and administrative expense was $6.6 million for the 2004 period compared to $6.1 million for the 2003 period. This expense included share-based payments expense of $205,000 for the 2004 period and $1.1 million for the 2003 period. This 8% increase in general and administrative expense was primarily due to increased activity related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work. Also, in the 2004 period, we expensed $267,000 of costs incurred with respect to certain securities offering activities for the sale of our common stock during the first two quarters of 2004 that did not result in a closing of a sale of common stock.

Share-Based Compensation Expense. Share-based compensation expense was $253,000 for the 2004 period and $1.4 million for the 2003 period. This compensation for the 2003 period arose primarily as a result of:

Stock options granted to certain members of our Board of Directors for which some of the options were fully vested upon issuance and had exercise prices below the market value of our common stock at the date of grant, which resulted in compensation expense;

Stock options, which were fully vested upon issuance, issued to our corporate secretary, who is not a director or employee and for whom option grants result in compensation charges under fair value accounting; and

Amortization of deferred compensation remaining from stock options granted in earlier periods.

This compensation expense decreased for the 2004 period because:

The options granted to members of our Board of Directors during the 2004 period had exercise prices equal to the market value of our common stock at the date of grant, resulting in no compensation expense;

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The options granted to our corporate secretary during the 2004 period vest over multiple periods, resulting in recognition of some of the compensation expense arising from those options being deferred to future periods; and

Deferred compensation related to previously granted stock options became fully amortized in previous periods.

Interest Income, Interest Expense and Other Income

Interest income was $309,000 for the 2004 period compared to $1.0 million for the 2003 period, a decrease of 69%. Included in the 2003 amount was $775,000 we received from the settlement of litigation related to a decline in the market value of certain commercial paper we held as an investment in 2001. Excluding the amount from this settlement, interest income for the 2003 period was $225,000. Interest income for the 2004 period increased compared to interest income for the 2003 period, exclusive of the litigation settlement, primarily due to higher average cash balances during the 2004 period as a result of the proceeds received from the sales of our common stock in December 2003 and December 2004 and higher yields on invested funds for the 2004 period compared to the 2003 period.

Interest expense was $500,000 for the 2004 period compared to $624,000 for the 2003 period, a decrease of 20%. This decrease was primarily due to certain capital leases becoming fully paid in late 2003 and early 2004.

Other income was $1.1 million for the 2004 period and the 2003 period. This income is earned primary from our sublease of space to M. D. Anderson Cancer Center under which there were no significant changes between the 2003 and 2004 periods.

Liquidity and Capital Resources

In the following discussion of liquidity and capital resources, references to the 2005 period refer to the year ended December 31, 2005 and references to the 2004 period refer to the year ended December 31, 2004.

We have incurred annual operating losses since our inception. At December 31, 2005, we had an accumulated deficit of $143.5 million. From inception through December 31, 2005, we have financed our operations primarily from the following sources:

$49.7 million of collaborative research and development payments from Aventis;

$41.4 million of equity sales in December 2003 and December 2004 through registered direct offerings under a shelf registration filed with the Commission;

$39.4 million of private equity sales to Aventis;

$32.2 million of net proceeds from our initial public offering in October 2000;

$26.6 million of private equity sales, net of offering costs, to others (including $10.8 million from the private sale of our common stock in June 2003);

$19.6 million of equity sales, net of offering costs, to Colgate-Palmolive pursuant to an alliance agreement entered into in November 2005;

$19.2 million from contract services, grants, interest and other income;

$9.9 million in mortgage financing from banks for our facilities;

$7.5 million of sales of ADVEXIN therapy product to Aventis for use in later-stage clinical trials; and

$5.7 million in leases and notes payable from commercial lessors and lenders to acquire equipment pledged as collateral for those leases and notes.

At December 31, 2005, we had cash, cash equivalents and short-term investments of $33.1 million, compared to $38.2 million at December 31, 2004. Cash and cash equivalents constituted $28.1 million and

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$30.2 million of these amounts at December 31, 2005, and December 31, 2004, respectively. This decrease in cash and cash equivalents at December 31, 2005, as compared to December 31, 2004 was due to activity during the year ended December 31, 2005, that included (1) $21.7 million used in operating activities, (2) $589,000 used by investing activities and (3) $20.3 million provided by financing activities. We expect to continue to focus our activities primarily on conducting Phase 3 and other clinical trials, conducting data analysis related to those trials, preparing regulatory documentation submissions to the FDA, producing ADVEXIN therapy and other clinical materials for use in our clinical trials and conducting pre-marketing activities for ADVEXIN therapy. We expect to continue our research and development of various other targeted molecular therapy technologies. If ADVEXIN therapy or any of our other product candidates are approved for commercial sale by the FDA, we expect to conduct activities supporting the marketing, sales, production and distribution of those products, either ourselves or in collaboration with other parties. The majority of our expenditures for the foreseeable future will most likely be for these activities as they relate to ADVEXIN therapy. These activities may increase the rate at which we use cash in the future as compared to the cash we used for operating activities during the year ended December 31, 2005. We believe our existing working capital can fund our operations for the next 18 to 24 months, although we may have to make adjustments to the scope of operations to achieve that objective, and unforeseen events could shorten that time period. Our existing resources may not be sufficient to support the commercial introduction of any of our product candidates. In order to fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders.

Net cash used in operating activities was $21.7 million for the 2005 period compared to $21.5 million for the 2004 period. This increase was due to:

A larger net loss in the 2005 period compared to the 2004 period; and

An aggregate decrease in accounts payable and accrued liabilities during the 2005 period compared to an aggregate increase in accounts payable and accrued liabilities during the 2004 period due to variations in the timing of payments to vendors that is a function of the nature of vendors to whom we have obligations and variations in the terms of payment to them;

with the above items offset by:

Depreciation that increased in the 2005 period compared to the 2004 period due to acquisitions of property and equipment during and subsequent to the 2004 period for which the first full year of depreciation was the 2005 period;

Share-based compensation expense that increased in the 2005 period compared to the 2004 period due to the issuance of shares to certain officers in connection with expiring stock options as discussed above under Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations Comparison of the Year Ended December 31, 2005 and December 31, 2004 Share-Based Compensation Expense ;

An increase in amortization of grant rights acquired during the 2005 period compared to the 2004 period since such amortization was recorded throughout 2005 but for only a portion of 2004 because the rights being amortized arose in connection with our acquisition of Magnum in October 2004;

A decrease in other assets during the 2005 period compared to an increase in other assets during the 2004 period due to (1) a prepayment of certain expenses in the 2004 period that did not occur in the 2005 period and (2) a decrease in federal grant funding receivable during the 2005 period compared to an increase in federal grant funding receivable during the 2004 period due to the receipt in the 2005 period of grant funding earned during that period whereas grant funding earned during the 2004 period was received in subsequent periods; and

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An increase in deferred revenue during the 2005 period that was greater than the increase during the 2004 period due to an increase in payments from third parties in advance of us performing work under agreements to provide manufacturing process development services for them.

Net cash used in investing activities was $589,000 for the 2005 period compared to $9.1 million for the 2004 period. This decrease was primarily due to (1) a lower level of equipment purchases in the 2005 period compared to the 2004 period and (2) a lower level of net activity in purchases and maturities of short-term investments in the 2005 period compared to the 2004 period due to normal variations in the amount and timing of purchases and sales of short-term investments based on our operating needs for cash and cash equivalents and the availability of cash from sales of our common stock. These decreases were offset by our purchase of marketable securities during the 2005 period through our investment in SR Pharma as discussed above under Item 1. Business Overview Investment in SR Pharma plc.

We have no obligations at this time to purchase significant amounts of additional property or equipment, but our needs may change. It may be necessary for us to purchase larger amounts of property and equipment to support our clinical programs and other research, development and manufacturing activities. We may need to obtain debt or lease financing to facilitate such purchases. If that financing is not available, we may need to use our existing resources to fund those purchases, which could result in a reduction in the cash and cash equivalents available to fund operating activities.

Net cash provided by financing activities was $20.3 million during the 2005 period compared to $24.4 million during the 2004 period. This change was due to:

A decrease in proceeds from sales of common stock to third parties and a lower level of stock option exercises in the 2005 period compared to the 2004 period;

A decrease in proceeds from notes payable in the 2005 period compared to the 2004 period as the 2004 period included proceeds received from an amendment of a mortgage note in that period, which is an event that did not occur again in the 2005 period; and

An increase in principal payments under notes payable and capital leases in the 2005 period compared to the 2004 period due to additional borrowings subsequent to the 2004 period to finance equipment acquisitions.

We have an agreement with VirRx, which began in 2002, to purchase shares of VirRx s Series A Preferred Stock. Key activity and provisions under this agreement include the following:

From inception of this agreement through December 31, 2005, and during the year ended December 31, 2005, we have purchased $2,325,000 and $600,000, respectively, of VirRx s Series A Preferred Stock for cash. These purchases are recorded as research and development expense. We purchased an additional $150,000 of this stock for cash on January 1, 2006, which was our final scheduled quarterly purchase of such stock. We have no plans at this time to purchase additional shares of this stock except in the event of VirRx s achievement of prescribed milestones discussed below.

VirRx is required to use the proceeds from these stock sales in accordance with the terms of a collaboration and license agreement between VirRx and us for the development of VirRx s technologies. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice, which would also terminate the requirement for us to make any additional stock purchases.

Provided the collaboration and license agreement remains in place, we are required to make additional milestone stock purchases, either for cash or through the issuance of our common stock, upon the completion of Phase 1, 2 and 3 clinical trials involving technologies licensed under this agreement. We are required to make a $5.0 million cash milestone payment to VirRx, for which we receive no VirRx stock, upon approval by the FDA of a BLA for the first collaboration product based on these technologies. To the extent we have already made cash milestone payments, we may receive a credit of 50% of the Phase 2 clinical trial milestone payments and 25% of the Phase 3 clinical trial milestone payments against this $5.0 million cash milestone payment. The additional

milestone stock purchases

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and cash payment are not anticipated to be required in the near future. We have an option to purchase all outstanding shares of VirRx at any time until March 2007.

