INTROGEN THERAPEUTICS INC
Form 424B3
November 29, 2005

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Filed pursuant to Rule 424(b)(3)
Registration No. 333-129687

PROSPECTUS

4,341,569 Shares of Common Stock

The selling stockholders named on page 30 of this prospectus will use this prospectus to resell all or a portion of up to 4,341,569 shares of our common stock.

We will not receive any proceeds from the sale of our common stock sold by the selling stockholders.

Our common stock is traded on The Nasdaq National Market under the symbol INGN. On November 28, 2005, the last reported sale price for the common stock on The Nasdaq National Market was $6.19 per share.

Before you invest, you are urged to carefully read this prospectus and all of the information incorporated by reference herein. Our business, and an investment in our common stock, involves significant risks. These risks and certain other information associated with an investment in our common stock are discussed in the Risk Factors section beginning on page 14 of this prospectus and in the documents incorporated by reference into this prospectus.

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

The date of this prospectus is November 29, 2005.

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SUMMARY

This summary presents a brief overview of Introgen Therapeutics, Inc. and the key aspects of the offering and may not contain all of the information that may be important to you or that you should consider before investing in our common stock. You should read the entire prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors. You should also review our consolidated financial statements, the notes to those financial statements and the other financial information incorporated by reference into this prospectus. All references to Introgen, the Company, the Registrant, we, us or our mean Introgen Therapeutics, Inc.

Product Development 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 non-integrating tumor suppressors, cytokines and molecular gene agents. 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 genes that increase production of normal cancer-fighting proteins. Rather than acting to repair or replace aberrant or missing genes and thereby creating a long-term or permanent change to the patient s genome, our products work in a different manner 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 genes that do not integrate into the patient s genome and 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 identifying therapeutic genes, which are genes that may be used to treat disease, and in using what we believe are safe and effective delivery systems to transport these genes 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.

We have entered into an alliance agreement with Colgate-Palmolive Company (Colgate-Palmolive) to develop and potentially market oral healthcare products. See the Alliance with Colgate-Palmolive Company section below for further discussion of this alliance agreement.

ADVEXIN® Therapy (p53)

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

We have received Fast Track designation for ADVEXIN therapy from the U.S. Food and Drug Administration (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,

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the FDA will take actions to expedite the evaluation and review of a Biologics License Application (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 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. 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, 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.

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.

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. 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 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

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reduction of tumor size greater than or equal to 50% of the pre-treatment size. We have been evaluating subpopulations of patients participating in these trials defined by various prognostic, medical and biological characteristics to provide refined targeting of ADVEXIN therapy. Analyses of the data from these patient subpopulations showed that the objective response rate (complete responses and partial responses) was 15% or greater. 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 systemic chemotherapy for the treatment of breast cancer prior to surgery and a Phase 1 clinical trial using ADVEXIN therapy in patients with locally recurrent breast cancer involving the chest wall. In the breast cancer study of 12 women with very large tumors, the combination of ADVEXIN and chemotherapy resulted in objective clinical responses with greater than 50% tumor reduction in all patients and the ability to remove all of the tumors surgically. These data are better than the expected results with chemotherapy alone and were presented at the 2004 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 significant symptomatic improvement in swallowing 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 therapy. This clinical trial was performed at Chiba University in Japan.

We are currently conducting additional Phase 1 and Phase 2 clinical trials of ADVEXIN therapy by itself and in combination with chemotherapy or radiation therapy in a variety of cancers. These 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 in December 2004 and various meetings of the American Society of Clinical Oncology, the American Association for Cancer Research and the American Society of Gene Therapy.

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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 pre-clinical studies provide new insight into the molecular pathways by which the p53 gene, the active component of ADVEXIN therapy, kills tumor cells. These pre-clinical 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 pre-clinical 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 six 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 the mda-7 gene, a promising tumor suppressor gene that we believe, like p53, has broad potential to induce apoptosis or cell death in many types of cancer. We have combined the mda-7 gene product with our adenoviral gene delivery system to form INGN 241. Our pre-clinical trials have shown that the protein produced by INGN 241 suppresses the growth of many cancer cells, including those of the breast, lung, ovaries, colon, prostate and the central nervous system, while not affecting the growth of normal cells. Because INGN 241 kills cancer cells even if other tumor suppressor genes, including p53, are not functioning properly, it appears that mda-7 functions via a novel mechanism of tumor suppression.

