INTROGEN THERAPEUTICS INC
Form 10-Q
May 12, 2008

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

Form 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2008.

or

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

For the transition period from to .

Commission file number 000-21291

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

Delaware	**74-2704230**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification Number)*

301 Congress Avenue, Suite 1850
Austin, Texas 78701
(Address of principal executive offices, including zip code)
(512) 708-9310
(Registrant s telephone number, including area code)

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

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

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o	Smaller reporting company o

(Do not check if a smaller reporting company)

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

As of May 9, 2008, the registrant had 44,013,449 shares of its common stock, $0.001 par value per share, issued and outstanding.

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PART I
FINANCIAL INFORMATION

Item 1. Financial Statements

INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands, except per share amounts)

	December 31, 2007	March 31, 2008 (Unaudited)
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 11,320	$ 16,479
Short-term investments	3,585	
Total cash, cash equivalents and short-term investments	14,905	16,479
Marketable securities	10,165	
Prepaid expense and other current assets	706	462
Total current assets	25,776	16,941
Property and equipment, net of accumulated depreciation of $14,994 and $15,241	4,442	4,321
Other assets	265	260
Total assets	$ 30,483	$ 21,522
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	$ 1,813	$ 3,045
Accrued liabilities and other	4,225	2,768
Deferred revenue and other	616	537
Current portion of notes payable	586	553
Total current liabilities	7,240	6,903
Notes payable, net of current portion	7,155	7,014
Deferred revenue and other, long-term	79	22
Total liabilities	14,474	13,939
Non-controlling and minority interests in consolidated subsidiaries	6	2
Commitments and Contingencies		
Stockholders Equity:		
Preferred stock, $.001 par value per share; 5,000 shares authorized; 4,900 shares issuable; zero Series A shares issued and outstanding in 2007 and 2008, respectively		

Common stock, $.001 par value per share; 100,000 shares authorized; shares issued and outstanding of 44,004 in 2007 and 44,013 in 2008	44	44
Additional paid-in capital	211,558	212,622
Accumulated deficit	(202,715)	(205,116)
Accumulated other comprehensive gain	7,116	31
Total stockholders equity	16,003	7,581
Total liabilities and stockholders equity	$ 30,483	$ 21,522

The accompanying notes are an integral part of these condensed consolidated financial statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(Amounts in thousands, except per share amounts)
(UNAUDITED)

	Three Months Ended March 31,	
	2007	**2008**
Contract services, grant and other revenue	$ 322	$ 186
Operating costs and expense:		
Research and development, including share-based compensation of $305 in 2007 and $175 in 2008	3,175	4,682
General and administrative, including share-based compensation of $950 in 2007 and $870 in 2008	3,267	2,531
Total operating costs and expense	6,442	7,213
Loss from operations	(6,120)	(7,027)
Interest income	442	99
Interest expense	(179)	(162)
Realized gain on sale of marketable securities		4,388
Other income	254	297
Loss before non-controlling and minority interests in consolidated subsidiaries	(5,603)	(2,405)
Non-controlling and minority interests in consolidated subsidiaries	(14)	4
Net loss	$ (5,617)	$ (2,401)
Net loss per share, basic and diluted	$ (0.13)	$ (0.05)
Shares used in computing basic and diluted net loss per share	43,655	44,007

The accompanying notes are an integral part of these condensed consolidated financial statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)
(UNAUDITED)

	Three Months Ended March 31,	
	2007	**2008**
Cash flows from operating activities:		
Net loss	$ (5,617)	$ (2,401)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-controlling interests in consolidated subsidiaries	14	(4)
Depreciation	279	247
Share-based compensation	1,255	1,045
Gain on sale of marketable securities		(4,388)
Changes in operating assets and liabilities:		
(Increase) decrease in other assets	(381)	249
Increase (decrease) in accounts payable	(846)	1,232
Increase (decrease) in accrued liabilities	68	(1,382)
Increase (decrease) in deferred revenue and other	(211)	(136)
Net cash used in operating activities	(5,439)	(5,538)
Cash flows from investing activities:		
Purchases of property and equipment		(126)
Purchases of short-term investments	(13,436)	
Maturities of short-term investments		3,585
Proceeds from sale of marketable securities		7,429
Net cash (used in) provided by investing activities	(13,436)	10,888
Cash flows from financing activities:		
Payment of offering costs related to sale of common stock	(1,571)	(75)
Proceeds from exercise of options for common stock	97	19
Principal payments under notes payable	(269)	(174)
Net cash used in financing activities	(1,743)	(230)
Effect of exchange rate changes on cash	(4)	39
Net decrease in cash	(20,622)	5,159
Cash and cash equivalents, beginning of period	25,578	11,320
Cash and cash equivalents, end of period	$ 4,956	$ 16,479
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 171	$ 152
Supplemental disclosure of non-cash investing and financing activities:		

Non-cash unrealized gain (loss) on marketable securities	$ 4,047	$ (2,736)

The accompanying notes are an integral part of these condensed consolidated financial statements.

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES
UNAUDITED NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. Business of the Company and Liquidity

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

We have not yet generated any significant revenue from unaffiliated third parties nor is there any assurance of future product revenue. We earn minimal revenue from contract services activities, grants and interest income, as well as rent from the lease of a portion of our facilities to The University of Texas M. D. Anderson Cancer Center. Our ability to generate revenue from the commercial sale of our products in the near future is uncertain. We may never generate revenue from the commercial sale of our products.

Our research and development activities involve a high degree of risk and uncertainty. Our ability to successfully develop, manufacture and market our proprietary products is dependent upon many factors. These factors include, but are not limited to, the need for and the ability to obtain additional financing, the reliance on collaborative research and development arrangements with corporate and academic affiliates and the ability to develop manufacturing, sales and marketing experience. Additional factors include uncertainties as to patents and proprietary technologies, competitive technologies, technological change and risk of obsolescence, development of products, competition, government regulations and regulatory approval, and product liability exposure. As a result of these factors and the related uncertainties, there can be no assurance of our future success.

We believe our cash, cash equivalents and short-term investments on hand at March 31, 2008, plus the amounts we may earn from contract services, grants and/or interest income during 2008, will be sufficient to fund our operations through at least March 31, 2009, and perhaps longer, at a level necessary to achieve our primary business objectives. However, in order to fund our operations beyond March 31, 2009, or to introduce any new product candidates, we may be required to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. If we raise additional funds through the issuance of equity securities, the percentage ownership of our stockholders could be significantly diluted. If we obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders. In the event these sources of financing become unavailable, we may have to adjust the scope of our operations and related cash needs to a level that can extend the period of time during which we can rely on existing resources to conduct our business activities. Such adjustments in the scope of our operations could include reducing the number of our personnel and perhaps delaying or discontinuing certain product development activities critical to achieving our business objectives.

2. Basis of Presentation and Significant Accounting Policies

The accompanying condensed consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles (GAAP) for interim financial information and pursuant to the rules and regulations of the Securities and Exchange Commission (SEC). The condensed consolidated balance sheet at December 31, 2007 has been derived from the audited consolidated financial statements at that date but does not include all of the information and footnotes required by generally accepted accounting principles for complete financial statements. These unaudited, interim financial statements do not include all of the information and footnotes required under GAAP for complete financial statements. In management s opinion, all accounting entries considered necessary for a fair presentation have been made in preparing these financial statements, and such entries are normal in nature. Operating results for the three-month period ended March 31, 2008 are not necessarily indicative of the results that may be expected for the entire fiscal year.

Our critical accounting policies and recently issued accounting pronouncements of significance to us are described in our most recent annual report on Form 10-K for the year ended December 31, 2007, filed with the Securities and

Exchange Commission on March 17, 2008. There have been no material changes in these items since that time. As noted in that annual report, Statement of Financial Accounting Standards No. 157, Fair Value Measurements, and Statement of Financial Accounting Standards No. 159,

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The Fair Value Option for Financial Assets and Financial Liabilities, were effective for us on January 1, 2008. Our adoption of those standards has no material effect on our financial statements.

These financial statements include the accounts of Introgen Therapeutics, Inc. and its consolidated subsidiaries (collectively referred to as Introgen). We account for Introgen Therapeutic, Inc. s investment in subsidiaries in accordance with the relevant provisions of GAAP. Accordingly, the subsidiaries accounts are included in these consolidated financial statements. We record a non-controlling interest for the portion of those subsidiaries we do not own to the extent such non-controlling interest constitutes a liability in our financial statements. If those subsidiaries have an accumulated net loss, the minority interest is zero.

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3. Consolidated Subsidiaries

During the three months ended March 31, 2007, we purchased 49% of the outstanding stock of Introgen Research Institute, Inc. for $10,000. The other 51% of IRI is owned by our corporate Secretary, who is also an Introgen stockholder.

We transferred to IRI a grant from the National Institutes of Health (NIH) originally awarded to us. IRI will be responsible for the remaining research contemplated by that grant and will receive future funding, if any, from the NIH under that grant. We have contractual relationships with IRI under which we may perform research and development services for them in the future. For the three months ended March 31, 2008 and 2007, we recorded grant income of $213,000 and $56,000, respectively, related to grants held by IRI.

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

4. Other Comprehensive Income or Loss

Other comprehensive income or loss is included as a component of stockholders equity and is composed of (1) foreign currency translation adjustments and (2) unrealized gains and losses on investments designated as available-for-sale securities. Other comprehensive income (loss) is calculated as follows (in thousands):

	Three Months Ended March 31,	
	2007	**2008**
Net loss	$ (5,617)	$ (2,401)
Foreign currency translation adjustments	(4)	39
Unrealized gain (loss) on marketable securities	4,047	
Total other comprehensive income (loss)	$ (1,574)	$ (2,362)

During the three months ended March 31, 2008, we sold all the shares of Silence Therapeutics plc we owned for their quoted market value on the Alternative Investment Market of the London Stock Exchange on the date of the sale. We received net proceeds of approximately $7.4 million from this sale. We purchased these shares for approximately $3.0 million in July 2005. These shares were presented as marketable securities in our financial statements in previous periods. This sale resulted in the recognition of a gain of $4.4 million which is recorded as a component of other income. As a result of this sale, the unrealized gain on marketable securities has been realized and is no longer a component of other comprehensive income (loss).