We have fixed debt service obligations under notes payable for which the liability is reflected on our balance sheet. We used the proceeds from these notes payable to finance facilities and equipment. Aggregate payments due under these obligations are as follows (in thousands):

Total debt service payments due during the year ending December 31:		
2006	$	1,293
2007		1,102
2008		777
2009		675
2010		670
Thereafter		9,486
Total debt service payments		14,003
Less portion representing interest		(5,463)
Total principal balance at December 31, 2005	$	8,540
Principal balance presented on the December 31, 2005 balance sheet as liabilities in these categories:		
Current portion of notes payable	$	756
Notes payable, net of current portion		7,784
Total principal balance at December 31, 2005	$	8,540

We have a fixed rent obligation under a ground lease for the land on which we built our facilities. Since this is an operating lease, there is no liability reflected on our balance sheet for this item, which is in accordance with generally accepted accounting principles. We make total annual rent payments of $156,000 under this lease which will continue until the expiration of the initial term of this lease in September 2026. Such payments are subject to adjustment in the future for inflation. Future minimum annual rental payments due under all operating leases are as follows (in thousands):

Year ending December 31, 2006	$	428
2007		344
2008		325
2009		225
2010		156
Thereafter		2,459
Total minimum lease payments under operating leases	$	3,937

In the normal course of business, we enter into various long-term agreements with vendors to provide services to us. Some of these agreements require up-front payment prior to services being rendered, some require periodic monthly payments and some provide for the vendor to bill us for their services as they are rendered. In substantially all cases, we may cancel these agreements at any time with minimal or no penalty and pay the vendor only for services actually rendered. Regardless of the timing of the payments under these agreements, we record the expense

incurred in the periods in which the services are rendered.

Pursuant to a consulting agreement, we pay consulting fees of approximately $175,000 per annum to EJ Financial, a company owned by the Chairman of our Board of Directors. EJ Financial provides us guidance on strategic product development, business development and marketing activities. We are obligated to continue paying this fee until we terminate the services of that company at our option.

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We have a consulting agreement with Jack A. Roth, M.D., Chairman of the Department of Thoracic Surgery and Director of the Keck Center for Gene Therapy at The University of Texas M. D. Anderson Cancer Center where he holds the Bud Johnson Clinical Distinguished Chair. Dr. Roth is the primary inventor of the technology upon which our ADVEXIN therapy is based and numerous other technologies we utilize. We licensed Dr. Roth s inventions from M. D. Anderson Cancer Center. Dr. Roth is our Chief Medical Advisor and chairman of our scientific advisory board. His duties involve the regular interaction and consultation with our scientists and others on our behalf. As compensation for his services and responsibilities, this consulting agreement provides for payments to Dr. Roth of $205,000 per annum, with that amount subject to adjustment for inflation in the future. These payments continue through the end of the consulting agreement term on September 30, 2009. We may terminate this agreement at our option upon one year s advance notice. If we had terminated this agreement as of December 31, 2005, we would have been obligated to make final payments totaling $205,000. Dr. Roth is one of our stockholders.

We have a consulting agreement with the placement agent and investment advisor who assisted us with the sale of our common stock in December 2004. We intend to pay them a fee of $25,000 per month on a month-to-month basis in consideration for their ongoing assistance with business development and financial matters.

We sublease a portion of our facilities to M. D. Anderson Cancer Center under a lease with a non-cancelable term that expires in 2009. M. D. Anderson Cancer Center is obligated to pay us rent and facilities operating expense reimbursements of approximately $94,000 per month through January 2006 and $28,000 per month thereafter.

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Quarterly Results of Operations

The following table sets forth certain unaudited quarterly financial data for the years ended December 31, 2004 and 2005. This information has been prepared on the same basis as the Consolidated Financial Statements and all necessary adjustments have been included in the amounts stated below to present fairly the selected quarterly information when read in conjunction with the Consolidated Financial Statements and notes thereto. Historical quarterly financial results and trends may not be indicative of future results.

	Three Months Ended							
	March 31, 2004	June 30, 2004	September 30, 2004	December 31, 2004	March 31, 2005	June 30, 2005	September 30, 2005	December 31, 2005
	(Unaudited) (In thousands, except per share amounts)							
Statement of Operations Data:								
Contract services, grant and other revenue	$ 109	$ 273	$ 209	$ 1,217	$ 509	$ 336	$ 398	$ 624
Operating expense:								
Research and development	4,295	5,948	5,734	4,497	5,239	5,700	5,090	5,371
General and administrative	1,444	2,147	1,710	1,.296	1,810	2,006	1,657	2,361
Loss from operations	(5,630)	(7,822)	(7,235)	(4,576)	(6,540)	(7,370)	(6,349)	(7,108)
Interest income (expense), net	(67)	(35)	(55)	(34)	34	35	8	89
Other income	250	306	269	242	275	274	277	272
Net loss	$ (5,447)	$ (7,551)	$ (7,021)	$ (4,368)	$ (6,231)	$ (7,061)	$ (6,064)	$ (6,747)
Basic and diluted net loss per share	$ (0.21)	$ (0.28)	$ (0.26)	$ (0.16)	$ (0.20)	$ (0.23)	$ (0.18)	$ (0.19)
Shares used in computing basic and diluted net loss per share	26,566	26,607	26,703	27,886	30,741	31,182	33,394	35,742

Contractual Obligations

The following table summarizes our contractual obligations as of December 31, 2005:

				More
		Two to	Four to	than Five

	Total	One Year or Less	Three Years	Five Years	Years
			(In thousands)		
Long-term debt	$ 14,003	$ 1,293	$ 1,879	$ 1,345	$ 9,486
Operating leases	3,937	428	669	381	2,459
Employment agreements	329	329			
Consulting agreements	862	298	410	154	
Total	$ 19,131	$ 2,348	$ 2,958	$ 1,880	$ 11,945

Off-Balance Sheet Arrangements

As of December 31, 2005, we did not have any significant off-balance sheet arrangements, as defined in Item 303(a)(4)(ii) of Regulation S-K.

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Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

Interest Rate Risk

Our exposure to market risk for changes in interest rates relates primarily to our fixed rate long-term debt and short-term investments in investment grade securities, which consist primarily of federal government obligations. Investments are classified as held-to-maturity and are carried at amortized cost. We do not hedge interest rate exposure or invest in derivative securities. A hypothetical 100-basis point decrease in the interest rates of our investments at the investment balances as of December 31, 2005 would decrease our interest income by approximately $331,000.

At December 31, 2005, the fair value of our fixed-rate debt approximated its carrying value based upon discounted future cash flows using current market prices.

Equity Price Risk and Foreign Currency Exchange Rate Risk

From time to time, we may invest in marketable securities of public companies, typically in the form of equity instruments, for business and strategic purposes. We own British Pound-denominated shares in SR Pharma, a publicly traded company listed on the Alternative Investment Market of the LSE. These marketable securities are classified as available-for-sale. Unrealized gains and losses in these marketable securities and the related foreign currency translation adjustments are reported as a separate component of accumulated other comprehensive income (loss) in stockholders equity until realized. We are exposed to market risk for changes in equity prices and foreign currency translation adjustments as a result of our investments in marketable securities.

These marketable securities are subject to significant fluctuation in fair value due to the volatility of the industry in which SR Pharma participates and changes in the relative foreign currency values. We do not hedge our equity price risk or foreign currency translation exposure or invest in derivative securities. A hypothetical 10% decrease in the stock price of our marketable securities as of December 31, 2005 would decrease the value of those marketable securities by approximately $290,000. A hypothetical 10% decrease in the value of the British Pound as of December 31, 2005 would decrease the fair value of our marketable securities by approximately $290,000. A hypothetical 10% decrease in the stock price of our marketable securities and a hypothetical 10% decrease in the value of the British Pound, in each case as of December 31, 2005, would decrease the fair value of our marketable securities by approximately $550,000.

Our purchase price for these SR Pharma marketable securities was approximately $3.0 million. At December 31, 2005, the fair value of these marketable securities was approximately $2.9 million, which is approximately $100,000 less than our cost. The impact of the foreign currency translation adjustment in the relative values of the Pound and the U.S. dollar was not material during this period.

Item 8. ***Financial Statements and Supplementary Data***

The information required by this Item is set forth in our Consolidated Financial Statements and notes thereto beginning on page F-3 of this Annual Report on Form 10-K.

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

Not applicable.

Item 9A. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures. Our management evaluated, with the participation of our Chief Executive Officer and our Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit

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under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in Commission rules and forms.

Changes in Internal Control over Financial Reporting. There was no change in our internal control over financial reporting that occurred during the last fiscal quarter covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management s Annual Report on Internal Control over Financial Reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Under the supervision and with the participation of our management, including our President and Chief Executive Officer and our Chief Financial Officer, we assessed the effectiveness of our internal control over financial reporting as of the end of the period covered by this report based on the framework in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions and that the degree of compliance with the policies or procedures may deteriorate.

Based on its assessment of internal control over financial reporting, management has concluded that, as of December 31, 2005, our internal control over financial reporting was effective to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with United States generally accepted accounting principles.

Our independent registered public accounting firm, Ernst & Young LLP, has issued an attestation report on our management s assessment of our internal control over financial reporting. The attestation report is included on page F-1 of this Annual Report on Form 10-K.

Item 9B. ***Other Information***

Not applicable.

PART III

Item 10. ***Directors and Executive Officers of the Registrant***

The information required by this Item is incorporated by reference to the information under the sections captioned Election of Directors, Executive Officers, Section 16(a) Beneficial Ownership Reporting Compliance and Code of Ethics contained in our 2006 Proxy Statement.

Item 11. ***Executive Compensation***

The information required by this Item is incorporated by reference to the information under the section captioned Executive Compensation contained in our 2006 Proxy Statement.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management***

The information required by this Item is incorporated by reference to the information under the sections captioned Security Ownership and Equity Compensation Plan Information contained in our 2006 Proxy Statement.

Item 13. ***Certain Relationships and Related Transactions***

The information required by this Item is incorporated by reference to the information under the sections captioned Certain Relationships and Related Transactions and Compensation Committee Interlocks and Insider Participation contained in our 2006 Proxy Statement.

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Item 14. ***Principal Accounting Fees and Services***

The information required by this Item related to principal accountant fees and services as well as related pre-approval policies is incorporated by reference to the information under the sections captioned Fees Paid to Ernst & Young LLP and Audit Committee Pre-Approval of Audit and Permissible Non-Audit Services of Independent Auditors contained in our 2006 Proxy Statement.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

1. *Consolidated Financial Statements*

The following financial statements are filed as part of this Annual Report on Form 10-K:

2. *Financial Statement Schedules*

All financial statement schedules are omitted because they are not applicable or not required, or because the required information is included in the Consolidated Financial Statements or notes thereto.