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

We have 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 that the mda-7 protein binds to a critical cellular enzyme known as PKR.

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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 pancreatic tumor cells by the mda-7 protein released from adjacent INGN 241-treated pancreatic cells.

Pre-clinical data indicate that INGN 241 works synergistically with celecoxib, marketed by Pfizer as Celebrex®, to inhibit the growth and increase apoptosis 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. The data appear in a recent issue of the medical journal *Surgery*.

In pre-clinical studies, we have observed that 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 that showed a cancer-selective effect of INGN 241. These data were reported in the medical journal *Cancer Research*.

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

Pre-clinical studies with INGN 241 in breast cancer cell lines have shown that 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 that while Herceptin exhibited no activity on Her-2/neu negative cells, INGN 241 did induce cell death in these cells.

Pre-clinical studies indicate that 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 that the number of cancer cells that can be killed by INGN 241 is greater than the number of cells that take up this novel investigational cancer therapy.

Findings and results arising from our development of INGN 241 have been published in the *Journal of Leukocyte Biology*, *Molecular Therapy*, *Oncogene*, *Surgery*, and *International Immunopharmacolgy*.

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 a Phase 2 clinical trial using INGN 241 in patients with metastatic melanoma.

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Data from our Phase 1 trial of INGN 241 in patients with solid tumors, which was published in *Molecular Therapy*, 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.

We have an exclusive license to the mda-7 gene for our therapeutic applications from Corixa Corporation (Corixa), which was acquired by GlaxoSmithKlein. 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 vaccine)

As a supplement to our gene-induced therapeutic protein programs, we are developing INGN 225 using the p53 gene to create a highly specific therapeutic cancer vaccine 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 ADVEXIN therapy can be used with a patient s isolated dendritic cells as an antigen delivery and immune enhancing therapeutic strategy. Pre-clinical testing has shown that the immune system can recognize and kill tumors after treatment with dendritic cells stimulated by the p53 gene, which suggests a vaccine consisting of dendritic cells stimulated by the p53 gene could have broad utility as a treatment for progression of solid tumors.

We are conducting a Phase 1/Phase 2 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/Phase 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/Phase 2 trial 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 chemotherapy. Historically the expected objective response rate in these patients to further chemotherapy is between 5% and 15%. 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 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 suppressor genes 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 gene delivery with rinses, patches, ointments and enhancing

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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 genes.

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

INGN 401 (FUS-1)

INGN 401 uses a nanoparticle vector system to deliver the tumor suppressor gene 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 gene and INGN 403 contains the mda-7 tumor suppressor gene, 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)

Through our strategic collaboration with VirRx, Inc. (VirRx), 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 indicates INGN 007 over-expresses a gene 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.

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Other Research and Development Programs

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

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

We are evaluating additional genes, including BAK, which hold promise as therapeutic candidates. BAK is a pro-apoptotic gene 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 gene. We had exclusive rights to use the BAK gene under a license with LXR Biotechnology, Inc. (LXR), the rights of which were subsequently sold to Tanox, Inc.

As a supplement to our gene-induced protein therapy product programs, 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 are working with M. D. Anderson Cancer Center to further evaluate this molecule as a cancer treatment.

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.

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.

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In addition, we agreed to use commercially reasonable efforts to develop one or more specialized oral formulations through completion of Phase II 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.

Introgen Enabling Technologies

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

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 gene delivery. These systems also may be applicable to indications where activity of the gene for disease treatment is required for longer periods of time or where systemic administration may be necessary.