5. Share-Based Compensation

We issued the following number of shares of common stock as a result of exercises of stock options granted from our stock option plans:

Three Months Ended March 31,	
2007	**2008**
108,400	9,350

6. Business Development Services Agreement with a Related Party

We have an agreement with a new member of our Board of Directors under which he will provide certain business development services to us in connection with potential co-development, collaborative, marketing partnership or certain other potential strategic transactions. In consideration for his services, upon the consummation of such a transaction, we will pay him a fee equal to one-half of one percent (0.5%) of certain monetary benefits received by our

stockholders or us. The maximum fee he can receive is $3,000,000. The fee we pay him will be reduced by expenses or other expenditures made or contemplated under such a transaction.

This fee is not payable for funding we receive that we are expected to expend for research and development programs, full-time equivalent payments to employees, loans, collaborative programs, business partnerships or strategic transactions, or otherwise. Transactions between our affiliates and us, whether now existing or created in the future, are excluded from this agreement. This

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agreement may be terminated at any time by written notice from us or this board member. In the event of such termination, the fee shall be paid with respect to a transaction produced through services performed by this board member before termination if the transaction is closed within two years after the date of termination of the agreement.

Item 2. Management s Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis should be read in conjunction with our Condensed Consolidated Financial Statements and the related notes thereto included in this Quarterly Report on Form 10-Q and the other documents we have filed with the Securities and Exchange Commission. In addition to historical information, this report and the following discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These statements address our future operations, financial condition, business strategies and other prospective items and include, among other subjects, matters concerning our expectations regarding:

Various regulatory applications, procedures and approvals relating to our product candidates, including but not limited to our expectations regarding the timing of such applications, procedures and approvals;

The growth of our operations, business and revenues and the growth rate of our costs and expenses;

Future increases in our research and development, sales and marketing and general and administrative expenses;

The sufficiency of our existing cash, cash equivalents, marketable securities and cash generated from operations;

Better efficacy of our product candidates through the use of biomarkers ;

Application of our research and development expertise to other diseases that result from cellular dysfunction and uncontrolled cell growth; and

Access to additional working capital.

The words believe, expect, anticipate and other similar expressions generally identify forward-looking statements These forward-looking statements are based on our current expectations and entail various risks and uncertainties. Given these risks and uncertainties, readers are cautioned not to place undue reliance on such forward-looking statements. We undertake no obligation to revise or publicly release the results of any revision to these forward-looking statements. These forward-looking statements are subject to certain risks and uncertainties that could cause our actual results to differ materially from those reflected in the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this report, and in particular, the risks discussed under the heading Risk Factors in Part II, Item 1A of this report and those discussed in other documents we file with the Securities and Exchange Commission.

Overview

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

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

We believe the use of targeted molecular therapies to induce the production of biopharmaceutical proteins represents a new approach for treating many cancers while avoiding the toxic side effects common to traditional therapies. We have developed significant expertise in developing targeted therapies that may be used to treat disease and in using what we believe are safe and

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effective delivery systems to transport these agents to the cancer cells. We believe we will be able to treat a number of cancers in a way that kills cancer cells without harming normal cells.

Our lead product candidate, ADVEXIN® therapy, combines the p53 tumor suppressor with a non-replicating, non-integrating, adenoviral delivery system we have developed and extensively tested. The p53 molecule is one of the most potent members of a group of naturally-occurring tumor suppressors, which act to kill cancer cells, arrest cancer growth and protect cells from becoming cancerous. We are developing other product candidates for the treatment of cancer using other molecules and delivery systems, such as the mda-7 and FUS1 tumor suppressors.

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

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

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

We have not yet generated any significant revenue from unaffiliated third parties nor is there any assurance of future product revenue. We earn minimal revenue from contract services activities, grants and interest income, as well as rent from the lease of a portion of our facilities to The University of Texas M. D. Anderson Cancer Center. Our ability to generate revenue from the commercial sale of our products in the near future is uncertain. We may never generate revenue from the commercial sale of our products.

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

The Introgen Approach

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

Most cancers are amenable to local treatment, such as surgery and radiation, which are administered far more often than systemic cancer treatments. Our locally delivered product candidates, such as ADVEXIN therapy and INGN 241 therapy, deposit therapeutic molecules at high concentrations directly into a patient s cancerous tumor by hypodermic syringe. We have systemic formulations for intravenous use in those cases for which a systemic therapy may be indicated and have applied ADVEXIN therapy using a nanoparticle formulation system to deliver our tumor suppressors.

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

The Introgen Strategy

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

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Develop and Commercialize ADVEXIN Therapy, INGN 241, INGN 225 and INGN 401 for Multiple Cancer Indications. We plan to continue our development programs to commercialize several of our product candidates in multiple cancer indications, including:

ADVEXIN therapy, using the p53 tumor suppressor;

INGN 241, using the mda-7 tumor suppressor (also known as interleukin 24 or IL-24);

INGN 225, using the p53 tumor suppressor as a highly specific cancer immunotherapy; and

INGN 401 systemic nanoparticle therapy, using the FUS-1 tumor suppressor.

Develop Our Portfolio of Targeted Molecular Therapies and Other Drug Products. Utilizing our research, clinical, regulatory and manufacturing expertise, we are evaluating development of additional molecular therapies for various cancers, including:

INGN 234, an oral rinse or mouthwash formulation containing the p53 tumor suppressor;

INGN 402 and 403, using nanoparticle formulations for systemic delivery of the p53 and mda-7 tumor suppressors; and

INGN 007, a replication-competent viral therapy.

Develop a Systemic Nanoparticle Administration Platform. Early pre-clinical and clinical studies with these new nanoparticle drugs have demonstrated a good safety profile and promising anti-cancer activity. In addition to FUS-1, we incorporate the p53 tumor suppressor and the mda-7 tumor suppressor in these nanoparticle formulations. We also have in-licensed technologies for systemic nanoparticle delivery of DNA, siRNA, miRNA, proteins, peptides and polypeptides.

Develop the Topical Use of Tumor Suppressors. We plan to continue developing topical product candidates for the treatment or prevention of oral and dermal cancers, specifically INGN 234 referred to above. We believe these treatments are a logical extension of our loco-regional delivery of cancer therapies and represent attractive product candidates since pre-malignant and malignant cells can be exposed to natural, biological tumor suppressors and DNA repairing agents. We are conducting this program in support of our Oral Care Alliance with Colgate-Palmolive.

Establish Targeted Sales and Marketing Capabilities. The oncology market can be effectively addressed by a small, focused sales force because it is characterized by a concentration of specialists in cancer centers and oncology clinics. We believe we can address this market by a combination of building a direct sales force as part of the ADVEXIN therapy commercialization process and pursuing marketing and distribution agreements with corporate partners for ADVEXIN therapy as well as additional products.

Expand Our Market Focus to Non-Cancer Indications. We plan to leverage our scientific, research and process competencies in molecular therapy and vector development to pursue targeted molecular therapies for a variety of other diseases and conditions. While our primary emphasis at this time is on cancer, we believe these therapies could hold promise for diseases such as cardiovascular disease and rheumatoid arthritis, which, like cancer, result from cellular dysfunction or uncontrolled cell growth.

We have an established process for evaluating new drug candidates and advancing them from pre-clinical to clinical development. We have identified and licensed multiple technologies, which we intend to combine with our adenoviral and non-viral vector systems and which we believe are attractive development targets for the treatment of various cancers. We intend to evaluate additional opportunities to in-license or acquire new technologies.

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Product Development Overview

ADVEXIN Therapy (p53)

ADVEXIN Therapy Overview and Regulatory Status

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

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

The European Medicines Agency (EMEA) Committee for Orphan Medicinal Products granted ADVEXIN therapy an Orphan Medicinal Product Designation in Europe for the treatment of Li-Fraumeni Syndrome. This designation has been ratified by the European Commission. The Orphan Medicinal Product Designation in Europe confers a number of regulatory benefits to ADVEXIN therapy, including access to protocol assistance, reduced regulatory fees and a ten-year period of marketing exclusivity from the date of marketing authorization by the European Commission. Li-Fraumeni Syndrome is an inherited cancer characterized by inherited mutations in the p53 tumor suppressor.

We have submitted, and the EMEA has accepted for review, a Marketing Authorization Application for ADVEXIN therapy under the EMEA s Exceptional Circumstances Approval rules for breakthrough therapies. The application is for the use of ADVEXIN therapy for the treatment of Li-Fraumeni Syndrome. Under these rules, approval, if granted by the EMEA, will be based on clinical results from the use of ADVEXIN therapy in Li-Fraumeni Syndrome and also from results of other trials with ADVEXIN therapy in a wide variety of non-inherited solid tumors that share the p53 biomarker abnormality, which characterizes Li-Fraumeni Syndrome.

The EMEA s Exceptional Circumstances Approval provisions are designed to facilitate access to needed treatments for certain Orphan Medicinal Products. A Marketing Authorization Application filed with the EMEA under these provisions can be reviewed on an expedited basis. This Exceptional Circumstance registration approach is designed by EMEA to be more streamlined than EMEA s Conditional Approval procedures, which are similar to the FDA s Accelerated Approval regulations.

An audit and inspection of Introgen s facilities and production processes was performed by a European Union Qualified Person (QP) during 2007. This inspection resulted in the QP concluding that ADVEXIN therapy has been manufactured at this site in accordance with the standards of Good Manufacturing Practices in place in the EU for Investigation Medicinal Products (IMPs). This inspection covered all aspects of ADVEXIN therapy manufacture, including production and purification, aseptic filling, labeling, and testing of raw materials, intermediates, and final product, and all quality systems in place for these aspects. This certification was obtained in preparation for the EMEA s inspection we anticipate upon review of the ADVEXIN therapy Marketing Authorization Application.

Most of our regulatory activities involving the EMEA are conducted by Gendux Molecular Limited, a wholly-owned subsidiary of ours based in Ireland.

We plan to analyze data from two Phase 3 clinical trials of ADVEXIN therapy in patients with advanced recurrent squamous cell carcinoma of the head and neck (recurrent head and neck cancer). These trials involve administration of ADVEXIN therapy, both as monotherapy and in combination with chemotherapy, in recurrent head and neck cancer.