3. *Exhibits*

(a) *Exhibits*

Exhibit Number	Description of Document
3.1(a)(6)	Certificate of Incorporation as currently in effect
3.1(b)(6)	Amendment to Certificate of Incorporation, effective as of December 21, 2001
3.1(c)(13)	Amendment to Certificate of Incorporation, effective as of August 6, 2004
3.2(4)	Bylaws of Introgen Therapeutics, Inc. (Introgen) as currently in effect
4.1(2)	Specimen Common Stock Certificate
4.2(5)	Certificate of Designations of Series A Non-Voting Convertible Preferred Stock
4.3(9)	Form of Stock Purchase Warrant
4.4(20)	Form of Stock Purchase Warrant
10.1(1)	Form of Indemnification Agreement between Introgen and each directors and officers
10.2(1)*	1995 Stock Plan and form of stock option agreement thereunder
10.3(3)*	2000 Stock Option Plan and forms of stock option agreement thereunder
10.3(14)*	2000 Stock Option Plan form of stock option agreement, as amended
10.4(3)*	2000 Employee Stock Purchase Plan and forms of agreements thereunder
10.5(1)	Form of Series C Preferred Stock Purchase Agreement among Introgen and certain investors
10.6(1)	Registration Rights Agreement, dated October 31, 1997
10.7(a)(1)	Assignment of Leases, dated November 23, 1998, by TMX Realty Corporation and Riverway Bank, and other related agreements

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Exhibit Number	Description of Document
10.7(b)(1)	Lease Agreement, dated June 7, 1996, by and between Introgen and Plaza del Oro Business Center
10.7(c)(2)	Amendment No. 1 to Lease Agreement, effective as of May 9, 1997
10.7(d)(2)	Amendment No. 2 to Lease Agreement, effective as of July 31, 1998
10.7(e)(2)	Amendment No. 3 to Lease Agreement, effective as of June 29, 2000
10.7(f)(13)	Modification Agreement effective April 1, 2004 by TMX Realty Corporation and Texas State Bank (formerly known as Riverway Bank), and other related agreements
10.8(a) (1)	Patent and Technology License Agreement, effective as of July 20, 1994, by and between The Board of Regents of The University of Texas System, M. D. Anderson Cancer Center and Introgen
10.8(b) (1)	Amendment No. 1 to Patent License Agreement, effective as of September 1, 1996
10.9 (3)	Sponsored Research Agreement for Clinical Trial, No. CS 93-27, dated February 11, 1993, between Introgen and M. D. Anderson, as amended
10.10	Reserved
10.11 (3)	Sponsored Research Agreement No. SR 93-04, dated February 11, 1993 between M. D. Anderson and Introgen, as amended
10.12	Reserved
10.13 (3)	Sponsored Research Agreement No. SR 96-004 between Introgen and M. D. Anderson, dated January 17, 1996
10.14	Reserved
10.15 (3)	License Agreement, dated March 29, 1996 between Introgen and SKCC
10.16(1)	Consulting Agreement between Introgen and Jack A. Roth, M.D., effective as of October 1, 1994
10.17(1)	Consulting Agreement between EJ Financial Enterprises, Inc. and Introgen, effective as of July 1, 1994
10.18(d)(15)*	Employment Agreement dated as of August 1, 2003 between Introgen and David G. Nance
10.19(1)	Service Agreement, effective as of July 1, 1994, between Introgen and Domecq Technologies, Inc.
10.20(a) (1)	Collaboration Agreement (p53 Products), effective as of October 7, 1994, between Introgen and RPR, as amended
10.20(b) (3)	Addendum No. 1 to Collaboration Agreement (p53 Products), dated January 23, 1996, between Introgen and RPR
10.20(c) (1)	1997 Agreement Memorandum, effective as of July 22, 1997, between Introgen and RPR
10.20(d) (3)	Letter Agreement, dated April 19, 1999, from Introgen to RPR regarding manufacturing process for ADVEXIN therapy
10.21(a) (1)	Collaboration Agreement (K-ras Products), effective as of October 7, 1994, between Introgen and RPR, as amended
10.21(b)(1)	Amendment No. 1 to Collaboration Agreement (K-ras Products), effective as of September 27, 1995, between Introgen and RPR
10.22 (3)	Collaborative Research and Development Agreement dated October 30, 1998 between Introgen, RPR and NCI
10.23 (1)	

		Non-Exclusive License Agreement, effective as of April 16, 1997, by Introgen and Iowa Research Foundation
10.24	(3)	Option Agreement, effective as of June 1, 1998, by Introgen and Imperial Cancer Research Technology Limited (ICRT)
10.25	(3)	Option Agreement, effective as of January 1, 1999, by Introgen and ICRT
10.26	(3)	Exclusive License Agreement, effective as of July 19, 1999, by Introgen and Corixa Corporation

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Exhibit Number	Description of Document
10.27(a)	Reserved
10.27(b)(1)	Letter dated January 28, 2000, from Introgen to LXR Biotechnology (LXR), notifying LXR of its exercise of its option
10.27(c) (2)	Exclusive License Agreement, effective as of May 16, 2000, by and between Introgen and LXR
10.28 (3)	Administrative Services and Management Agreement, effective as of January 1, 1999, by and between Introgen and Gendux, Inc.
10.29 (3)	Research and Development Agreement, effective as of January 1, 1999, by and between Introgen and Gendux, Inc.
10.30 (3)	Delivery Technology License Agreement, effective as of January 1, 1999, by and between Introgen and Gendux, Inc.
10.31 (3)	Target Gene License Agreement, effective as of January 1, 1999, by and between Introgen and Gendux, Inc.
10.32 (1)	Non-Exclusive License Agreement, effective as of August 17, 1998, by and between Introgen and National Institutes of Health
10.33	Reserved
10.34(2)	Master Lease Agreement, effective as of August 4, 1999, by and between Introgen and Finova Capital Corporation
10.35(2)	Construction Loan Agreement, effective as of July 24, 2000, by and between Introgen and Compass Bank
10.36 (5)	Restated p53 and K-ras Agreement, effective as of June 30, 2001, by and among Introgen, Aventis Pharmaceuticals Inc. (API) and Aventis Pharma S.A. (Aventis)
10.37(5)	p53 Assignment Agreement, effective as of June 30, 2001, by and among Introgen, API and Aventis
10.38(5)	K-ras Assignment Agreement, effective as of June 30, 2001, by and among Introgen, API and Aventis
10.39(5)	Registration Rights Agreement, effective as of June 30, 2001, by and among Introgen, API and RPR
10.40(5)	Voting Agreement, effective as of June 30, 2001, by and among Introgen, API and RPR
10.41(7)	Master Services Agreement, effective as of July 9, 2001, by and between Introgen and PPD Development, LLC
10.42(8)	Series A Preferred Stock Purchase Agreement, effective as of March 7, 2002, by and between Introgen and VirRx, Inc.
10.43(8)	Collaboration and License Agreement, effective as of March 7, 2002, by and between Introgen and VirRx, Inc.
10.44(9)	Securities Purchase Agreement, effective as of June 18, 2003, by and among Introgen and the Investors named therein
10.45(10)	Placement Agent Agreement, effective as of November 26, 2003, by and among Introgen, SG Cowen Securities Corporation and First Albany Capital Inc.
10.46(11)	Placement Agent Agreement, dated December 6, 2004, by and between Introgen and Mulier Capital Limited
10.47(16)*	Stock Purchase Agreement dated May 2, 2005, by and between Introgen and David G. Nance
10.48(16)*	

	Stock Purchase Agreement dated May 2, 2005, by and between Introgen and J. David Enloe, Jr.
10.49(17)	Letter Agreement dated July 26, 2005, by and between Introgen and SR Pharma plc
10.50(18)	Letter Agreement dated April 20, 2005 by and between Introgen and Suiter Limited

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Exhibit Number	Description of Document
10.51(19)*	Stock Purchase Agreement dated October 26, 2005, by and between Introgen and David G. Nance
10.52(20)	Letter Agreement Amendment dated July 14, 2005, by and between Introgen and Suiter Limited
10.53	Oral Healthcare Alliance Agreement dated November 4, 2005, by and between Introgen and Colgate-Palmolive Company
10.54	Common Stock Purchase Agreement dated November 4, 2005, by and between Introgen and Colgate-Palmolive Company
10.55(21)	Letter Agreement dated February 24, 2006, by and between Introgen and Aventis Pharmaceuticals, Inc.
14.1(12)	Code of Conduct and Ethics
21.1	List of subsidiaries of Introgen
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (See page 65)
31.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended
32.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(1) Incorporated by reference to the same-numbered exhibit filed with our Registration Statement on Form S-1 (No. 333-30582) filed with the Commission on February 17, 2000.

(2) Incorporated by reference to the same-numbered exhibit filed with Amendment No. 2 to our Registration Statement on Form S-1 (No. 333-30582) filed with the Commission on September 8, 2000.

(3) Incorporated by reference to the same-numbered exhibit filed with Amendment No. 3 to our Registration Statement on Form S-1 (No. 333-30582) filed with the Commission on October 4, 2000.

(4) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended December 31, 2000, (File No. 000-21291), filed with the Commission on February 14, 2001.

(5) Incorporated by reference to the same-numbered exhibit filed with our Annual Report on Form 10-K for the fiscal year ended June 30, 2001 (File No. 000-21291), filed with the Commission on September 19, 2001.

(6) Incorporated by reference to the same-numbered exhibit filed with our Transition Report on Form 10-KT for the six-month transition period ended December 31, 2001 (File No. 000-21291), filed with the Commission on March 20, 2002.

(7) Incorporated by reference to the same-numbered exhibit filed with Amendment No. 1 to our Transition Report on Form 10-KT for the six-month transition period ended December 31, 2001 (File No. 000-21291), filed with the Commission on March 26, 2002.

(8) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended March 31, 2002 (File No. 000-21291), filed with the Commission on May 15, 2002.

(9) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the Commission on June 18, 2003.

(10) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the Commission on November 26, 2003.

(11) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the Commission on December 10, 2004.

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(12) See Access to Company Information on page 1 of this Annual Report on Form 10-K.

(13) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended June 30, 2004 (File No. 000-21291), filed with the Commission on August 16, 2004.