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 gene for the treatment of lung cancer. The data reported in this publication demonstrate that combining this innovative delivery system with the mda-7 gene results in potent anti-cancer effects and systemic tumor growth inhibition in an animal model of lung cancer. We believe combining potent anti-cancer genes, 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 gene delivery system, which is replication disabled, in selected therapeutic scenarios, in applications beyond INGN 007.

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Additional Enabling Technologies

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

Multi-Gene Vector System. This technology is designed to combine multiple genes 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 gene at a time for disease treatment.

Pro-Apoptotic Gene Delivery System. This technology is designed to allow the activity of pro-apoptotic, or apoptosis-inducing, genes during treatment only, while temporarily suppressing the ability of the apoptotic gene 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 limit the activity of the gene for disease treatment to particular cell types. It is intended to be applied to both viral and non-viral vectors.

Manufacturing and Process Development

Commercialization of a molecular and gene-based 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 Practices 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 for our own products allow, we also manufacture pre-clinical and clinical materials for outside parties for a fee under contract services arrangements.

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 GlaxoSmithKlein), Aventis Pharmaceutical Products, Inc. (Aventis), Columbia University, VirRx and LXR, with the LXR rights being subsequently sold to Tanox, Inc.

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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.

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 the p53 gene, 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 gene in the treatment of cancer patients whose tumors express a normal p53 protein.

Combination Therapy with the p53 Gene

Our portfolio development includes seeking protection for clinical therapeutic strategies that combine the use of the p53 gene 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 gene 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 gene 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 gene 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 gene 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 gene-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 adenoviruses for gene-based products and include procedures applicable to the p53 gene, as well as any of the other of our potential gene-based products. We have also licensed from Aventis a United States application and corresponding international applications directed to processes for the production of purified

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adenoviruses, which are useful for gene-based 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 Suppressor Genes

We either own or have exclusively licensed rights in a number of other patents and applications directed to the clinical application of various tumor suppressor genes other than the p53 gene, including the mda-7, BAK, the 3p21.3 gene family (FUS-1) and anti-sense K-ras genes. 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 genes.

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 the p53 gene, 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 gene molecules. We have exclusively licensed a number of United States and international applications directed to various improved vectors for use in gene-based protocols, gene-based applications employing more than one gene for disease treatment, as well as applications directed to the delivery of genes 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 gene.

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

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The Offering

Common stock offered by Introgen Therapeutics, Inc.:	None
Common stock offered by selling stockholders:	4,341,569
Use of proceeds:	We will not receive any proceeds from the sale of our common stock sold by the selling stockholders.
Registration rights:	Under the registration rights agreement that we entered into with certain of the selling stockholders, we are obligated to use our best efforts to cause the registration statement, of which this prospectus is a part, to become effective and to keep the registration statement effective for a period of up to 90 days, subject to certain exceptions. However, we may elect to keep the registration statement effective for a longer period of time.
Risk factors:	See Risk Factors for a discussion of the factors you should carefully consider before deciding to invest in shares of our common stock.

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RISK FACTORS

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

If we are unable to commercialize ADVEXIN® 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 gene, 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

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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;

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.

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

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

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

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

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

We have generated operating losses since we began operations in June 1993. As of September 30, 2005, we had an accumulated deficit of approximately $136.7 million. We expect to incur substantial additional operating expenses and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities increase. As we expand our operations and develop systems to support commercialization of our product candidates, these losses, among other things, have had, and are expected to continue to have, an adverse impact on our total assets, stockholders equity and working capital.

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

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

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

We expect we will fund our operations over approximately the next 12 to 15 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;

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.

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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 National Cancer Institute, Chiba University in Japan, VirRx and Corixa (which was acquired by GlaxoSmithKlein), 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 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 revenues are likely to be lower than if we directly marketed and sold our products, and any revenues we receive will depend upon the efforts of such third parties. We have no experience in marketing or selling pharmaceutical products and we currently have no sales, marketing or distribution capability. We may be unable to develop sufficient sales, marketing and distribution capabilities to commercialize our products successfully.