We received Fast Track designation for ADVEXIN therapy from the FDA under its protocol assessment program as a result of the FDA s agreement with the design of our two Phase 3 clinical trials of ADVEXIN therapy. Under this Fast Track designation, the FDA will take actions to expedite the evaluation and review of the Biologics License Application (BLA) for ADVEXIN therapy. A BLA is the application for approval to market and sell ADVEXIN therapy in the United States. We plan to pursue with the FDA an Accelerated Approval of ADVEXIN therapy, which is one alternative provided under a Fast Track designation.

We reviewed historically successful FDA registration strategies for numerous cancer drugs, noting that during approximately the past 15 years, 14 cancer drugs have been approved based upon submissions of Phase 2 clinical data. A number of the Phase 2 trials supporting these approvals employed single-arm studies involving relatively small patient populations. Virtually all of those drugs relied on surrogate endpoints for approval and a substantial number of

the products were for orphan drug indications.

We conducted a series of meetings with the FDA and the European Medicines Agency (EMEA) to develop and implement the filing strategies for ADVEXIN therapy. We now plan to submit non-sequential registration dossiers in Europe and the US on or before

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June 30, 2008, based on data from our Phase 2 and Phase 3 clinical trials of ADVEXIN therapy for treatment of recurrent head and neck cancer.

The FDA has concluded that ADVEXIN therapy continues to show promise with respect to an unmet medical need since there are limited treatment alternatives in the United States for recurrent head and neck cancer. The FDA has concluded that the clinical development program for ADVEXIN therapy for recurrent head and neck cancer continues to meet the criteria for Fast Track designation. By using new clinical data and new analyses of those data, we hope to more specifically target recurrent head and neck cancer in patients using indicators known as biomarkers, as discussed further below under ADVEXIN Therapy as a Targeted Molecular Therapy. We believe this Personalized Medicine approach will improve efficacy by identifying the patients most likely to benefit from ADVEXIN therapy.

We submitted a Submission Of a Partial Application (SOPA Request) to the FDA Division of Cellular and Gene Therapies proposing a rolling BLA for ADVEXIN therapy for the treatment of recurrent head and neck cancer. This request was based primarily on data from our Phase 2 clinical trials. We have proposed to the FDA that, since the basis of the proposed rolling BLA was Phase 2 clinical data which utilized 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 new data and analyses from the Phase 2 ADVEXIN therapy clinical trials for recurrent head and neck cancer and conduct efficacy analyses on one or both of our Phase 3 trials. Given that we have two Phase 3 clinical trials in recurrent 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.

In addition to our original Phase 3 protocol determination to assess patient s mutation status and other Personalized Medicine characteristics, we subsequently reached agreement with the FDA that biomarker evaluations as described in its 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. This initiative also encouraged sponsors to examine novel approaches to define tumor responses that correlate with clinical benefit. Our Phase 3 statistical analysis plan and clinical protocols describe assessments of p53 biomarker profiles based not only on p53 mutational gene sequence evaluations but also on p53protein levels as determined by prospectively identified immunohistochemistry procedures. We have employed several biomarker and response criteria to evaluate ADVEXIN therapy efficacy as described below.

We are currently conducting the efficacy analysis of one of our ADVEXIN therapy Phase 3 studies. This analysis involves comparing ADVEXIN therapy to methotrexate for the treatment of recurrent head and neck cancer. The efficacy assessment of the randomized, controlled clinical trial is based upon analysis of biomarkers and clinical outcomes. The efficacy evaluation of the Phase 3 study will incorporate the biomarker analyses identified in Phase 2 clinical trials of ADVEXIN therapy of recurrent head and neck cancer. The Phase 3 Statistical Analysis Plan was finalized with input from the FDA. We have followed advice from the FDA to accelerate our Phase 3 safety analysis and to perform an efficacy analysis for this study. An independent Data Safety Monitory Board review in 2006 noted no safety issues with the Phase 3 study. We completed the submission of the Phase 2 data to the FDA in the second quarter of 2007. These data contained information on response rate, survival and biomarker findings associated with the use of ADVEXIN therapy in recurrent head and neck cancer.

Preliminary results from one of the Phase 3 trials in patients with recurrent head and neck cancer were presented at the American Association for Cancer Research (AACR) annual meeting in San Diego, California in April, 2008. Biomarkers of the p53 tumor suppressor gene target of ADVEXIN treatment were predictive in identifying patients more likely to benefit from ADVEXIN therapy. We believe these results confirm the predictive value of p53 biomarkers hypothesized from previous Phase 1 and 2 ADVEXIN clinical trials. The earlier studies included patients with recurrent squamous cell carcinoma of the head and neck (SCCHN), non-small cell lung cancer, prostate cancer and Li-Fraumeni Syndrome cancers. Previously reported preliminary results demonstrated a correlation between p53 biomarkers and increased tumor responses and survival following ADVEXIN therapy.

In the preliminary analysis of the Phase 3 recurrent head and neck cancer trial, tumor response was correlated with a statistically significant increased survival. An analysis from recurrent SCCHN patients treated with ADVEXIN monotherapy in Phase 1, 2 and 3 trials showed that p53 profiles favorable for ADVEXIN efficacy demonstrated a statistically significant correlation with tumor response. In this preliminary analysis, tumor response was observed in 79 percent of patients with p53 biomarkers favorable for ADVEXIN efficacy compared to 25 percent of patients with unfavorable p53 biomarkers for ADVEXIN. This difference was statistically significant.

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A comprehensive analysis of our Phase 3 data and additional pivotal studies of ADVEXIN in recurrent head and neck cancer, including prospective biomarker analyses demonstrating statistically significant correlations between p53 biomarkers and increased response and survival following ADVEXIN therapy, will be presented at medical conferences later this year. These and other data will be the basis for regulatory submissions in the United States and in Europe.

During 2008, we plan to:

Complete efficacy, safety and biomarker analyses of one or both of our two Phase 3 clinical trials for recurrent head and neck cancer and plan to submit those data to the FDA and EMEA in support of ADVEXIN therapy registration programs; and

Complete filings with the EMEA in support of an Exceptional Circumstance Approval Application for Li-Fraumeni Syndrome cancers.

There is no assurance we will be able to achieve these regulatory milestones during the time period we currently anticipate. We may encounter delays in the regulatory process relating to these milestones due to additional information requirements from regulatory authorities, unintentional omissions in our applications, additional government regulation or other delays in the review process. We may update our expectations regarding these regulatory milestones from time to time to reflect new information as it becomes available to us.

ADVEXIN Therapy as a Targeted Molecular Therapy

We identified a set of predictive indicators, commonly referred to as biomarkers, associated with high response rates and increased survival in Phase 2 clinical trials of ADVEXIN therapy in patients with recurrent head and neck cancer. These trials are discussed in more detail below under Other ADVEXIN Therapy Activities. We believe these biomarkers support the use of ADVEXIN therapy as a targeted molecular therapy.

The FDA, the National Cancer Institute (NCI), and the Centers for Medicare & Medicaid Services are undertaking the Oncology Biomarker Qualification Initiative to expedite the development of novel cancer treatments that reflect the Personalized Medicine approach. These agencies define biomarkers as clinical or biological indicators of disease or therapeutic effects, which can be measured through dynamic imaging tests, laboratory tests on blood or tissue samples as well as by clinically defined parameters. This initiative was developed to employ biomarkers as a way of speeding the development and evaluation of new cancer therapies. The identification of predictive indicators of ADVEXIN therapy activity is responsive to these initiatives by predicting the patient populations most likely to benefit from a specific cancer therapy.

We have compiled molecular biomarker data from several of our clinical studies in patients with head and neck, lung, prostate and Li-Fraumeni Syndrome cancers. Some of these studies are described in more detail in preceding and subsequent paragraphs.

The targeted molecular therapy provided by ADVEXIN therapy is evidenced by its use to successfully treat a Li-Fraumeni Syndrome cancer patient on a compassionate use basis under a protocol authorized by the FDA. Li-Fraumeni Syndrome cancer patients have inherited defects in the p53 tumor suppressor that is the target of ADVEXIN therapy. Our treatment of a tumor in a Li-Fraumeni Syndrome patient with ADVEXIN therapy led to improvement of tumor-related symptoms and resulted in a complete response in the treated lesion as determined by positron emission tomography (PET) computerized tomography (CT) scans. PET-CT scans measure the metabolic activity of tumors and are being increasingly utilized in the management of cancer patients because they provide more sensitive assessments of treatment effects compared to conventional CT and magnetic resonance imaging scans.

This Li-Fraumeni Syndrome study defined important biomarkers to guide the administration of ADVEXIN therapy to patients with other cancers who display p53 pathway abnormalities. Our molecular analysis of biopsies of the Li-Fraumeni Syndrome tumor before and after treatment identified key markers of p53 pathway abnormalities that are used to predict and evaluate the effects of ADVEXIN therapy. These markers included detection of abnormal levels of p53 protein that identify aberrant p53 pathways and the induction of molecular markers of tumor growth control and tumor cell death that validate ADVEXIN therapy s mechanisms of action. We believe these biomarkers can be used to identify patients most likely to benefit from ADVEXIN therapy.

The EMEA Committee for Orphan Medicinal Products has granted ADVEXIN therapy an Orphan Medicinal Product Designation in Europe for the treatment of Li-Fraumeni Syndrome. This designation has been ratified by the European Commission. The Orphan Medicinal Product Designation in Europe confers a number of regulatory benefits to ADVEXIN therapy, including access to protocol assistance, reduced regulatory fees and a 10-year period of marketing exclusivity from the date of approval.

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We have submitted, and the EMEA has accepted for review, a Marketing Authorization Application for ADVEXIN therapy under the EMEA s Exceptional Circumstances Approval rules for breakthrough therapies. The application is for the use of ADVEXIN therapy for the treatment of Li-Fraumeni Syndrome. Under these rules, approval, if granted by the EMEA, will be based on clinical results from the use of ADVEXIN therapy in Li-Fraumeni Syndrome and also from results of other trials with ADVEXIN therapy in a wide variety of non-inherited solid tumors that share the p53 biomarker abnormalities, which characterize Li-Fraumeni Syndrome.