(14) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended September 30, 2004 (File No. 000-21291), filed with the Commission on November 15, 2004.

(15) Incorporated by reference to the same-numbered exhibit filed with Amendment No. 1 to our Form 10-K/ A for the fiscal year ended December 31, 2003 (File No. 000-21291), filed with the Commission on April 29, 2004.

(16) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the Commission on May 4, 2005.

(17) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the Commission on August 1, 2005.

(18) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended June 30, 2005 (File No. 000-21291), filed with the Commission on August 9, 2005.

(19) Incorporated by reference to the exhibit filed with our Current Report on Form 8-K, filed with the Commission on November 1, 2005.

(20) Incorporated by reference to the same-numbered exhibit filed with our Quarterly Report on Form 10-Q, for the quarter ended September 30, 2005 (File No. 000-21291), filed with the Commission on November 9, 2005.

(21) Incorporated by reference to the exhibit filed with our Current Report on Form 8-K, filed with the Commission on February 24, 2006.

Confidential treatment has been granted for portions of this exhibit.

Confidential treatment has been requested for portions of this exhibit.

* Indicates management contract or compensatory plan or arrangement.

(b) *Exhibits*

See Item 15(3) above.

(c) *Financial Statement Schedules*

See Item 15(2) above.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

INTROGEN THERAPEUTICS, INC.
By: /s/ DAVID G. NANCE

David G. Nance
President, Chief Executive Officer and Director
(Principal Executive Officer)
By: /s/ JAMES W. ALBRECHT, JR.

James W. Albrecht, Jr.
Chief Financial Officer
(Principal Financial and Accounting Officer)

Date: March 16, 2006

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints David G. Nance and James W. Albrecht, Jr. and each of them acting individually, as his or her attorney-in-fact, each with full power of substitution, for him or her in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed on behalf of the Registrant by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ DAVID G. NANCE (David G. Nance)	President, Chief Executive Officer, and Director (Principal Executive Officer)	March 16, 2006
/s/ JAMES W. ALBRECHT, JR (James W. Albrecht, Jr.)	Chief Financial Officer (Principal Financial and Accounting Officer)	March 16, 2006
/s/ JOHN N. KAPOOR, PH.D. (John N. Kapoor, Ph.D.)	Chairman of the Board and Director	March 16, 2006
/s/ WILLIAM H. CUNNINGHAM, PH.D (William H. Cunningham, Ph.D.)	Director	March 12, 2006
/s/ MALCOLM GILLIS, PH.D (Malcolm Gillis, Ph.D.)	Director	March 16, 2006

/s/ CHARLES E. LONG (Charles E. Long)	Director	March 16, 2006
/s/ PETER BARTON HUTT (Peter Barton Hutt)	Director	March 16, 2006

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Introgen Therapeutics, Inc. and Subsidiaries

We have audited management s assessment, included in the accompanying Management s Report on Internal Control Over Financial Reporting, that Introgen Therapeutics, Inc. and Subsidiaries maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Introgen Therapeutics, Inc. s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management s assessment and an opinion on the effectiveness of the company s internal control over financial reporting based on our audit.

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

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

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

In our opinion, management s assessment that Introgen Therapeutics, Inc. and Subsidiaries maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Introgen Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Introgen Therapeutics, Inc. and Subsidiaries as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three fiscal years in the period ended December 31, 2005 of Introgen Therapeutics, Inc. and Subsidiaries and our report dated March 10, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Austin, Texas

March 10, 2006

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Introgen Therapeutics, Inc. and Subsidiaries

We have audited the accompanying consolidated balance sheets of Introgen Therapeutics, Inc. and Subsidiaries as of December 31, 2005 and 2004, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Introgen Therapeutics, Inc. and Subsidiaries at December 31, 2005 and 2004, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Introgen Therapeutics, Inc. and Subsidiaries s internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 10, 2006 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Austin, Texas

March 10, 2006

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONSOLIDATED BALANCE SHEETS

	December 31,	
	2004	2005
	(Amounts in thousands)	
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 30,187	$ 28,090
Short term investments	7,993	5,032
Total cash, cash equivalents and short term investments	38,180	33,122
Marketable securities		2,892
Prepaid expense and other current assets	659	297
Total current assets	38,839	36,311
Property and equipment, net of accumulated depreciation of $10,983 and $12,588, respectively	7,277	6,181
Grant rights acquired	1,582	163
Other assets	359	326
Total assets	$ 48,057	$ 42,981
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	$ 2,683	$ 2,258
Accrued liabilities	3,572	3,296
Deferred revenue	30	472
Current portion of notes payable	573	756
Total current liabilities	6,858	6,782
Notes payable, net of current portion	7,901	7,784
Deferred revenue, long-term	1,132	1,404
Total liabilities	15,891	15,970
Commitments and Contingencies (Note 10)		
Stockholders Equity:		
Preferred stock, $.001 par value per share; 5,000 shares authorized; 4,900 shares issuable; 100 and zero Series A shares issued and outstanding in 2004 and 2005, respectively	1	
Common stock, $.001 par value per share; 100,000 shares authorized; 30,622 and 37,147 shares issued and outstanding in 2004 and 2005, respectively	30	37
Additional paid-in capital	149,652	170,675
Deferred compensation	(161)	(68)
Accumulated deficit	(117,356)	(143,459)

Accumulated other comprehensive loss		(174)
Total stockholders equity	32,166	27,011
Total liabilities and stockholders equity	$ 48,057	$ 42,981

The accompanying notes are an integral part of these Consolidated Financial Statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2003	2004	2005
	(Amounts in thousands, except per share amounts)		
Contract services, grant and other revenue	$ 304	$ 1,808	$ 1,867
Operating costs and expense:			
Research and development	14,973	20,474	21,400
General and administrative	6,102	6,597	7,834
Total operating costs and expense	21,075	27,071	29,234
Loss from operations	(20,771)	(25,263)	(27,367)
Interest income	1,017	309	787
Interest expense	(624)	(500)	(621)
Other income	1,052	1,067	1,098
Net loss	$ (19,326)	$ (24,387)	$ (26,103)
Net loss per share, basic and diluted	$ (0.84)	$ (0.91)	$ (0.80)
Shares used in computing basic and diluted net loss per share	22,902	26,943	32,780

The accompanying notes are an integral part of these Consolidated Financial Statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY

	Series A Non-Voting Convertible Preferred Stock		Common Stock		Additional			Accumulated Other	
	Shares	Amount	Shares	Amount	Paid-In Capital	Deferred Compensation	Accumulated Deficit	Comprehensive Loss	Total
					(Amounts in thousands)				
Balance, December 31, 2002	100	$ 1	21,487	$ 21	$ 94,430	$ (974)	$ (73,643)	$	$ 19,835
Issuance of common stock in a private equity offering in June 2003, net of offering costs of $729			2,000	3	10,769				10,772
Issuance of common stock in a direct equity offering in December 2003, net of offering costs of $1,473			2,859	3	18,540				18,543
Issuance of common stock in connection with exercise of stock options and warrants			193		98				98
Addition to deferred compensation relating to issuance of stock options, net of reversals					433	39			472
Amortization of deferred compensation and share-based compensation						891			891
Net loss							(19,326)		(19,326)
Balance, December 31, 2003	100	$ 1	26,539	$ 27	$ 124,270	$ (44)	$ (92,969)	$	$ 31,285
			3,451	3	22,891				22,894

Issuance of common stock in a direct equity offering in December 2004, net of offering costs of $1,366								
Issuance of common stock in connection with exercise of stock options			380		644			644
Issuance of common stock in connection with asset acquisition			252		1,477			1,477
Addition to deferred compensation relating to issuance of stock options, net of reversals					370	(297)		73
Amortization of deferred compensation and share-based compensation						180		180
Net loss							(24,387)	(24,387)
Balance, December 31, 2004	100	$ 1	30,622	$ 30	$ 149,652	$ (161)	$ (117,356)	$ $ 32,166
Issuance of common stock in a direct equity offering in November 2005, net of offering costs of $414			3,611	4	19,581			19,585
Issuance of common stock in connection with exercise of stock options			457		615			615
Issuance of common stock in connection with the grant of stock			113		687			687
Addition to deferred compensation relating to issuance of stock options					142	(142)		
	(100)	(1)	2,344	3	(2)			

Conversion of preferred stock to common stock							
Amortization of deferred compensation and share-based compensation				235			235
Comprehensive loss					(26,103)		(26,103)
Net loss							
Unrealized loss on marketable securities						(149)	(149)
Foreign currency translation adjustment, cumulative translation loss of $25 at December 31, 2005						(25)	(25)
Total comprehensive loss							(26,277)
Balance, December 31, 2005	$	37,147	$ 37	$ 170,675	$ (68)	$ (143,459)	$ (174)	$ 27,011

The accompanying notes are an integral part of these Consolidated Financial Statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2003	2004	2005
	(Amounts in thousands)		
Cash flows from operating activities:			
Net loss	$ (19,326)	$ (24,387)	$ (26,103)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	1,475	1,322	1,605
Share-based compensation	1,362	253	922
Amortization of grant rights acquired		159	1,419
Changes in assets and liabilities:			
(Increase) decrease in other assets	523	(532)	395
Increase (decrease) in accounts payable	280	629	(425)
Increase (decrease) in accrued liabilities	538	773	(275)
Increase (decrease) in deferred revenue	204	270	714
Net cash used in operating activities	(14,944)	(21,513)	(21,748)
Cash flows from investing activities:			
Purchases of property and equipment	(233)	(1,097)	(509)
Purchases of short-term investments		(38,383)	(31,869)
Maturities of short-term investments		30,390	34,830
Purchase of marketable securities			(3,041)
Net cash used in investing activities	(233)	(9,090)	(589)
Cash flows from financing activities:			
Proceeds from sale of common stock, net of offering costs	29,315	22,894	19,585
Proceeds from exercise of options for common stock	98	644	615
Proceeds from notes payable	314	1,448	772
Principal payments under notes payable and capital leases	(1,620)	(593)	(707)
Net cash provided by financing activities	28,107	24,393	20,265
Effect of exchange rate changes on cash			(25)
Net increase (decrease) in cash	12,930	(6,210)	(2,097)
Cash and cash equivalents, beginning of period	23,467	36,397	30,187
Cash and cash equivalents, end of period	$ 36,397	$ 30,187	$ 28,090
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 624	$ 472	$ 580

Cash paid for taxes for the issuance of common stock in connection with the grant of common stock	$	$	$ 411
Supplemental disclosure of non-cash investing and financing activities:			
Grant rights acquired in asset acquisition	$	$ (1,741)	$
Common stock issued for the asset acquisition	$	$ 1,477	$
Liabilities assumed in asset acquisition	$	$ 272	$
Issuance of common stock in connection with the grant of stock	$	$	$ 687
Purchases of equipment under capital lease obligations	$ 314	$	$
Proceeds from insurance financing notes	$	$ 123	$ 117

The accompanying notes are an integral part of these Consolidated Financial Statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2005

1. Formation and Business of the Company

Introgen Therapeutics, Inc., a Delaware corporation, and our subsidiaries are biopharmaceutical companies focused on the discovery, development and commercialization of targeted molecular therapies for the treatment of cancer and other diseases. We are developing product candidates to treat a wide range of cancers using tumor suppressors, cytokines and other targeted molecular therapies. These agents are designed to increase production of normal cancer-fighting proteins that act to overpower cancerous cells, stimulate immune activity and enhance conventional cancer therapies.