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

ADVEXIN therapy and most of our other product candidates under development could be broadly described as gene therapies. A number of clinical trials are being conducted by other pharmaceutical companies involving gene therapy, including compounds similar to, or competitive with, our product candidates. The announcement of adverse results from these clinical trials, such as serious unwanted and unexpected side effects attributable to treatment, 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.

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

We report to the FDA and other regulatory agencies serious adverse events, including those 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 gene therapy product or gene-induced product for sale in the United States. The commercial success of our products will depend in part on public acceptance of the use of gene therapy products or gene-induced products, which are a new type of disease treatment for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy products or gene-induced products are unsafe, and these treatment methodologies may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy products or gene-induced products could also result in greater government regulation and stricter clinical trial oversight.

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

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Our ability to develop and protect a competitive position based on our biotechnological innovations, innovations involving genes, gene-induced therapeutic protein agents, viruses for delivering the genes to cells, formulations, gene therapy delivery systems 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 gene 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 infringed by, and therefore potentially preclude our commercialization of, products like ADVEXIN therapy that are used for adenoviral p53 therapy.

Schering-Plough has filed with the European Patent Office, or EPO, an opposition against our European patent directed to combination therapy with p53 and conventional chemotherapy and/or radiation. An opposition is an administrative proceeding instituted by a third party and conducted by the EPO to determine whether a patent should be maintained or revoked in part or in whole, based on evidence brought forth by the party opposing the patent. The EPO held an initial oral proceeding in October 2003 and determined our patent should be maintained as amended. Schering-Plough has appealed this decision, which is set to be heard and decided in February 2006. Resolution of this appeal will require we expend time, effort and money. If Schering-Plough ultimately prevails in having our European patent revoked on appeal, then the scope of our protection for our product in Europe will be reduced. We would not expect, however, such a result to have a significant detrimental impact on our commercialization efforts in Europe.

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

The biotechnology and pharmaceutical industry has been characterized by extensive litigation regarding patents and other intellectual property rights, and companies have employed intellectual property litigation to gain a competitive advantage. We are aware of a number of issued patents and patent applications related to gene therapy, the treatment of cancer and the use of the p53 and other tumor suppressor genes.

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Schering-Plough Corporation, including its subsidiary Canji, Inc., controls various United States applications and a European patent and applications, some of which are directed to therapy using the p53 gene, and others to adenoviruses containing the p53 gene, or adenoviral p53, and to methods for carrying out therapy using adenoviral p53. Adenoviral p53 technology underlies our ADVEXIN therapy product candidate. 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 you such a defense would prevail.

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

We have recently been involved in patent opposition proceedings before the EPO, in which we have sought to have the EPO revoke three different European patents owned or controlled by Canji/Schering-Plough. These European patents relate to the use of a p53 gene, or the use of tumor suppressor genes, in the preparation of therapeutic products. In one opposition involving a Canji European patent directed to the use of a tumor suppressor gene, 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 gene and that is owned by Johns Hopkins and, we understand, controlled by Schering-Plough, the EPO recently revoked the patent in its entirety. The patent owner has appealed this decision and a 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 the p53 gene. In a third case involving the use of a p53 gene, the European patent at issue was initially upheld, but finally revoked in a hearing held in late April 2004.

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

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

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

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

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

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

We compete with pharmaceutical and biotechnology companies, including Canji, Inc. and Genvec, Inc., which are pursuing forms of treatment similar to ours for the diseases ADVEXIN therapy and our other product candidates target. We are aware 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, Inc., 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

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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 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.

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 revenues.

To complete our clinical trials and commercialize our product candidates, if approved, we will need access to, or development of, facilities to manufacture a sufficient supply of our product candidates.

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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.

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.

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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 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.

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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 Quarterly Report on Form 10-Q. 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;

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the incurrence of amortization expenses; and

possible dilution to our stockholders.

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

If we 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 stock-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 2005 and subsequent periods.

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

Dr. John N. Kapoor, the Chairman of our Board of Directors, is also associated with EJ Financial Enterprises, Inc., a healthcare investment firm that is wholly owned by him, and therefore may have conflicts

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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 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 are 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. Magnum s primary asset is the right to receive funding under a research grant from the National Institutes of Health. Such grant activities and related funding will supplement research and development programs we have in progress. During the year ended December 31, 2004, we earned $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.