The EMEA s Exceptional Circumstances Approval provisions are designed by EMEA to facilitate access to needed treatments for certain Orphan Medicinal Products. A Marketing Authorization Application filed with the EMEA under these provisions can be reviewed on an expedited basis. This registration approach is more streamlined than EMEA s Conditional Approval procedures, which are similar to the FDA s Accelerated Approval regulations. As a result of the encouraging clinical findings in treating Li-Fraumeni Syndrome, we are making ADVEXIN therapy available on a compassionate use basis to qualified Li-Fraumeni Syndrome patients with tumors refractory to standard treatment.

Li-Fraumeni Syndrome is an inherited genetic disorder that greatly increases the risk of developing several types of cancer typically with initial occurrence at a young age. The majority of Li-Fraumeni Syndrome families have inherited mutations in the p53 tumor suppressor. The findings described above have been presented at the annual meetings of the American Society of Gene Therapy (ASGT) and the American Society of Clinical Oncology (ASCO).

Other ADVEXIN Therapy Activities

We performed a Phase 2 clinical trial of ADVEXIN therapy combined with neoadjuvant chemotherapy and surgery in women with locally advanced breast cancer. The results of this study were published in the journal *Cancer.* Objective clinical responses were seen following the combined therapy in 100% of the patients with a median of 80% reduction in tumor size. Following tumor shrinkage, complete tumor removal by subsequent surgery was achieved in 100% of the patients. At a median follow-up of 37 months (range, 30-41 months), four patients (30%) developed systemic recurrence and two patients died. The estimated breast cancer-specific survival rate at three years was 84%. There was no increase in systemic toxicity. Neoadjuvant treatments are administered prior to surgery and represent a novel and increasingly applied approach to making surgical tumor resections less invasive, improving outcomes and facilitating breast conservation.

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 therapy and radiation treatment resulted in 63% biopsy-proven complete responses at three months, which is approximately four times the expected rate using radiotherapy alone. The results of this study were published in *Clinical Cancer Research.*

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

We have completed other clinical trials of ADVEXIN therapy, 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 600 patients with ADVEXIN therapy, establishing a large safety database. Findings from several of our clinical trials have been published in *Clinical Cancer Research* and *Proceedings of the American Society for Clinical Oncology* as well as presented at numerous conferences, including the San Antonio Breast Cancer Conference and various meetings of the ASCO, ASGT and the American Association for Cancer Research.

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.

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Pre-clinical studies have provided insight into the molecular pathways by which the p53 tumor suppressor, the active component of ADVEXIN therapy, kills tumor cells. These studies were undertaken to provide additional molecular data supporting the activity observed during the clinical development of ADVEXIN therapy and to provide additional information regarding the specific pathways, including anti-angiogenesis or the reduction of blood vessels supplying the tumor, that mediate the observed clinical effects of ADVEXIN therapy. The studies were conducted by our collaborators at Okayama University in Japan, The University of Texas M. D. Anderson Cancer Center and other academic institutions and were published in *Molecular Cancer Therapeutics* and other scientific journals.

Other data suggest the enhanced therapeutic effects of a combination of ADVEXIN therapy and Erbitux® therapy 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.

We hold a worldwide, exclusive license to a family of patent applications directed to combination therapy using ADVEXIN therapy with inhibitors of epidermal growth factor receptors (EGFr inhibitors) such as Erbitux®, Vectibix®, Tarceva® and Iressa®. We licensed this family of patents from M. D. Anderson Cancer Center. This important technology is based on the discovery by scientists at M. D. Anderson Cancer Center that p53 therapies (which is the basis for our ADVEXIN therapy) and mda7 therapies (which is the basis for our INGN 241 product candidate discussed below) can work synergistically with inhibitors of epidermal growth factor receptors to arrest tumor growth. Preclinical studies have shown that this therapeutic approach results in a greater level of cancer cell death than when either therapy is used alone.

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

We have completed a Phase 1/early Phase 2 clinical trial using INGN 241 to evaluate safety, mechanism of action and efficacy in approximately 22 patients with solid tumors. This trial indicated that in patients with solid tumors, INGN 241 was well tolerated, was biologically active and displayed minimal toxicity associated with its use. Although INGN 241 was administered directly to tumors, evidence of distant biologic activity was observed, suggesting this therapy may have utility in treating primary tumors as well as metastatic disease. We are conducting a Phase 2 clinical trial using INGN 241 in patients with metastatic melanoma. We are also conducting a Phase 3 clinical trial using INGN 241 in combination with radiation therapy for solid tumors.

Data from our Phase 1/early Phase 2 clinical trial of INGN 241 in patients with solid tumors demonstrated 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 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 conducted pre-clinical work indicating that in addition to its known activity as a tumor suppressor, the protein produced by mda-7 may also stimulate the body s immune system to kill metastatic tumor cells and to protect the body against cancer, thereby offering the potential of providing an added advantage in treating various cancers because it may attack cancer using two different mechanisms. Because the mda-7 tumor suppressor may act as a cytokine, or immune system modulator, it is also known as interleukin 24, or IL-24. The mda-7 molecule may also work as a radiation sensitizer to make several types of human cancer cells more susceptible to radiation therapy. We

have seen evidence of this effect in pre-clinical and clinical settings.

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

Pre-clinical data indicate the combination of INGN 241 and Velcade® (Bortezeamib), marketed by Millennium Pharmaceuticals, Inc., can result in increased tumor cell killing in human ovarian cancer cells. These data showed that co-administration of INGN 241 and Velcade®, a known protein degradation inhibitor, further elevated mda-7 protein levels and caused a significant increase in killing of ovarian cancer cells. These findings are published in *Cancer Gene Therapy*.

Pre-clinical data indicate INGN 241 works synergistically with celecoxib, marketed by Pfizer as Celebrex®, to inhibit the growth and increase killing of breast cancer cells. 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.

Pre-clinical data indicate INGN 241 and bevacizumab, marketed by Roche Holding AG and Genentech, Inc. (Genentech) as Avastin®, each inhibit tumor angiogenesis through distinct mechanisms in models of lung cancer. Study results demonstrate the combination of INGN 241 and Avastin® significantly increases anti-tumor activity compared with either agent used separately. We have observed synergistic activity resulting in a positive therapeutic effect in the treatment of lung cancer in laboratory animals following the combination of the two agents. In contrast, treatment with Avastin® alone demonstrated only minor tumor regression in those animals. These findings have been published in *Molecular Therapy*, the journal of the American Society of Gene Therapy.

Pre-clinical data indicate the combination of INGN 241 and Tarceva®, marketed by Genentech, more significantly inhibits tumor cell growth than Tarceva® administered alone. The preclinical data suggest the two agents work in concert to inhibit activity of the epidermal growth factor receptor, a potent driver for cell growth in many types of cancer.

Our pre-clinical work indicates INGN 241 effectively kills cancer cells that are resistant to cisplatin, one of the most commonly used chemotherapeutic agents. These pre-clinical studies identified a novel defect in a protein degradation pathway in the cisplatin-resistant cells. This defect enhances the activity of INGN 241, suggesting that INGN 241 may have particular utility in treating cancers that do not respond to cisplatin. We have also observed that INGN 241 can restore cisplatin sensitivity to certain cancer cells that have become cisplatin-resistant.

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

We have published preclinical data describing how an important tumor survival pathway impacts the anticancer activity of INGN 241. Inhibition of this pathway, known as NF-kB, enhanced the tumor killing effects of INGN 241 in cell culture and in preclinical models of human tumors. Researchers at Introgen and The University of Texas M. D. Anderson Cancer Center conducted theses studies. The data appear in the publication *Molecular Cancer Therapeutics*.

We have published preclinical data demonstrating that vitamin E succinate (VES) enhances the cytotoxic effects of INGN 241 in ovarian cancer cells. VES is a derivative of Vitamin E that has demonstrated potent antitumor activity in cell and animal models of cancer. Researchers at Introgen and The University of Texas M. D. Anderson Cancer Center collaborated on the studies. The results appear in the publication *Cancer Letters*.

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

Pre-clinical work has demonstrated administration of INGN 241 results in the development of systemic immune responses against tumor cells and suggests INGN 241 could be used as a novel cancer molecular immunotherapy. In pre-clinical studies, implantation of

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INGN 241-treated tumor cells into mice resulted in significant inhibition of tumor growth. Significantly, mice immunized with INGN 241-treated cells showed inhibition of tumor growth after a subsequent challenge with additional tumor cells.

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

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

Pre-clinical studies have demonstrated that INGN 241 can induce human lung cancer cells to undergo apoptosis, or programmed cell death, through the synergistic action of INGN 241 and a class of tumor-targeted drugs known as heat shock protein 90 (Hsp90) inhibitors. We have observed the combination of INGN 241 and two Hsp90 inhibitors can result in the enhancement of cell death in lung cancer cells. This combination treatment inhibited tumor cell movement, suggesting an anti-metastatic effect.

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

We have exclusive licenses from Columbia University and The University of Texas M. D. Anderson Cancer Center to mda-7 tumor suppressor technology for our therapeutic applications. The technology licensed from M. D. Anderson Cancer Center was developed pursuant to sponsored and collaborative research programs over the past several years. 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. We have an exclusive license to a family of patent applications covering methods and compositions of the mda-7 tumor suppressor with several types of currently available therapies, including conventional chemotherapies, vascular endothelial growth factor inhibitors, such as Avastin® (bevacizumab), non- steroidal anti-inflammatory drugs, which include COX-2 inhibitors such as Celebrex®, (celecoxib) and proteasome inhibitors, which can increase therapeutic functionality, such as Velcade® (bortezemib).

INGN 225 (p53 molecular immunotherapy)

We are developing INGN 225 using the p53 tumor suppressor in a different manner to create a molecular immunotherapy for cancer that stimulates a particular type of immune system cell known as a dendritic cell. Research published in *Current Opinion in Drug Discovery & Development* concluded that the p53 tumor suppressor can be used with a patient s isolated dendritic cells as an antigen delivery and immune enhancing therapeutic strategy. Pre-clinical testing has shown that the immune system can recognize and kill tumors after treatment with dendritic cells stimulated by the p53 tumor suppressor, which suggests a molecular immunotherapy consisting of dendritic cells stimulated by p53 could have broad utility as a treatment for progression of tumors.