Our primary approach to the treatment of cancers is to deliver targeted molecular therapies that increase production of normal cancer-fighting proteins. Our products work by acting as templates for the transient *in vivo* production of proteins that have pharmacological properties. The resultant proteins engage disease-related molecular targets or receptors to produce a specific therapeutic effect.

We believe the use of molecular therapies that are cleared from the body after administration in order to induce the production of biopharmaceutical proteins is an emerging field presenting a new approach for treating many cancers without the toxic side effects common to traditional therapies. We have developed significant expertise in developing targeted therapies that may be used to treat disease, and in using what we believe are safe and effective delivery systems to transport these agents to cancer cells. We believe we are able to treat a number of cancers in a way that kills cancer cells without harming normal cells.

Our lead product candidate, ADVEXIN® therapy, combines the p53 tumor suppressor with a non-replicating, non-integrating, adenoviral delivery system we have developed and extensively tested. The p53 molecule is one of the most potent members of a group of naturally-occurring tumor suppressors, which act to kill cancer cells, arrest cancer growth and protect cells from becoming cancerous. We are developing other product candidates for the treatment of cancer using other molecules and delivery systems, such as the mda-7 tumor suppressor.

We believe our research and development expertise gained from our targeted molecular therapies for cancer is also applicable to other diseases that, like cancer, result from cellular dysfunction and uncontrolled cell growth. As a result, we are conducting research in collaboration with medical institutions to understand the safety and effectiveness of our targeted molecular therapy product candidates in the treatment of other diseases.

We typically license the technologies on which our products are based from third parties. These licenses generally grant us exclusive rights for pre-clinical and clinical development, manufacturing, marketing and commercialization of product candidates based on those technologies.

Our product research and development efforts include pre-clinical activities as well as the conduct of Phase 1, 2 and 3 clinical trials. We rely on third parties to treat patients in their facilities under these clinical trials. We produce ADVEXIN therapy and other product candidates in manufacturing facilities we own and operate using production methods we developed. We hold a number of patents or patents pending on certain product candidates and manufacturing processes used to produce certain product candidates.

We have not yet generated any significant revenue from unaffiliated third parties, nor is there any assurance of future product 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 revenue from the commercial sale of our products in the near future. We may never generate revenue from the commercial sale of our products.

Our research and development activities involve a high degree of risk and uncertainty, and our ability to successfully develop, manufacture and market our proprietary products is dependent upon many factors. These factors include, but are not limited to, the need for and the ability to obtain additional financing, the reliance

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on collaborative research and development arrangements with corporate and academic affiliates and the ability to develop manufacturing, sales and marketing experience. Additional factors include uncertainties as to patents and proprietary technologies, competitive technologies, technological change and risk of obsolescence, development of products, competition, government regulations and regulatory approval, and product liability exposure. As a result of these factors and the related uncertainties, there can be no assurance of our future success.

Since our inception in 1993, we have used our resources primarily to conduct research and development activities for ADVEXIN therapy and, to a lesser extent, other product candidates. As of December 31, 2005, we had an accumulated deficit of approximately $143.5 million. We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities continue and as we evolve our operations and systems to support commercialization of our product candidates. These losses, among other things, have caused and may cause our total assets, stockholders equity and working capital to decrease in the future.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying Consolidated Financial Statements include our accounts and all of our subsidiaries. Intercompany transactions and balances are eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expense during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents include amounts on deposit with financial institutions and investments that are readily convertible to cash and so near their maturity that they present insignificant risk of changes in value because of changes in interest rates. These investments have original maturities of three months or less. Our investments generally consist of securities in the form of United States federal government obligations.

Short-term Investments

Our short-term investments are carried at an amount that approximates amortized cost and consist primarily of fixed income securities issued by the United States government. We have the positive intent and ability to hold such securities until their respective maturity dates, which are less than one year from the date of purchase. As of December 31, 2005, the carrying value approximates the market value of these investments.

Marketable Securities

Our marketable securities consist of issued share capital of other public companies and are classified as available-for-sale. Unrealized gains and losses are computed using the published share price of the applicable stock exchange at the close of business on the last day of the reporting period and are reported as a separate component of accumulated other comprehensive income (loss) in shareholders equity until realized.

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Fair Value of Financial Instruments

Our financial instruments consist primarily of cash and cash equivalents, short term investments, marketable securities, and accounts payable. We believe all of these financial instruments are recorded at amounts that approximate their current market values.

Risks and Uncertainties

Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash and cash equivalents, short term investments, and marketable securities. We place these financial instruments with high credit quality financial institutions and issuers.

Intangible Assets

Grant rights acquired, which are presented as an intangible asset on our balance sheet, resulted from our asset acquisition related to the Magnum purchase in October 2004. We amortize that asset to expense on a straight-line basis over the estimated remaining life of that asset. We review purchased intangible assets for impairment whenever changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Such evaluations compare the carrying amount of an asset to future undiscounted net cash flows expected to be generated by the asset over its expected useful life. If the asset is considered to be impaired, we record an impairment charge equal to the amount by which the carrying value of the asset exceeds its fair value determined by utilizing a discounted cash flow technique.

Property and Equipment

Property and equipment are carried at cost, less accumulated depreciation. Maintenance, repairs and minor replacements are charged to expense as incurred. Depreciation is provided generally using accelerated methods based on useful lives of fifteen years for research, manufacturing and administrative facilities and five to seven years for equipment. Interest incurred during construction of facilities is capitalized as a cost of those facilities.

Property and equipment consists of the following items (in thousands):

	December 31,	
	2004	**2005**
Facilities	$ 12,415	$ 12,524
Equipment	5,845	6,245
Total property and equipment	18,260	18,769
Less accumulated depreciation	(10,983)	(12,588)
Net property and equipment	$ 7,277	$ 6,181

Substantially all of our facilities are pledged as collateral for the mortgage notes payable described in Note 8. A portion of our equipment is pledged as collateral for the equipment notes payable described in Note 8.

Federal Income Taxes

We recognize deferred tax liabilities and assets for the expected future tax consequences of events that have been recognized differently between the financial statements and tax returns. Under this method, deferred tax liabilities and assets are determined based on the difference between the financial statement carrying amounts and tax bases of liabilities and assets using enacted tax rates and laws in effect in the years in

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which the differences are expected to reverse. Deferred tax assets are evaluated for realization based on more-likely-than-not criteria in determining if a valuation should be provided.

Accrued Liabilities

Accrued liabilities consist of the following significant items (in thousands):

	December 31,	
	2004	**2005**
Clinical costs due unrelated parties	$ 803	$ 267
Pre-clinical costs due related parties	631	677
Pre-clinical costs due unrelated parties	138	124
Property taxes	421	366
Franchise and use taxes	219	312
Payroll	64	78
Vacation	249	349
Legal and accounting fees	549	490
Other vendor charges not yet billed	498	633
Total accrued liabilities	$ 3,572	$ 3,296

In conducting our pivotal Phase 3 clinical trials of ADVEXIN therapy, we procure services from multiple third party vendors. The cost of these services constitutes a significant portion of the cost of these trials and of our research and development expense in general. Some of our vendors do not necessarily bill us for their services on a regular basis and, accordingly, make it difficult for us to determine the costs we have incurred relative to their services for any given accounting period. As a result, we make significant accounting estimates as to the amount of costs we have incurred relative to these vendors in each accounting period. These estimates are based on many factors, including, among others, costs set forth in our contracts with these vendors, the period of time over which the vendor has rendered the services and the rate of enrollment of patients in our clinical trials. Using these estimates, we record expense and accrued liabilities in each accounting period that we believe fairly represent our obligations to these vendors. Actual results could differ from these estimates resulting in increases or decreases in the amount of expense recorded and the related accrual.

Revenue Recognition

Contract services revenue is recognized when the related services are completed and delivered to the customer. Deferred revenue is recorded as cash received in advance of completion of these services.

Grant revenue is recognized as research expense relating to a grant is incurred and the work contemplated under the grant has been performed.

Rental income from the sublease of laboratory space to third parties under leases that have variable monthly rent amounts over the term of the lease is recognized on a straight-line basis over the term of the lease. Any cash payments received in excess of rental income recognized is recorded as deferred revenue. Rental income is included in other income in the accompanying Consolidated Statement of Operations.

Research and Development Costs

In conducting our clinical trials of ADVEXIN therapy and other product candidates, we procure services from numerous third-party vendors. The cost of these services constitutes a significant portion of the cost of

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these trials and of our research and development expense in general. These vendors do not necessarily provide us billings for their services on a regular basis and, accordingly, are often not a timely source of information to determine the costs we have incurred relative to their services for any given accounting period. As a result, we make significant accounting estimates as to the amount of costs we have incurred relative to these vendors in each accounting period. These estimates are based on numerous factors, including, among others, costs set forth in our contracts with these vendors, the period of time over which the vendor will render the services and the rate of enrollment of patients in our clinical trials. Using these estimates, we record expense and accrued liabilities in each accounting period that we believe fairly represent our obligations to these vendors. Actual results could differ from these estimates, resulting in increases or decreases in the amount of expense recorded and the related accrual. We have consistently applied these estimation procedures in the past and plan to continue applying such procedures in the same manner during the foreseeable future. Our experience has been that our estimates have reasonably reflected the expense we actually incur.