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 the notes to our consolidated financial statements and the footnotes thereto as of December 31, 2004, and for the year then ended, included in our Annual Report on Form 10-K, as filed with the SEC on March 15, 2005.

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.

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DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

Certain statements in this prospectus and the documents incorporated herein by reference are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities and Exchange Act of 1934, as amended (the Exchange Act), that involve risks and uncertainties. Any statements contained herein (including without limitation statements to the effect that we estimate, expect, anticipate, plan, believe, project, continue, may, or will or statements concerning potential or variations thereof or comparable terminology or the negative thereof) that are not statements of historical fact should be construed as forward-looking statements. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Actual results could differ materially and adversely from those anticipated in such forward-looking statements as a result of certain factors, including those described in the prospectus under Risk Factors. Because of these and other factors that may affect our operating results, past performance should not be considered an indicator of future performance and investors should not use historical results to anticipate results or trends in future periods. We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements. Readers should carefully review the risk factors described in other documents we file from time to time with the SEC including our quarterly reports on Form 10-Q.

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

USE OF PROCEEDS

All proceeds from the sale of common stock in this offering will go to the stockholders selling common stock under this prospectus. We will not receive any proceeds from the sale of common stock sold by the selling stockholders.

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SELLING STOCKHOLDERS

The following table provides certain information as of November 22, 2005 regarding the beneficial ownership of our common stock by the stockholders selling common stock under this prospectus prior to and after the offering. Beneficial ownership is determined under the rules of the SEC and generally includes voting and investment power with respect to securities.

Our registration of the common stock does not necessarily mean that the selling stockholders will sell all or any of these securities. We have assumed for purposes of the table below that the selling stockholders will sell all of the shares offered for sale.

Name	Shares Owned Prior to Offering (1)	Shared Being Offered Hereby	Shares Owned After Offering (1), (2)	Percentage Owned After Offering (1)
Aventis Pharmaceuticals Inc. (3)	4,322,369	4,322,369		
Ann Lurie Revocable Trust	19,200	19,200		
Total	4,341,569	4,341,569		

(1) The number and percentage of shares beneficially owned is determined in accordance with Rule 13d-3 of the Exchange Act, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rule, beneficial ownership includes any shares as to which an individual has sole or shared voting power or investment power and also any shares as to which an individual has

the right to acquire within 60 days of the date of this prospectus through the exercise of any stock option or other right.

(2) Assumes that each selling stockholder sells all shares registered under this Registration Statement.

(3) Aventis Inc. (AI) is the beneficial owner of the 4,322,369 shares of common stock. Aventis Holdings Inc. (AHI), a subsidiary of AI, beneficially owns the 4,322,369 shares of common stock, which includes direct ownership of 1,978,648 shares. Aventis Pharmaceuticals Inc., a subsidiary of AHI, directly owns 2,343,721 of the shares beneficially owned by AI and AHI. The shares directly owned by API are being registered under this Registration Statement.

Relationship with Introgen

Aventis Inc. currently beneficially owns an aggregate of 4,322,369 shares of our common stock. Pursuant to a purchase agreement executed on June 30, 2001, we sold and issued 100,000 shares of a new class of Series A Non-Voting Convertible Preferred Stock, $.001 par value per share, convertible into 2,343,721 shares of our common stock, to Aventis Pharmaceuticals Inc. for $25,000,000. We received the cash payment and issued the shares on July 2, 2001. Aventis Pharmaceuticals Inc., formerly known as Aventis Pharmaceuticals Products Inc., is a subsidiary of Aventis Inc. and sanofi-aventis SA. Aventis Inc. beneficially holds greater than five percent of our outstanding common stock. Effective as of June 21, 2005, we issued 2,343,721 shares of our common stock to Aventis Pharmaceuticals Inc. upon conversion of the shares of our Series A Non-Voting Convertible Preferred Stock held by Aventis Inc.