Moffitt Cancer Center is conducting a Phase 2 randomized, controlled study of INGN 225 involving as many as 80 patients with metastatic, small-cell lung cancer. Mutations in the p53 tumor suppressor occur in approximately 90 percent of the patients with this disease such that this patient population is well-suited for testing the clinical efficacy of INGN 225. The National Institutes of Health National Cancer Institute awarded to Moffitt Cancer Center a grant of approximately $1.3 million to fund this trial. We have the right to, and expect we will, use the clinical data generated from this study as part of our INGN 225 commercial development efforts.

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

The results from the Phase 1/2 trial in patients with extensive-stage small cell lung cancer who were previously treated with chemotherapy demonstrated a 45 percent response rate in patients with platinum-resistant small-cell lung cancer who received

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chemotherapy following INGN 225. The historical response rate is generally less than 15 percent in these patients. Among the 43 patients evaluable for survival following INGN 225 treatment, survival was also improved compared to historical controls.

INGN 234 (p53 topical)

We are developing INGN 234 for the prevention of oral cancers and the treatment of oral leukoplakia. We conducted a Phase 1 clinical trial in which p53 was administered in an oral mouthwash formulation to prevent precancerous oral lesions from developing into cancerous lesions.

We are conducting pre-clinical work on other topical administrations of tumor suppressors to control or prevent oral or dermal cancers. We are investigating multiple delivery platforms, including both viral and non-viral approaches. We are also investigating combining delivery of our therapies with rinses, patches, ointments and enhancing polymers. We believe the opportunity exists to develop non-toxic treatments for pre-malignant and malignant cells that can be easily exposed to natural biological tumor suppressor and DNA repairing molecules.

We have entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. See Part I, Item 2. Management s Discussion and Analysis of Financial Condition and Results of Operation Business and Collaborative Arrangements Alliance with Colgate-Palmolive Company below for further discussion of this alliance agreement.

INGN 401 (FUS-1)

INGN 401 uses systemically administered nanoparticles to express the tumor suppressor FUS-1. We exclusively license the FUS-1 technology from M. D. Anderson Cancer Center.

A Phase 1/early Phase 2 clinical trial is in process at M. D. Anderson Cancer Center testing INGN 401 in patients with advanced non-small cell lung cancer who have been treated previously with chemotherapy. INGN 401 was successfully delivered into the tumors of stage IV lung cancer patients and was found to be active in patients metastatic non-small cell lung cancer tumors. This finding is the first clinical demonstration that a gene can be injected intravenously and be taken up and expressed at high levels in cancer cells at distant sites.

The interim results of this clinical trial were presented by the M. D. Anderson Cancer Center investigators at the 2007 annual meeting of the American Association of Cancer Research. That presentation noted this clinical trial consists of thirteen patients first treated with front line cisplatin combination chemotherapy, which failed to halt their disease. They received INGN 401 as a second line therapy. At the time of this presentation, the median survival time for the patients in this study was 14.6 months which compares favorably to a seven-month median survival time for patients receiving conventional second line therapy. No significant drug-related toxicity has been observed with respect to INGN 401. The clinical trial continues and no maximum tolerated dose has been established.

Pre-clinical data suggests 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.

Pre-clinical data suggests that a combination of ADVEXIN therapy and INGN 401, administered intravenously in nanoparticle formulations, is capable of significantly shrinking metastatic tumors in models of human lung cancer. The data indicates that while ADVEXIN therapy and INGN 401 are each effective as a monotherapy, more powerful results were observed when the treatments were combined. The data also indicates that the nanoparticle treatments had no demonstrable adverse effects on normal cells.

INGN 401 has demonstrated synergistic activity with gefitinib (Iressa®), 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.

Data and findings from our work to develop INGN 401 have been published in *Cancer Gene Therapy* and *Cancer Research.* We are working with investigators at MDACC to design a pivotal clinical trial for INGN 401.

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

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

INGN 007 (oncolytic viral therapy)

We are developing INGN 007, a replication-competent viral therapy, which is also called an oncolytic virus, 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 molecule that allows the vector to saturate the entire tumor. This testing has demonstrated that INGN 007 has a favorable safety profile and significantly inhibits tumor growth. Findings from this work to develop INGN 007 have been published in *Cancer Research* and were presented at a meeting of the ASCO. We are developing this replication-competent viral therapy through our strategic collaboration with VirRx. We have submitted to the FDA our Investigational New Drug application for INGN 007 in solid tumors.

Other Research and Development Programs

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

We license from M. D. Anderson Cancer Center a group of molecules known as the 3p21.3 family. Pre-clinical research performed on these molecules by collaborators at The University of Texas Southwestern Medical Center and M. D. Anderson Cancer Center suggests that the 3p21.3 family plays a critical role in the suppression of tumor growth in lung and other cancers. This family of molecules includes the FUS-1 tumor suppressor we are testing as INGN 401 and the NPRL2 gene. We are working with M. D. Anderson Cancer Center to further evaluate other 3p21.3 family molecules as clinically relevant therapeutics.

The NPRL2 gene is believed to be important in the genesis of multiple types of cancer, including lung cancer and renal cell cancer. Preclinical data with the NPRL2 tumor suppressor gene demonstrated that systemic treatment using NPRL2 nanoparticles in combination with cisplatin resulted in a 90% inhibition of tumor growth in human lung cancer cells compared to control treatments. The ability to use a biomarker assay for NPRL2 to identify patients who might not experience significant benefit from treatment with cisplatin alone could represent an important advance in cancer treatment. Development of NPRL2 systemic nanoparticles may help patients whose tumors are resistant to cisplatin by re-sensitizing tumors to this commonly used therapy. Study results involving the NPRL2 treatment have been published in *Cancer Research*, a biomedical journal, and *Cancer Wise*, an electronic publication of M. D. Anderson Cancer Center.

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

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

Introgen Enabling Technologies

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

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Nanoscale Viral Delivery Systems

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

Nanoparticle Systemic Delivery Platform

We hold an exclusive, worldwide license to a portfolio of patents from M. D. Anderson Cancer Center focused on the delivery of biologically active proteins, polypeptides and peptides using novel nanoparticle delivery complexes. These systemically-delivered nanoparticles are applicable to a wide variety of bioactive protein-derived molecules. This technology is directed to specially designed nanoparticles that carry and deliver therapeutic bioactive proteins, polypeptides and peptides to targeted cells, such as cancer cells.

These nanoparticle formulations have certain therapeutic advantages. While peptides alone may be rapidly removed from circulation, requiring frequent administration and high doses, our nanoparticle-polypeptide formulations can increase therapeutic activity and protect against rapid degradation normally associated with peptide therapy. Our peptide nanoparticles can include special targeting molecules to further enhance cellular uptake and to improve therapeutic efficacy. We believe these formulations can be expected to have a systemic effect.

We have 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 using this technology in INGN 401, INGN 402 and INGN 403.

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

Replicating Viral Delivery Systems

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

Additional Enabling Technologies

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

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

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

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

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Manufacturing and Process Development

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

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

As a result of an audit and inspection by a European Union Qualified Person (QP), we are certified with the Medicines and Healthcare Products Regulatory Agency (MHRA) that our facilities and production processes are compliant with European Good Manufacturing Practices for the manufacture and testing of ADVEXIN therapy. The MHRA is the competent authority in the UK and is a component of the EMEA.

Business and Collaborative Arrangements

Alliance with Colgate-Palmolive Company

In November 2005, we entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. In connection with the alliance agreement and pursuant to a common stock purchase agreement, Colgate-Palmolive purchased 3,610,760 shares of our common stock at a price of $5.539 per share for a total of approximately $20.0 million. Under the common stock purchase agreement, Colgate-Palmolive 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 are conducting 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. The alliance agreement excludes certain of our cancer product candidates, including ADVEXIN therapy, INGN 241, INGN 225 and INGN 401.

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

VirRx, Inc.

We are working with VirRx to investigate other vector technologies, specifically replication-competent viral therapies, for delivering products into targeted cells. These technologies form the basis for our INGN 007 product candidate. We own approximately 49% of the outstanding common stock of VirRx.

Under a collaboration and license agreement with VirRx, we are required to make additional milestone stock purchases, either for cash or through the issuance of our common stock, upon the completion of Phase 1, 2 and 3 clinical trials involving technologies licensed under this agreement. We are required to make a $5.0 million cash milestone payment to VirRx, for which we will receive no VirRx stock, upon approval by the FDA of a BLA for the

first collaboration product based on these technologies. To the extent we

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have already made cash milestone payments, we may receive a credit of 50% of the Phase 2 clinical trial milestone payments and 25% of the Phase 3 clinical trial milestone payments against this $5.0 million cash milestone payment.

The additional milestone stock purchases and cash payments are not anticipated to be required in the near future. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice, which would also terminate the requirement for us to make any additional stock purchases.

Academic and Other Collaborations

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

The University of Texas M. D. Anderson Cancer Center

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

We have license agreements with The Board of Regents of The University of Texas System and M. D. Anderson Cancer Center, a component institution of The University of Texas System, whereby we have exclusive, worldwide licenses to make, use and sell certain technology. Under the terms of the license, we will pay M. D. Anderson Cancer Center a royalty based on net sales by us or our affiliates or by sublicense agreement of products incorporating any of such technologies. We are obligated by the license agreements to reimburse any of M. D. Anderson Cancer Center s costs that may be incurred in connection with obtaining patents related to the licensed technologies.

Our strategy for product development is designed to take advantage of the significant multidisciplinary resources available at M. D. Anderson Cancer Center. Through these efforts, we have licensed numerous technologies and patents over the past several years that we believe could hold promise for development into commercial products.

National Cancer Institute

We have multiple cooperative research and development agreements, or CRADA, with the NCI. Under one of these agreements, the NCI will conduct a Phase 2 clinical study to treat cancer patients with genetically engineered therapies targeted to abnormal p53 pathways. This clinical study will combine our p53 formulations with a novel p53 targeted treatment developed by investigators at the NCI. This agreement continues until March 2012 and is terminable earlier upon the mutual consent of the parties. We are paying the NCI approximately $19,000 per quarter through March 2009 to support their technical, statistical and administrative activities under this CRADA.

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

Research and License Agreements for mda-7 Tumor Suppressor Programs

We have exclusive licenses from Columbia University and M. D. Anderson Cancer Center to mda-7 tumor suppressor related technology for our therapeutic applications. The technology licensed from M. D. Anderson Cancer Center was developed pursuant to sponsored and collaborative research programs over the past several years. The agreement is effective until the last to expire of the subject patents. It is terminable upon the breach or insolvency of either party. Under the sublicense agreement, we have agreed to

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make additional payments to Columbia University upon the achievement of development milestones, as well as royalty payments on product sales.