Net Loss Per Share

Net loss per share is computed using the weighted average number of shares of common stock outstanding. Due to losses incurred in all periods presented, the shares associated with stock options, warrants and non-voting convertible preferred stock are not included because they are anti-dilutive.

Share-Based Compensation

Statement of Financial Accounting Standards (SFAS) No. 123, Accounting for Stock-Based Compensation, allows companies to adopt one of two methods for accounting for stock options. We have elected the method that requires disclosure only of share-based compensation. Because of this election, we continue to account for our employee share-based compensation plans, using the intrinsic value method, under Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees, as clarified by Interpretation No. 44, Accounting for Certain Transactions Involving Stock Compensation. Accordingly, deferred compensation is recorded for share-based compensation grants based on the excess of the fair market value of the common stock on the measurement date over the exercise price. The deferred compensation is amortized ratably over the vesting period of each unit of share-based compensation grant, generally four years. If the exercise price of the share-based compensation grants is equal to the fair value of our shares on the date of grant, no compensation expense is recorded.

In December 2004, SFAS No. 123R, Share-Based Payment, was issued. This statement establishes standards for the accounting for transactions in which an entity exchanges its equity investments for goods and services. It also addresses transactions in which an entity incurs liabilities in exchange for goods or services that are based on the fair value of the entity s equity instruments or that may be settled by the issuance of those equity instruments. The statement does not change the accounting guidance for share-based payments with parties other than employees. The statement requires measurement of the cost of employee service received in exchange for an award of equity instruments based on the grant-date fair value of the award, with limited exceptions. That cost is to be recognized over the period during which an employee is required to provide service in exchange for the award, which is usually the vesting period of the award. A public entity will initially measure the cost of employee services received in exchange for an award of a liability instrument based on the instrument s current fair value. The fair value of that award will be remeasured subsequently at each reporting date through the settlement date. Changes in fair value during the requisite service period will be recognized as compensation over that period. The grant date fair value of employee share options and similar instruments will be estimated using option pricing models adjusted for the unique characteristics of these instruments.

We will be required to comply with SFAS No. 123R for the annual reporting period beginning January 1, 2006. We have not yet determined which fair-value method and transitional provision we will follow. We

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expect the adoption of SFAS No. 123R will have a significant impact on our results of operations. We do not expect such adoption to significantly impact our financial position or liquidity. See the table in the following paragraph for the pro forma impact on net loss and net loss per share from calculating share-based compensation costs under the fair value alternative of SFAS No. 123. The calculation of compensation cost for share-based payment transactions after the effective date of SFAS No. 123R may be different from the calculation of compensation cost under SFAS No. 123, but such differences have not yet been quantified.

The fair value of options granted for all periods presented was estimated on the applicable grant dates using the Black-Scholes option pricing model. Significant weighted average assumptions used to estimate fair value for all years include: risk-free interest rates ranging from 3% to 6%; expected lives of ten years; no expected dividends; and volatility factors ranging from 62% to 107%. Had compensation expense been determined consistent with the provisions of SFAS No. 123, our net loss would have been increased to the following pro forma amounts (in thousands, except per share information):

	Year Ended December 31,		
	2003	2004	2005
Net loss, as reported	$ (19,326)	$ (24,387)	$ (26,103)
Add: Share-based employee compensation expense included in reported net loss	1,169	32	1,098
Deduct: Total share-based employee compensation expense determined under fair value based method for all awards	(4,126)	(2,834)	(5,268)
Pro forma net loss	$ (22,283)	$ (27,189)	$ (30,273)
Loss per share:			
Basic and Diluted as reported	$ (0.84)	$ (0.91)	$ (0.80)
Basic and Diluted pro forma	$ (0.97)	$ (1.01)	$ (0.92)

See Note 6 for a discussion of stock purchase warrants issued in connection with our sales of common stock in June 2003 and December 2004.

Accumulated Other Comprehensive Loss

Accumulated other comprehensive loss is included as a component of stockholders equity and is composed of foreign currency translation adjustments and unrealized gains and losses on investments designated as available-for-sale securities. Accumulated comprehensive loss is calculated as follows (in thousands):

	Year Ended December 31,		
	2003	2004	2005
Net loss	$ (19,326)	$ (24,387)	$ (26,103)
Foreign currency translation loss			(25)
Unrealized loss on marketable securities			(149)

Total comprehensive loss	$ (19,326)	$ (24,387)	$ (26,277)

3. Acquisition of Magnum Therapeutics Corporation

In October 2004, we acquired all of the outstanding capital stock of Magnum, a company owned prior to this acquisition by one of our executive officers. We paid approximately $1.75 million for the Magnum stock by (1) issuing approximately 252,000 shares of our common stock valued at approximately $1.48 million at the acquisition date and (2) assuming liabilities of approximately $272,000. With respect to the common

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stock we issued for the acquisition, 50% of the shares were held by an independent escrow agent for a period of approximately one year subsequent to the acquisition date to satisfy the indemnification obligations of the selling shareholder under terms of the purchase agreement. Such shares were released from escrow in January 2006.

Magnum s primary asset is the funding it receives under a research grant from the NIH, which supplements our ongoing research and development programs. During the years ended December 31, 2005 and 2004, we earned $1.0 million and $1.1 million of revenue under this grant. In the event certain of Magnum s technologies result in commercial products, we may be obligated to pay royalties related to the sales of those products to certain third parties.

The results of Magnum s operations have been included with ours for the period subsequent to the October 2004 acquisition date. Since Magnum was a development stage company at the time we acquired it, this acquisition has been accounted for as an asset acquisition and not as a business combination.

The total purchase consideration has been allocated to the assets acquired based on their respective fair values at the date of acquisition. The following presents the fair value of the net assets acquired (in thousands):

Cash and cash equivalents	$ 9
Acquired grant rights	$ 1,741

4. Intangible Assets

Intangible Assets With Definite Lives

Our intangible assets with definite lives that are subject to amortization, all of which arose from our acquisition of Magnum in October 2004 described in Note 3, are as follows (in thousands):

	December 31,					
	2004			2005		
	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
Asset Acquisition:						
Acquired Grant Rights	$ 1,741	$ (159)	$ 1,582	$ 1,741	$ (1,578)	$ 163
Ending Balance	$ 1,741	$ (159)	$ 1,582	$ 1,741	$ (1,578)	$ 163

Research and development expense includes amortization of intangibles of $1,419,000 for the year ended December 31, 2005 and $159,000 for the year ended December 31, 2004. We had no intangibles on our balance sheet in years prior to 2004, such that there was no amortization expense in those years. Amortization of intangibles for the year ended December 31, 2005 reflects a change in the estimated useful life of the acquired grant rights from 22 months to 17 months. The effect of this change was to increase amortization expense in 2005 and decrease amortization expense in 2006 by $470,000 or $0.01 per share. Estimated annual amortization expense for fiscal year 2006 is $163,000 and zero thereafter.

5. Investment in SR Pharma plc

In July 2005, we purchased approximately 8.3% of the issued share capital of SR Pharma for approximately $3.0 million. SR Pharma is a European biotechnology company publicly traded on the Alternative Investment Market of the LSE that is developing oncology and other products. This investment is classified as marketable securities on

our balance sheet. Marketable securities are classified as available-for-sale and are presented at estimated fair value with any unrealized gains or losses included in other

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comprehensive income (loss). At December 31, 2005, these marketable securities had a fair market value of $2.9 million.

6. Stockholders Equity

Stock Sales

In November 2005, we sold approximately 3.6 million shares of our common stock in a direct equity sale to Colgate-Palmolive pursuant to a shelf registration statement for an aggregate purchase price of approximately $20.0 million. Our net proceeds from this transaction, after related fees and expense, were approximately $19.6 million. See Note 9 for further discussion of our agreement with Colgate-Palmolive.

In December 2004, we sold approximately 3.5 million shares of our common stock in a direct equity offering pursuant to a shelf registration statement for an aggregate purchase price of approximately $24.3 million. Our net proceeds from this transaction, after related fees and expense, were approximately $22.9 million. In connection with this transaction, we have issued or will issue warrants to the placement agents representing us in this stock sale to purchase up to 225,238 shares of our common stock at a price of $6.65 per share and to purchase up to 88,707 shares of our common stock at a price of $8.00 per share. These warrants are exercisable beginning in December 2005 and expire in December 2009.

In December 2003, we sold 2,859,427 newly-issued shares of our common stock in a registered direct offering for an aggregate purchase price of approximately $20.0 million. Our net proceeds from this transaction, after related fees and expense, were approximately $18.5 million.

In June 2003, we sold 2.0 million newly-issued shares of our common stock to selected institutional investors through a private placement for an aggregate purchase price of $11.5 million. Our net proceeds from this transaction, after related fees and expense, were $10.8 million. In connection with this sale, we issued warrants to purchase 400,000 shares of our common stock at $7.89 per share. These warrants are exercisable at any time by the warrant holders through June 2008. Beginning in June 2005, we may force the exercise of these warrants if the average closing market price of our common stock during any 20 consecutive trading days is greater than $15.78 per share.

Common Stock Grant to Officers

Options to purchase 191,200 shares of our common stock held by certain of our officers reached the end of their stated contractual ten year life during the 2005 period, resulting in the expiration of the right to exercise those options. To provide those officers an economic equivalent to those expired options, we granted them an aggregate of 178,362 shares of our common stock during the 2005 period, of which 113,349 shares were issued to those officers and 65,013 shares were withheld by us in consideration for our payment on their behalf of approximately $411,000 of federal income taxes. This expense related to employee federal income taxes, plus compensation expense not requiring cash of $687,000, resulted in total share-based compensation expense of $1.1 million related to these transactions.

Our insider trading policy restricts sales of our common stock by our officers and employees. Accordingly, the expiring options described above could not be exercised pursuant to a cashless exercise program prior to their respective expiration dates due to these insider trading restrictions.

Conversion of Series A Non-Voting Convertible Preferred Stock to Common Stock

In 2001, we sold 100,000 shares of $0.001 par value, Series A Non-Voting Convertible Preferred Stock to Aventis for $25.0 million. In June 2005, these shares were converted into 2,343,721 shares of our common stock. The preferred shares were cancelled and replaced by newly issued shares of our common stock. The

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preferred shares cancelled are no longer issuable. We received no cash or other consideration in connection with this conversion.