PLAN OF DISTRIBUTION

The selling stockholders and any of their pledgees, donees, transferees, assignees and successors-in-interest may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or varying prices, at or related to prevailing market prices or at negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

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ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account pursuant to their prospectus;

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

privately negotiated transactions;

short sales (including, where permitted, transfers to cover short sales);

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 under the Securities Act, if available, rather than under this prospectus.

The selling stockholders may also engage in short sales against the box, puts and calls and other transactions in our securities or derivatives of our securities and may sell or deliver shares in connection with these trades.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved.

The selling stockholders may negotiate and pay broker-dealers commissions, discounts or concessions for their services. Broker-dealers engaged by a selling stockholder may allow other broker-dealers to participate in resales. However, the selling stockholders and any broker-dealers involved in the sale or resale of shares may qualify as underwriters within the meaning of Section 2(11) of the Securities Act. In addition, the broker-dealers commissions, discounts or concessions may qualify as underwriters compensation under the Securities Act. If a selling stockholder qualifies as an underwriter, it will be subject to the prospectus delivery requirements of the Securities Act.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholders and their affiliates. In addition, we will make copies of this prospectus available to the selling stockholders, and we have informed them of the need for delivery of copies of this prospectus to purchasers at or prior to the time of any sale of shares offered hereby. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

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Under the registration rights agreement that we entered into with Aventis, we are obligated to use our best efforts to cause the registration statement, of which this prospectus is a part, to become effective and to keep the registration statement effective for a period of up to 90 days, subject to certain exceptions. However, we may elect to keep the registration statement effective for a longer period of time. We are required to pay all fees and expenses incident to the registration of the shares. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2004, and management s assessment of the effectiveness of our internal control over financial reporting as of December 31, 2004, as set forth in its reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements and management s assessment are incorporated by reference in reliance on Ernst & Young LLP s reports, given on its authority as experts in accounting and auditing.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference the information we file with them, which means that we can disclose important information to you by referring you to documents that we have previously filed with the SEC or documents that we will file with the SEC in the future. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference into this prospectus any filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus until the termination of this offering, as well as the following documents:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2004, filed with the SEC on March 15, 2005;
- those portions of our Definitive Proxy Statement, filed with the SEC on April 28, 2005, that are deemed filed with the SEC;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2005, filed with the SEC on May 10, 2005;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2005, filed with the SEC on August 9, 2005;
- our Quarterly Report on Form 10-Q for the quarter ended September 30, 2005, filed with the SEC on November 9, 2005;
- our Current Report on Form 8-K filed with the SEC on April 25, 2005;

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our Current Report on Form 8-K filed with the SEC on May 4, 2005;

our Current Report on Form 8-K filed with the SEC on May 10, 2005;

our Current Report on Form 8-K filed with the SEC on July 25, 2005;

our Current Report on Form 8-K filed with the SEC on August 1, 2005;

our Current Report on Form 8-K filed with the SEC on October 26, 2005;

our Current Report on Form 8-K filed with the SEC on November 1, 2005;

our Current Report on Form 8-K filed with the SEC on November 8, 2005; and

the description of our common stock contained in our Registration Statement on Form 8-A, filed with the SEC on September 8, 2000, and any further amendment or report filed hereafter for the purpose of updating such description.

You may request a copy of any of these filings, at no cost to you, by writing or telephoning us at the following address and telephone number: Introgen Therapeutics, Inc., 301 Congress Avenue, Suite 1850, Austin, Texas 78701; telephone number (512) 708-9310.

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

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and periodic reports, proxy statements and other information with the SEC. You may inspect these documents without charge at the principal office of the SEC located at 450 Fifth Street, N.W., Washington, D.C. 20549, and you may obtain copies of these documents from the SEC s Public Reference Room at its principal office. Information regarding the operation of the Public Reference Room may be obtained by calling 1-800-SEC-0330. The SEC maintains a web site that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC s web site is www.sec.gov.

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DISCLOSURE OF SEC POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

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

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