Moffitt Cancer Center

We are collaborating with the H. Lee Moffitt Cancer Center and Research Institute to advance our INGN 225 molecular cancer immunotherapy program. Moffitt Cancer Center has conducted pre-clinical research with us and has completed a Phase1/2 clinical trial in patients with small cell lung cancer. The National Institutes of Health National Cancer Institute awarded Moffitt Cancer Center a grant of approximately $1.3 million to conduct a Phase 2 clinical trial of INGN 225. We have the right to, and expect we will, use the clinical data generated from this study as part of our INGN 225 commercial development efforts.

Marketing and Sales

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

Patents and Intellectual Property

Our Portfolio

Our success will depend in part on our ability to develop and maintain proprietary aspects of our technology. To this end, we have an intellectual property program directed at developing proprietary rights in technology that we believe may be important to our success. We also rely on a licensing program to ensure continued strong technology development and technology transfer from companies and research institutions with whom we work. We have entered into a number of exclusive license agreements or options with companies and institutions, including M. D. Anderson Cancer Center, Sidney Kimmel Cancer Center, Aventis Pharmaceutical Products, Inc. (Aventis), which is now Sanofi-Aventis, Columbia University, VirRx and LXR, with the LXR rights being subsequently sold to Tanox, which in turn has been acquired by Genentech. 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. Currently, the last to expire patents key to our ADVEXIN therapy expire in 2020. We have applications pending that could extend our coverage for our ADVEXIN therapy beyond these dates. Patents key to our INGN 241 product, using the mda-7 tumor suppressor, expire in the time frame of 2013 to 2016, although we have pending patent cases that could extend our protection beyond these expiration dates. 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 independent development programs and work with M. D. Anderson Cancer Center, we currently have an exclusive license to a number of United States and corresponding international patents and patent applications directed to adenoviruses that contain p53, referred to as adenoviral p53, adenoviral p53 DNA, adenoviral p53 pharmaceutical compositions, the production of adenoviral p53 compositions and the use of such compositions in various cancer therapies and protocols.

We have exclusively licensed from Aventis patent applications directed to adenoviral p53 and its clinical applications. We have an exclusive license to a United States patent application and corresponding international applications directed to the use of the p53 tumor suppressor in the treatment of cancer patients whose tumors express a normal p53 protein.

Combination Therapy with Tumor Suppressors, including p53 and mda-7/IL24

Our portfolio development includes seeking protection for clinical therapeutic strategies that combine the use of either the p53 tumor suppressor or the mda-7/IL-24 tumor suppressor with traditional cancer therapies. In this regard, also arising out of our work

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with M. D. Anderson Cancer Center, we have an exclusive license to a number of issued United States patents and applications with corresponding international patents and applications directed to cancer therapy using either the p53 tumor suppressor or the mda-7/IL-24 tumor suppressor in combination with conventional radiotherapy and/or other anti-cancer compounds. Such compounds include:

DNA-damaging agents and conventional chemotherapies;

Immunotherapeutics (e.g., Herceptin®);

COX-2 inhibitors (e.g., celecoxib);

Hsp90 inhibitors;

Proteasome inhibitors;

VEGF inhibitors (e.g., Avastin®); and

EGFr inhibitors (e.g., Tarceva®, Iressa®).

These United States patents and applications and corresponding international patents and applications concern the therapeutic application of the p53 tumor suppressor or the mda-7/IL-24 tumor suppressor before, during or after treatment with radiotherapy or other anti-cancer compounds.

To further extend our portfolio as it relates to combinatorial anti-cancer therapy, we have licensed from Aventis a United States patent and corresponding international patents and applications directed to therapy using the p53 tumor suppressor together with taxanes such as Taxol® or Taxotere®. We have exclusively licensed a United States patent application and corresponding international applications directed to the use of the p53 tumor suppressor in combination with surgical intervention in cancer therapy.

Adenovirus Production, Purification and Formulation

Another focus of our research has involved the development of procedures for the commercial-scale production of our potential adenoviral-based products, including that of ADVEXIN therapy. We own four issued United States patents and related European patents, as well as a number of pending United States applications and corresponding international applications directed to highly purified adenoviral compositions, commercial-scale processes for producing adenoviral-based compositions having a high level of purity and storage-stable formulations. These patents and patent applications include procedures for preparing commercial quantities of recombinant adenovirus products and include procedures applicable to the p53 tumor suppressor, as well as any of our other potential products.

We have licensed from Aventis in the p53 field a United States patent and corresponding international applications directed to processes for the production of purified adenoviruses, which are useful for our product applications. With respect to storage-stable formulations, we were issued a United States patent directed to compositions and methods concerning improved, storage-stable adenovirus formulations. This patent is not limited to our ADVEXIN therapy product candidate and may eventually replace formulations currently in use.

Other Tumor Suppressors

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

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 licenses include various applications and patents relating to p53, combination therapy with 2-methoxyestradiol, anti-proliferative factor technologies, retroviral delivery systems, stimulation of anti-p53 and screening and product assurance technologies.

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We have exclusively licensed a number of United States and international applications directed to various improved vector applications employing more than one molecular therapy for disease treatment, as well as applications directed to the delivery of molecular therapies for disease treatment without the use of a vector, or non-viral therapy. For example, a United States patent, exclusively licensed to us, was issued that is directed to adenoviruses that exhibit tissue specific replication. We have exclusive rights in an issued United States patent and corresponding international applications directed to a low toxicity analogue of IL-24, also called F42K. We also have been issued exclusively licensed patents in Europe directed to our nanoparticle delivery system for delivering tumor suppressor genes.

Trade Secrets

We rely on trade secrets law to protect technology where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. We generally require employees, academic collaborators and consultants to enter into confidentiality agreements covering our trade secrets and other confidential information. Despite these measures, we may not be able to adequately protect our trade secrets or other proprietary information.

We are a party to various license agreements that give us rights to use specified technologies in our research and development processes. If we are not able to continue to license this technology on commercially reasonable terms, our product development and research may be delayed. In the case of technologies we have licensed, we may not have the ability to make the final decisions on how the patent application process is managed, and accordingly may be unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology.

Our research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be diminished.

Financial Overview

Since our inception in 1993, we have used our resources primarily to conduct research and development activities for ADVEXIN therapy and, to a lesser extent, for other product candidates. At March 31, 2008, we had an accumulated deficit of $205.1 million. We anticipate we will incur losses in the future that may be greater than losses incurred in prior periods. At March 31, 2008, we had cash, cash equivalents and short-term investments of $16.5 million.

During the three months ended March 31, 2008, we sold all the shares of Silence Therapeutics plc we owned for their quoted market value on the Alternative Investment Market of the London Stock Exchange on the date of the sale. We received net proceeds of approximately $7.4 million from this sale. We purchased these shares for approximately $3.0 million in July 2005. These shares were presented as marketable securities in our financial statements in previous periods.

We have used cash primarily as follows (in thousands):

	Three Months Ended March 31,	
	2007	**2008**
Operating activities	$ 5,439	$ 5,538
Purchases of property and equipment		126
Principal payments on notes payable	269	174
Payment of offering costs related to previous sales of common stock	1,571	75

We have received cash primarily as follows (in thousands):

	Three Months Ended March 31,	
	2007	**2008**

Proceeds from sale of marketable securities	$	$7,429
Proceeds from stock option exercises	97	19

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We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities continue and as we evolve our operations and systems to support commercialization of our product candidates. These losses, among other things, have caused and may cause our total assets, stockholders equity and working capital to decrease.

We currently earn revenue or income from research grants from U.S. Government agencies, contract services and process development activities, the lease of a portion of our facilities to M. D. Anderson Cancer Center and interest income on cash placed in short-term, investment grade securities. To fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders.

We have an effective registration statement on Form S-3 (Commission File No. 333-140424) for the sale by us of shares of our common stock with an aggregate offering price of up to $150.0 million.

Stock Options

From time to time, we grant options to purchase our common stock to our directors, officers, employees and other service providers in recognition of their contribution to achieving our corporate objectives and as an incentive for their future contributions to us. These options typically vest under the following general terms:

Options issued to members of our Board of Directors vest monthly over 12 months.

Options issued to our Chief Executive Officer vest 100% on the date of grant.

Options issued to all other persons vest over four years at the rate of 25% per year on each annual anniversary of the grant date.

Our outstanding stock options have an exercise price equal to the market price of our common stock on their date of grant. At March 31, 2008, we had options outstanding to purchase the following numbers of shares of our common stock:

Vested Options	Unvested Options	Total Options	Range of Exercise Prices Per Share
6,196,492	2,185,025	8,381,517	$0.52 to $8.94

We issued the following number of shares of common stock as a result of exercises of stock options granted from our stock option plans:

Three Months Ended March 31,	
2007	2008
108,400	9,350

Stock Purchase Warrants

From time to time, we issue stock purchase warrants, generally to investors or placement agents, in connection with sales of our common stock. As of March 31, 2008, we have fully vested warrants outstanding to purchase an aggregate of 1,400,032 shares of our common stock at prices ranging from $4.60 per share to $8.00 per share. These warrants expire on various dates through December 2015.

With respect to warrants for 686,087 of these shares exercisable through June 2008 at $4.60 per share, we may force their exercise if the average closing market price of our common stock during any 20 consecutive trading days is greater than $15.78 per share. These warrants also provide for the downward adjustment of their exercise price in the event we sell shares of our common stock at a price less than their current exercise price.

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Agreement With Board Member

We have a business development agreement with a new member of our Board of Directors under which he will provide certain business development services to us in connection with potential co-development, collaborative, marketing partnership or certain other potential strategic transactions. In consideration for his services, upon the consummation of such a transaction, we will pay him a fee equal to one-half of one percent (0.5%) of certain monetary benefits received by our stockholders or us. The maximum fee he can receive is $3,000,000. The fee we pay him will be reduced by expenses or other expenditures made or contemplated under such a transaction.