Under a voting agreement related to these shares, Aventis must vote these shares 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 June 2011 or the sale of these shares pursuant to an effective registration statement on the open market or to an Aventis non-affiliate, as defined in the voting agreement. A registration rights agreement related to these shares 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.

After this conversion, we have 5.0 million shares of authorized and unissued preferred shares, of which 100,000 shares have been cancelled and 4.9 million shares are undesignated and issuable.

Stock Option Plans

The 2000 Stock Option Plan (Stock Option Plan) was initiated in October 2000 and all stock option grants since that time have been under this plan. The Stock Option Plan provides for the granting of options, either incentive or non-statutory, or stock purchase rights to our employees, directors and consultants to purchase shares of our common stock. This plan provides for annual increases each January 1 in the number of shares available for issuance in an amount equal to the lesser of 1.6 million shares, 5% of the outstanding shares on the date of the annual increase, or a lesser amount as may be determined by the Board of Directors. After this latest annual increase and at January 1, 2006, there were 2,652,000 shares of common stock reserved for future option grants under this plan. In the event of a merger, reorganization or change in our controlling ownership, all options outstanding under the Stock Option Plan become fully vested and immediately exercisable unless the successor corporation assumes or substitutes other options in their place. The Stock Option Plan will terminate in 2010 and may be amended or terminated by the Board of Directors.

Prior to October 2000, stock options were granted under our 1995 Stock Plan. We no longer issue options under this plan. The terms of this plan are substantially the same as the Stock Option Plan. No shares of common stock were reserved for future option grants under this plan at December 31, 2005.

For options issued to persons other than our employees or members of our board of directors, we compute compensation expense based on the fair value of the options. For options issued to our employees or members of our board of directors, if the option exercise price is less than the quoted market price of our common stock on the date the option is granted, we compute compensation expense based on the intrinsic value of the options. For options issued to our employees or members of our board of directors for which the option exercise price is equal to or greater than the quoted market price of our common stock on the date the option is granted, we compute no compensation expense. We record compensation expense in our financial statements ratably over the vesting period of each option.

Additional deferred compensation and paid-in capital recorded in stockholders equity related to stock options was $39,000, ($297,000) and ($142,000) during the years ended December 31, 2003, 2004 and 2005, respectively.

Expense recorded from the amortization of deferred compensation related to stock options was $891,000, $180,000 and $235,000 during the years ended December 31, 2003, 2004 and 2005, respectively.

Reversals of deferred compensation and additional paid-in capital for unamortized deferred compensation related to the forfeiture of non-vested options by terminated employees was zero during the years ended December 31, 2005 and 2004 and $93,000 during the year ended December 31, 2003.

In addition to share-based compensation expense resulting from the amortization of deferred compensation, we also have incurred share-based compensation expense for which there is no related deferred

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compensation. In 2005, we recorded compensation expense of $1.1 million as a result of granting shares to certain of our officers in connection with expiring stock options (see *Common Stock Grant to Officers* above). In 2004, we recorded compensation expense of (1) $35,000 resulting from the acceleration of vesting of options previously granted to a certain member of the Board of Directors upon his resignation from the Board of Directors and (2) $38,000 as a result of granting stock options fully vested upon issuance to a non-employee consultant for whom options granted are subject to fair value accounting. In 2003, we recorded compensation expense of $471,000 as a result of granting stock options fully vested upon issuance to (1) certain members of our Board of Directors for which some of the options have exercise prices below the market value of our common stock at the date of grant and (2) our corporate secretary, who is not a director or employee and for whom options granted are subject to fair value accounting.

The following is a summary of option activity under these plans:

	Options Outstanding	Weighted Average Exercise Price per Share
Balance, December 31, 2002	3,986,093	$ 2.18
Granted	1,269,890	4.91
Exercised	(193,488)	1.46
Cancelled	(306,094)	3.20
Balance, December 31, 2003	4,756,401	2.91
Granted	1,472,551	6.03
Exercised	(380,294)	1.72
Cancelled	(290,384)	6.02
Balance, December 31, 2004	5,558,274	3.65
Granted	1,256,138	6.55
Exercised	(456,714)	1.35
Cancelled	(379,329)	2.81
Balance, December 31, 2005	5,978,369	4.49
Exercisable at December 31, 2005	3,583,200	$ 3.65

The weighted average fair value of options granted during the years ended December 31, 2003, 2004 and 2005 were $4.63, $5.43 and $5.71, respectively.

All options granted during the periods set forth in the table above have an exercise price equal to the fair value of our common stock as of the date of grant, with the exception of 265,000 options granted in 2003 to certain members of our Board of Directors and our corporate secretary at exercise prices of $4.00 and $5.00 per share. These exercise prices were below the quoted market value of our common stock of $5.58 per share on the date these options were granted.

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The following table summarizes information about stock options outstanding as of December 31, 2005:

Options Outstanding				Options Exercisable	
Range of Exercise Price	Outstanding as of December 31, 2005	Weighted Average Remaining Contractual Life (In years)	Weighted Average Exercise Price	Exercisable as of December 31, 2005	Weighted Average Exercise Price
$0.39-$3.50	1,490,913	3.75	$ 1.08	1,349,863	$ 1.03
$3.75-$4.92	1,139,775	6.58	4.43	903,775	4.49
$5.00-$6.18	1,691,461	7.60	5.21	912,781	5.14
$6.25-$9.65	1,656,220	9.02	6.87	416,781	7.04
	5,978,369	6.84	4.49	3,583,200	3.65

Employee Stock Purchase Plan

Under our 2000 Employee Stock Purchase Plan (Stock Purchase Plan), 780,000 shares of common stock are reserved for purchase by eligible employees, at 85% of the appropriate market price. The Stock Purchase Plan provides for an increase on each January 1 in the number of shares available for issuance, in an amount equal to the lesser of 480,000 shares, 1.5% of the outstanding shares of common stock on the date of the annual increase or such lesser amount as may be determined by the Board of Directors. The Stock Purchase Plan provides that eligible employees may authorize payroll deductions of up to 10% of their qualified compensation. The maximum number of shares that an employee may purchase in a single offering period is 10,000 shares. The Stock Purchase Plan will terminate in 2010 and may be amended or terminated by the Board of Directors. During the year ended June 30, 2001, 22,561 shares of common stock were purchased by employees under this plan. There have been no common stock purchases since that time, as we have suspended operation of the Stock Purchase Plan until further notice by the Board of Directors.

Shares Reserved For Future Issuance

We have reserved a total of 10,123,979 shares of our common stock for issuance in the future with respect to (1) our Stock Option Plan, (2) our Stock Purchase Plan and (3) stock purchase warrants issued in connection with our sales of common stock in June 2003 and December 2004.

Common Stock Purchase Warrant

We previously had an agreement with a third party under which they were to perform investor relations services on our behalf focusing on the sophisticated, global financial community. The agreement provided for us to issue this third party a warrant to purchase up to 500,000 shares of our common stock under certain circumstances. We have cancelled this agreement in accordance with its terms and have no obligation to issue this stock purchase warrant.

7. Federal Income Taxes

As of December 31, 2005, we have generated federal net operating loss carryforwards of approximately $111 million, orphan drug credits of approximately $9.9 million and research and development credits of approximately $978,000 available to reduce future income taxes. These carryforwards begin to expire in 2007. A change in ownership, as defined by federal income tax regulations, could significantly limit our ability to utilize these

carryforwards. Additionally, because United States tax laws limit the time during which these carryforwards may be applied against future taxes, we may not be able to take full advantage of these attributes for federal income tax purposes.

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Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred taxes as of December 31 are as follows (in thousands):

	2004	2005
Deferred tax assets:		
Current deferred tax assets		
Accrued liabilities	$ 601	$ 799
Unrealized gains and losses		64
Other	33	
Valuation allowance for current deferred tax assets	(625)	(862)
Net current deferred tax assets	9	1
Noncurrent deferred tax assets		
Net operating loss carryforwards	33,261	40,242
Research and development tax credits	1,448	1,625
Orphan drug tax credits	7,908	9,878
Tax basis of property and equipment in excess of book basis	2,477	2,949
Stock compensation	1,662	1,380
Deferred rent	419	520
Investments		860
Other		62
Valuation allowance for noncurrent deferred tax assets	(46,510)	(57,377)
Net noncurrent deferred tax assets	665	139
Deferred tax liabilities:		
Current deferred tax liabilities		
Prepaid expense	(89)	(80)
Total current deferred tax liabilities	(89)	(80)
Noncurrent deferred tax liabilities		
Acquired grant rights	(585)	(60)
Total noncurrent deferred tax liabilities	(585)	(60)
Net current deferred tax asset (liability)	(80)	(79)
Net noncurrent deferred tax asset (liability)	$ 80	$ 79

As we have had cumulative losses and there is no assurance of future taxable income, a valuation allowance has been established to fully offset the net deferred tax asset. During the year ended December 31, 2004, the valuation allowance increased $16.1 million primarily due to losses from operations and decreased by $644,000 due to the

difference between book and tax basis of acquired Magnum assets and assumed liabilities. During the year ended December 31, 2005, the valuation allowance increased by $11.1 million due primarily to losses from operations. Approximately $407,000 of the valuation allowance relates to tax benefits for stock option deductions included in the net operating loss carryforward, which when realized, will be allocated directly to contributed capital to the extent the benefits exceed amounts attributable to deferred compensation expense.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Undistributed earnings of our foreign subsidiaries are considered permanently reinvested and, accordingly, no provision for U.S. federal or state income taxes has been provided thereon.

Our provision for income taxes differs from the expected tax expense (benefit) amount computed by applying the statutory federal income tax rate of 34% to income from continuing operations before taxes due to the following:

	Year Ended December 31,		
	2003	2004	2005
Federal statutory rate	(34.0)%	(34.0)%	(34.0)%
State taxes, net of federal benefit	(2.8)	(2.6)	(2.8)
Increase in deferred tax valuation allowance	39.5	66.0	42.5
Stock option compensation	2.4	(7.4)	1.1
Orphan drug tax credits		(20.9)	(5.0)
Research and development tax credits	(2.9)	(2.5)	(0.7)
Other	(2.2)	1.4	(1.1)
	%	%	%

8. Notes Payable

In May 2004, we amended the mortgage note payable to a bank related to our facilities. The original $6.0 million principal balance of our mortgage note payable was increased to $7.8 million. The proceeds from this increase were used to pay in full the principal and interest outstanding on a second mortgage note payable with an original principal balance of approximately $3.3 million, which resulted in that second mortgage note being retired. In addition to this note retirement, the proceeds from this loan amendment were used to pay the costs related to this transaction of $96,000 and to add $668,000 to our cash and cash equivalents.

The amended mortgage note payable bears interest at 6.25%. The note is payable in monthly installments of $56,400 until May 2006. At that time, we may, at our option, extend the note to a November 2009 maturity date. Upon such extension, the interest rate is modified to the lesser of (a) 2.5% above the five-year U.S. Treasury Bond Note rate or (b) 8.5%, and principal and interest on the note become payable in equal monthly installments based on a 225-month amortization period. The principal balance outstanding on the note s extended maturity date is payable in full at that time. The note payable had an outstanding balance of $7,482,000 and $7,675,000 at December 31, 2005 and 2004, respectively. The second mortgage note payable that was retired using the proceeds from the amendment of the mortgage note payable had an outstanding balance of zero at December 31, 2005 and December 31, 2004. Our facilities are pledged as security for the mortgage note payable.

We financed $655,000 and $560,000 of equipment acquisitions under notes payable to commercial finance companies during the years ended December 31, 2005 and 2004, respectively. The notes are payable monthly over terms of 36 to 60 months from the time of the draw and bear interest at fixed interest rates ranging from zero to 10.6% at December 31, 2005. These notes payable are secured by the equipment being financed.

In connection with our construction of facilities, we capitalized interest of $6,000 as a cost of those facilities during the year ended December 31, 2004. No such construction occurred during the years ended December 31, 2005 and 2003 for which interest capitalization was required.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Aggregate annual maturities on notes payable as of December 31, 2005, are as follows (in thousands):

Year ending December 31, 2006	$	756
2007		623
2008		340
2009		257
2010		267
Thereafter		6,297
Total	$	8,540

We believe the fair market value of our debt approximates its carrying value as of all balance sheet dates presented herein. At December 31, 2003, the current portion of notes payable and capital lease obligations included $125,000 of capital lease obligations retired in full in 2004.

9. License and Research Agreements

Patent and Technology License Agreement With The University of Texas System

We have a license agreement with The Board of Regents of The University of Texas System (the System) and M. D. Anderson Cancer Center, a component institution of the System, whereby we have an exclusive, worldwide license to use certain technology. Beginning with the first commercial sale of a product incorporating the licensed technologies, we will pay M. D. Anderson Cancer Center, for the longer of fifteen years or the life of the patent, a royalty based on net sales by us or our affiliates or by sublicense agreement of products incorporating any of such technologies. We are obligated by the agreement to reimburse any of M. D. Anderson Cancer Center s costs that may be incurred in connection with obtaining patents related to the licensed technologies.

VirRx, Inc.

We are working with VirRx to investigate other vector technologies, specifically replication-competent viral therapies, for delivering products into targeted cells. These technologies form the basis for our INGN 007 product candidate.

We have an agreement with VirRx, which began in 2002, to purchase shares of VirRx s Series A Preferred Stock for $150,000 on the first day of each fiscal quarter through January 1, 2006. From inception of this agreement through December 31, 2005, and during the year ended December 31, 2005, we have purchased $2,325,000 and $600,000, respectively, of this stock for cash. We record these purchases as research and development expense. VirRx is required to use the proceeds from these stock sales in accordance with the terms of a collaboration and license agreement between VirRx and us for the development of VirRx s technologies. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice.

Provided the collaboration and license agreement remains in place, we are required to make additional milestone stock purchases, either for cash or through the issuance of our common stock, upon the completion of Phase 1, 2 and 3 clinical trials involving technologies licensed under this agreement. We are required to make a $5.0 million cash milestone payment to VirRx, for which we receive no VirRx stock, upon approval by the FDA of a Biologics License Application for the first collaboration product based on these technologies. To the extent we have already made cash milestone payments, we may receive a credit of 50% of the Phase 2 clinical trial milestone payments and 25% of the Phase 3 clinical trial milestone payments against this $5.0 million cash milestone payment. The additional milestone stock purchases and cash payment are not

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

anticipated to be required in the near future. We have an option to purchase all outstanding shares of VirRx at any time until March 2007.

In accordance with the provisions of Financial Accounting Standards Board Interpretation 46(R), Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51, VirRx is not consolidated in our financial statements.

Alliance Agreement with Colgate-Palmolive Company

In November 2005, we entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. In connection with the alliance agreement and pursuant to a common stock purchase agreement, Colgate-Palmolive purchased 3,610,760 shares of our common stock at a purchase price of $5.539 per share for a total of approximately $20.0 million. These shares are subject to trading and transfer restrictions for one year from the date of purchase. Under the common stock purchase agreement, Colgate-Palmolive also agreed to vote these shares and any other shares of our capital stock owned by it in favor of corporate actions approved by our Board of Directors. This voting agreement is subject to suspension or termination upon certain events specified in the common stock purchase agreement.

Pursuant to the alliance agreement, we will conduct research and development activities involving specialized formulations of our molecular therapies (such as p53, mda-7 and FUS-1) targeted at precancerous conditions of the oral cavity and at oral cancer. The objective is to market these formulations as oral healthcare products. Excluded from the alliance agreement is our current portfolio of cancer product candidates, including ADVEXIN therapy, INGN 241, INGN 225 and INGN 401.

Under the alliance agreement, Colgate-Palmolive has a first right to negotiate development, manufacturing, marketing and distribution rights with us for specifically designed oral healthcare products for use in the human oral cavity that may result from these research and development activities. In addition, we agreed to use commercially reasonable efforts to develop one or more specialized oral formulations through completion of Phase 2 clinical trials within the seven-year term of the alliance agreement. We can terminate our development efforts earlier under certain circumstances, including if the prospects for these products do not warrant further investment, or if we expend $15.0 million in this effort. In calculating the amount of our expenditures on these efforts, we may include grant funding received by us or our collaborators for work performed by third parties (e.g., universities and other institutions) that is directly related to program activities, as specified in the alliance agreement. The term of the alliance agreement continues to November 2012, unless earlier terminated by the parties as provided in the alliance agreement.

Other Technology Option and License Agreements

We have various other technology option and license agreements with various third parties related to certain molecular therapies or delivery systems that are part of other product candidates we are developing. These agreements require us to make milestone and license payments to these parties if and when we achieve certain prescribed clinical trial and product development milestones. We also license certain enabling technologies under technology option and license agreements with other third parties, which require annual payments aggregating $40,000 until cancelled at our option.

10. Commitments and Contingencies

Lease Commitments

We are obligated under various operating leases for land, office and laboratory space that expire at various dates through September 2026. Rent expense was $365,000, $316,000 and $301,000 for the years ended

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

December 31, 2005, 2004 and 2003, respectively. Future minimum lease payments under non-cancelable operating leases as of December 31, 2005, are as follows (in thousands):

	Operating Leases
Year ending December 31, 2006	$ 428
2007	344
2008	325
2009	225
2010	156
Thereafter	2,459
Total minimum lease payments	$ 3,937

Insurance and Litigation

We are subject to numerous risks and uncertainties because of the nature and status of our operations, and to claims and legal actions arising in the normal course of business. We maintain insurance coverage for events and in amounts that we deem appropriate. Management believes that uninsured losses, if any, would not be materially adverse to our financial position or results of operations.

Employment Agreement

We have an employment agreement with our President and Chief Executive Officer that provides for a base salary and bonuses through July 31, 2006.

11. Related Parties

The Chairman of our Board of Directors, who is also one of our stockholders, owns a company to which we pay consulting fees of approximately $175,000 per year. We are obligated to continue paying this fee until such time as we, at our option, terminate the services of that company. As of December 31, 2005, this person held options to purchase 142,200 shares of our common stock.

We have a consulting agreement with an individual primarily responsible for the creation of the technology upon which ADVEXIN therapy is based, who is also a stockholder. Under this consulting agreement, we paid this individual fees of $202,000, $200,000 and $188,000 during the years ended December 31, 2005, 2004 and 2003 respectively. This consulting agreement provides for payments of $205,000 per annum through the end of its term on September 30, 2009, with such future payments subject to adjustment for inflation. We may terminate this agreement at our option upon one year s advance notice.

We have a consulting agreement with the placement agent and investment advisor who assisted us with the sale of our common stock in December 2004. We intend to pay them a fee of $25,000 per month on a month-to-month basis in consideration for their ongoing assistance with business development and financial matters.

We sublease a portion of our facilities to M. D. Anderson Cancer Center under a lease with a non-cancelable term that expires in 2009. M. D. Anderson Cancer Center is obligated to pay us rent of approximately $94,000 per month until January 2006 and approximately $28,000 per month thereafter for a total of $405,000 in 2006, $340,000 in 2007 and 2008 and $170,000 in 2009. Rental income was $1,068,000, $1,045,000 and $1,012,000 for the years ended December 31, 2005, 2004 and 2003, respectively.

We fund certain research performed by M. D. Anderson Cancer Center to further the development of technologies that could have potential commercial viability. By sponsoring and funding this research, we have

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

the right to include certain patentable inventions arising therefrom under our patent and technology license agreement with The University of Texas System described in Note 9. The expense for this research was approximately $243,000, $581,000 and $885,000 for the years ended December 31, 2005, 2004 and 2003, respectively.

We received funding from Aventis for a Phase 2 clinical trial for breast cancer conducted under our supervision. We recorded revenue of zero, $13,000 and $56,000 for the years ended December 31, 2005, 2004 and 2003, respectively, related to this work.

In October 2004, we acquired all of the outstanding capital stock of Magnum, a company owned prior to this acquisition by one of our executive officers. See Note 3 for further discussion.

12. London Stock Exchange

We are evaluating the feasibility of listing our common stock on the LSE, which would be in addition to the listing of our common stock on the NASDAQ National Market System in the United States. We believe an LSE listing may allow us to better leverage our assets on a global basis and, specifically, in Europe and Asia.

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EXHIBIT INDEX

Exhibit Number	Description of Document
10.53	Oral Healthcare Alliance Agreement dated November 4, 2005, by and between Introgen and Colgate-Palmolive Company
10.54	Common Stock Purchase Agreement dated November 4, 2005, by and between Introgen and Colgate-Palmolive Company
21.1	List of subsidiaries of Introgen
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (See page 65)
31.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Securities Exchange Act, as amended
32.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Confidential treatment has been requested for portions of this exhibit.