This fee is not payable for funding we receive that we are expected to expend for research and development programs, full time equivalent payments to employees, loans, collaborative programs, business partnerships or strategic transactions, or otherwise. Transactions between our affiliates and us, whether now existing or created in the future, are excluded from this agreement. This agreement may be terminated at any time by written notice from us or this board member. In the event of such termination, the fee shall be paid with respect to a transaction produced through services performed by this board member before termination if the transaction is closed within two years after the date of termination of the agreement.

Critical Accounting Policies and Recently Issued Accounting Pronouncements

Our critical accounting policies and recently issued accounting pronouncements of significance to us are described in our most recent annual report on Form 10-K for the year ended December 31, 2007, filed with the Securities and Exchange Commission on March 17, 2008. There have been no material changes in these items since that time. As noted in that annual report, Statement of Financial Accounting Standards No. 157, Fair Value Measurements, and Statement of Financial Accounting Standards No. 159, The Fair Value Option for Financial Assets and Financial Liabilities, were effective for us on January 1, 2008. Our adoption of those standards has no material effect on our financial statements.

Results of Operations

Our operations consist primarily of the research and development of our product candidates and technologies described above in Part I, Item 2. Management s Discussion and Analysis of Financial Condition and Results of Operations Product Development Overview. Our research and development expense includes, but is not limited to, expense related to personnel, facilities and equipment, pre-clinical research, clinical trials, manufacturing of materials for use in clinical trials, conducting data analysis and conducting regulatory documentation submissions to the FDA. Our research and development expense can be divided between programs in the pre-clinical stage and programs in the clinical stage, and general research and development expense attributable to all programs. We manage our business by tracking research and development expense in these categories in lieu of tracking research and development expense on a project-by-project basis. Tables setting forth the amount of research and development expense we have incurred in each of these categories are presented below under Comparison of Three Months Ended March 31, 2008 and March 31, 2007.

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

The likelihood that a product candidate will be commercially successful may be affected by a variety of factors, including, among others, the quality of the product candidate, the validity of the target and disease indication, early clinical data, competition, manufacturing capability and commercial viability. Because of the discretion of the FDA, EMEA and similar agencies throughout the world, as well as the foregoing factors, we cannot predict with reasonable accuracy:

The future expense we will incur developing these product candidates;

When we will complete our work in developing these product candidates;

When, if ever, we will earn significant revenue from approved products that might result from these product development programs.

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

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

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

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

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

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

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

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

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

We expect our operating expenses discussed below could increase in the future as we continue to expand our research and development programs and work to commercialize our product candidates. If we are successful in receiving approval from regulatory agencies to sell one or more of our product candidates, we expect to incur expenses in the future that we have not incurred in the past, such as product manufacturing costs and sales and marketing expenses. If we are able to obtain more debt financing to support these activities, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on additional indebtedness we may incur. If we raise additional funds through the issuance of equity securities, the percentage ownership of our stockholders could be significantly diluted. If we are able to sell one or more of our product candidates, we expect to receive revenue in the future that we have not received in the past.

Comparison of Three Months Ended March 31, 2008 and March 31, 2007

The following comparisons are for the three months ended March 31, 2008 and March 31, 2007. References to the 2008 period refer to the three months ended March 31, 2008 and references to the 2007 period refer to the three months ended March 31, 2007. All dollar amounts are in thousands unless noted otherwise.

Contract Services, Grant and Other Revenue

	Three Months Ended March 31,	
	2007	**2008**
Contract services, grant and other revenue	$ 322	$ 186

Percent increase (decrease) from previous period	N/A	(42)%

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The change in contract services, grant and other revenue for the 2008 period compared to the 2007 period was a result of :

Decreased research activity funded by federal grants as the work under these grants approached completion and either:

No new grants were added to replace the expiring grants; or

New grants related to our product development technologies were funded in the name of and directly to our academic collaborators which, while such grants can provide us access to the benefits of the funded research, do not produce grant revenue recorded in our financial statements;

which was offset by:

Increased contract services revenue for research work we performed for third parties as a result of our active efforts to expand our offering of these services.

Research and Development Expense

	Three Months Ended March 31,	
	2007	**2008**
Pre-clinical stage programs expense	$ 353	$ 447
Clinical stage programs expense	1,991	3,356
General research and development expense	831	879
Total research and development expense	$ 3,175	$ 4,682
Percent increase (decrease) in total from previous period	N/A	47%

Research and development expense included share-based compensation expense of $175,000 for the 2008 period and $305,000 for the 2007 period.

We experienced a reduction in research and development expense in the 2007 period due to typically non-recurring events in that period consisting of:

Reaching an agreement with a third party in the 2007 period that resulted in us not having to pay certain of their invoices that were previously included in our accounts payable; and

Credits to expense resulting from the reduction in the 2007 period of amounts previously accrued for possible liabilities..

Our research and development expense in the 2008 period was substantially the same as what this expense would have been in the 2007 period absent these events, which is reflective of the consistent nature of our research and development activities between those periods.

General and Administrative Expense

	Three Months Ended March 31,	
	2007	**2008**
General and administrative expense	$ 3,267	$ 2,531
Percent increase (decrease) from previous period	N/A	(23)%

General and administrative expense included share-based compensation expense of $870,000 for the 2008 period and $950,000 for the 2007 period.

The change in the 2008 period compared to the 2007 period was a result of:

Decreased legal fees incurred with respect to certain matters arising during the normal course of our business;

Decreased fees related to investor and public relations activities; and

Decreased share-based compensation expense, which is discussed further below under Share-Based Compensation Expense.

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Share-Based Compensation Expense

	Three Months Ended March 31,	
	2007	2008
Share-based compensation expense	$ 1,255	$ 1,045
Percent increase (decrease) from previous period	N/A	(17)%

The change the 2008 period compared to the 2007 period was primarily a result of:

The absence of a broad-based grant of stock options to substantially all employees in calendar 2007 as had typically been the case in prior years. This absence resulted in a decrease in this expense in the 2008 period as the expense for similar such grants from approximately four years earlier became fully amortized without new, additional expense amortization from a calendar 2007 grant;

The forfeiture of stock options resulting from normal employee attrition; and

Variances in the risk-free interest rate, the volatility of our stock price and other factors considered in our determination of share-based compensation expense using the Black-Scholes option pricing model.

Interest Income

	Three Months Ended March 31,	
	2007	2008
Interest income	$ 442	$ 99
Percent increase (decrease) from previous period	N/A	(78)%

The change in the 2008 period compared to the 2007 period was a result of:

A lower overall average balance of cash, cash equivalents and short-term investments in the first quarter of the 2008 period compared to the 2007 period as a result of the investment of proceeds from our sales of our common stock in November 2006 and December 2006 for which there were no similar transactions in calendar 2007 or during the 2008 period; and

Generally lower interest rates during the 2008 period compared to the 2007 period;

which were partially offset by

Earnings on the proceeds received from the sale of marketable securities in the 2008 period as further discussed in the Financial Overview section above.

Interest Expense

	Three Months Ended March 31,	
	2007	2008
Interest expense	$ 179	$ 162
Percent increase (decrease) from previous period	N/A	(9)%

This expense decreased for the 2008 period compared to the 2007 period due to reductions in the total principal balance outstanding under notes payable on which we are paying interest as a result of normal debt service payments.

Realized Gain on Sale of Marketable Securities

	Three Months Ended March 31,	
	2007	2008
Realized gain on sale of marketable securities	$	$ 4,388

Percent increase (decrease) from previous period	N/A	100%

The change in the 2008 period compared to the 2007 period was a result of our sale of all the shares we owned of Silence Therapeutics as further discussed in the Financial Overview section above.

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Other Income

	Three Months Ended March 31,	
	2007	2008
Other income	$ 254	$ 297
Percent increase (decrease) from previous period	N/A	17%

The dollar amount of other income was generally comparable between the 2008 and 2007 periods, which is consistent with the nature of our activities that generate other income. The percentage variations in this income is not material to our business due to the relatively low dollar amounts involved. This income is earned primarily from our sublease of space to M. D. Anderson Cancer Center and other miscellaneous activities.

Liquidity and Capital Resources

In the following discussion of liquidity and capital resources, references to the 2008 period refer to the three months ended March 31, 2008 and references to the 2007 period refer to the three months ended March 31, 2007. All dollar amounts are in thousands unless noted otherwise.

We have incurred annual operating losses since our inception. At March 31, 2008, we had an accumulated deficit of $205.1 million.

Our cash equivalents and short-term investments are generally comparable financial instruments, with short-term investments having original maturity dates in excess of three months. At December 31, 2007, our marketable securities consisted of issued share capital of other public companies and were classified as available-for-sale. Our balances are as follows:

	December 31, 2007	March 31, 2008
Cash and cash equivalents	$ 11,320	$ 16,479
Short-term investments	3,585	
Total cash, cash equivalents and short-term investments	14,905	16,479
Marketable securities	10,165	
Total cash, cash equivalents, short-term investments and marketable securities	$ 25,070	$ 16,479

During the three months ended March 31, 2008, we sold all of our marketable securities at their quoted market value for net cash proceeds of approximately $7.4 million.

The change in our cash and cash equivalents, exclusive of short-term investments and marketable securities, consisted of the following amounts, the details of which are presented in our condensed consolidated statements of cash flows in Item 1. Financial Statements above:

	Three Months Ended March 31,	
	2007	2008
Net cash (used in) operating activities	$ (5,439)	$ (5,538)
Net cash (used in) provided by investing activities	$(13,436)	$10,888
Net cash (used in) financing activities	$ (1,743)	$ (230)

From inception through March 31, 2008, we have financed our operations primarily from the following sources, the amounts of which are presented net of related expenses paid in cash (in millions):

$ 69.1

Equity sales in December 2003, December 2004, November 2006 and December 2006 through registered direct offerings under a shelf registration filed with the SEC	
Collaborative research and development payments from Aventis Pharmaceutical Products, Inc, which is now Sanofi-Aventis, from 1994 to 2000	49.7
Private equity sales to Aventis from 1994 to 1999	39.4
Initial public offering in October 2000	32.2
Private equity sales to various other parties	29.8

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Contract services, grants, interest and other income	30.7
Equity sales to Colgate-Palmolive under a shelf registration filed with the SEC and pursuant to an alliance agreement entered into in November 2005	19.6
Mortgage financing from banks for our facilities	9.9
Sales of ADVEXIN therapy product to Aventis for use in later-stage clinical trials from 1997 to 2000	7.5
Gain on sale of shares of shares of Silence Therapeutics plc in January 2008	7.4
Leases and notes payable from commercial lessors and lenders to acquire equipment pledged as collateral for those leases and notes	6.5

We expect to continue focusing our activities primarily on conducting Phase 3 and other clinical trials, conducting data analysis related to those trials, preparing regulatory documentation submissions to the FDA, producing ADVEXIN therapy and other clinical materials for use in our clinical trials and conducting pre-marketing activities for ADVEXIN therapy. We expect to continue our research and development of various other targeted molecular therapy technologies. If ADVEXIN therapy or any of our other product candidates are approved for commercial sale by the FDA, we expect to conduct activities supporting the marketing, sales, production and distribution of those products, either ourselves or in collaboration with other parties.

We believe our cash, cash equivalents and short-term investments on hand at March 31, 2008, plus the amounts we may earn from contract services, grants and/or interest income during 2008, will be sufficient to fund our operations through at least March 31, 2009, and perhaps longer, at a level necessary to achieve our primary business objectives. However, in order to fund our operations beyond March 31, 2009, or to introduce any new product candidates, we may be required to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. If we raise additional funds through the issuance of equity securities, the percentage ownership of our stockholders could be significantly diluted. If we obtain additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on such indebtedness, and the terms of the debt securities issued could impose significant restrictions on our operations. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders. In the event these sources of financing become unavailable, we may have to adjust the scope of our operations and related cash needs to a level that can extend the period of time during which we can rely on existing resources to conduct our business activities. Such adjustments in the scope of our operations could include reducing the number of our personnel and perhaps delaying or discontinuing certain product development activities critical to achieving our business objectives.

Net Cash Used in Operating Activities

	Three Months Ended March 31,	
	2007	2008
		(
Net cash used in operating activities	$(5,439)	$ 5,538)

The net cash we used in our operating activities relates to the following items:

Net loss - The net loss reported in our statement of operations includes certain expenses that do not involve the use of cash. The following table illustrates the portion of our net loss for which we use cash:

	Three Months Ended March 31,	
	2007	2008

Net loss	$ (5,617)	$ (2,401)
Less expenses not requiring the use of cash:		
Non-controlling interests in income of consolidated subsidiary	14	(4)
Depreciation	279	247
Share-based compensation	1,255	1,045
Gain on sale of marketable securities		(4,388)
Portion of net loss for which we use cash	$ (4,069)	$ (5,501)
Percent increase from previous period	N/A	35%

See Comparison of Three Months Ended March 31, 2008 and March 31, 2007 above for a discussion of the changes in the components of our net loss.

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Accounts payable and accrued liabilities Changes in these accounts arise primarily from variations in the timing of payments to vendors and employees that arise in the ordinary course of business. This timing is a function of:

- Variations in our general business activities;
- The nature of vendors to whom we have obligations;
- The nature of payment terms we receive from vendors;
- The timing of when we receive invoices from vendors;
- The timing of when we elect to make payments to vendors based on our available cash balances and cash flow needs; and
- The timing of our regularly scheduled paydays for our employees relative to the end of our accounting periods.

The changes in our accounts payable and accrued liabilities for the 2008 and 2007 periods are related to one or more of the above items, with no single component of those aggregate changes being material to our business as a whole. In addition to the above items, we experienced a smaller decrease in accounts payable and accrued liabilities collectively in the 2008 period compared to the 2007 period due to:

- Reaching an agreement in the 2007 period with a third party that we would not have to pay certain of their invoices that were previously included in our accounts payable;
- Payment in the 2007 period of $1.6 million to a placement agent in connection with their work supporting the sale of our common stock in November 2006 and December 2006 that was accrued as of December 31, 2006; and
- Elimination in the 2007 period of a liability accrued at December 31, 2006 for consulting services that we determined would not have to be paid.

Deferred revenue and other - These accounts relate to:

- Cash payments for contract manufacturing, process development and product production services work received in advance of completing the work to which the payments relate, which increases our deferred revenue. This deferred revenue decreases, with no effect on cash, as we complete the work and recognize the related revenue;
- Rental income we receive from the sublease of laboratory space to third parties under leases that have variable monthly rent amounts over the term of the lease. We recognize this income on a straight-line basis over the term of the lease. Cash payments received in excess of rental income recognized is recorded as deferred revenue. This deferred revenue decreases, with no effect on cash, when the cash payments we receive are less than the rental income recognized on a straight-line basis; and
- At December 31, 2006, the long-term portion of fees payable to a placement agent that assisted with our sale of common stock in November 2006 and December 2006. There is no long term portion of this obligation at December 31, 2007.

The amount of the change in deferred revenue and other in the 2008 period compared to the 2007 period was not material to our financial position or results of operations.

Other assets Other assets decreased in the 2008 and increased in the 2007 period. Changes in other assets vary in direction and amount based on the timing of and dollars involved in transactions related to items such as prepaid expenses, grant funding receivable and deposits. The aggregate changes in other assets during the 2008

and 2007 periods resulted from such activities that arose during the normal course of our business, with no component of those aggregate changes being material to our business as a whole.

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Depreciation is an expense in our net loss that does not use cash. This expense decreased in the 2008 period compared to the 2007 period due to the absence of significant property and equipment acquisitions during the 2008 period and our use of declining balance depreciation methods that results in decreasing depreciation charges over the life of an asset.

Share-based compensation is an expense in our net loss that does not use cash. See Share-Based Compensation Expense above for a discussion of the changes in this expense between periods.

The gain on sale of marketable securities in the 2008 period resulted from the sale of the shares we owned in Silence Therapeutics as discussed further under Investment in Silence Therapeutics plc in the Financial Overview section above.

Net Cash Provided by and Used in Investing Activities

	Three Months Ended March 31,	
	2007	**2008**
Net cash (used in) provided by investing activities	$(13,436)	$10,888

The change in the 2008 period compared to the 2007 period was primarily due to:

The sale of our marketable securities for net cash proceeds of approximately $7.4 million in the 2008 period;

A higher level of net activity in sales of short-term investments in the 2008 period compared to the 2007 period arising from (1) normal variations in the amount and timing of purchases and sales of short-term investments based on our operating needs for cash and cash equivalents and (2) the availability of cash from sales of our common stock; and

A higher amount of equipment purchases to support our business being necessary in the 2008 period compared to the 2007 period.

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

Net Cash Used in Financing Activities

	Three Months Ended March 31,	
	2007	**2008**
Net cash used in financing activities	$(1,743)	$ (230)

The change in the 2008 period compared to the 2007 period was primarily due to:

The payment during the 2007 period of approximately $1.6 million of fees payable to a placement agent that were accrued as of December 31, 2006, which were for the placement agent s work supporting the sale of our common stock in November 2006 and December 2006; and

A decrease in proceeds from exercise of options for common stock in the 2008 period compared to the 2007 period, which is activity that can vary based upon the discretionary actions of the individuals holding such options.

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Debt Service, Lease and Other Contractual Obligations

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

Total debt service payments for April 1, 2008 through December 31, 2008	$ 837
Total debt service payments due during the year ending December 31:	
2009	949
2010	820
2011	735
2012	735
Thereafter	8,902
Total debt service payments	12,978
Less portion representing interest	(5,411)
Total principal balance at March 31, 2008	$ 7,567
Principal balance presented on the March 31, 2008 balance sheet as liabilities in these categories:	
Current portion of notes payable	$ 553
Notes payable, net of current portion	7,014
Total principal balance at March 31, 2008	$ 7,567

We have fixed, noncancellable rent obligations under operating leases consisting primarily of the following:

A ground lease for the land on which we built our primary research and manufacturing facilities with annual rent payments of $156,000 through September 2026. These payments are subject to adjustment in the future for inflation;

A lease for a building housing our second production facility with annual rent payments of $101,000 through January 2009; and

A lease for our corporate office space with annual rent payments of $234,000 through July 2009.

The latter two leases are subject to adjustment annually for changes in operating expenses.

Since these leases are operating leases under generally accepted accounting principles, no liability related to them is reflected on our balance sheet. Future minimum annual rental payments due under these leases and all other operating leases, the last of which is due in 2026, are as follows (in thousands):

April 1, 2008 through December 31, 2008	$ 394
Year ending December 31,	
2009	320
2010	166
2011	161
2012	156
Thereafter	2,147
Total minimum lease payments under operating leases	$ 3,344

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

Pursuant to a consulting agreement, we have paid consulting fees of approximately $175,000 per annum to EJ Financial, a company owned by a member of our Board of Directors. EJ Financial has provided us guidance on strategic product development, business development and marketing activities. Effective December 31, 2007, this consulting agreement was ended by mutual agreement between EJ Financial and us. Accordingly, we no longer make payments under this agreement.

We have a consulting agreement with Jack A. Roth, M.D., Chairman of the Department of Thoracic Surgery and Director of the Keck Center for Gene Therapy at The University of Texas M. D. Anderson Cancer Center where he holds the Bud Johnson Clinical Distinguished Chair. Dr. Roth is the primary inventor of the technology upon which our ADVEXIN therapy is based and numerous other technologies we utilize. We licensed Dr. Roth s inventions from M. D. Anderson Cancer Center. Dr. Roth is our Chief Medical Advisor and chairman of our scientific advisory board. His duties involve the regular interaction and consultation with our scientists and others on our behalf. As compensation for his services and responsibilities, this consulting agreement provides for payments to Dr. Roth of $215,000 per annum. These payments continue through the end of the consulting agreement term on September 30, 2009. We may terminate this agreement at our option upon one year s advance notice. If we had terminated this agreement as of March 31, 2008, we would have been obligated to make final payments totaling $215,000. Dr. Roth is one of our stockholders.

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A placement agent assisted with our sale of common stock in November 2006 and December 2006. As consideration for its services, we are obligated make future payments of fees to the placement agent totaling $225,000. These fees are payable in monthly installments of approximately $25,000 through December 2008.

We sublease a portion of our facilities to M. D. Anderson Cancer Center, a component institution of The University of Texas System, which is one of our shareholders. They are obligated to pay us rent and facilities operating expense reimbursements of approximately $32,000 per month during the non-cancelable term of this lease, which expires in 2009.

Non-Audit Services of Independent Registered Public Accounting Firm

Pursuant to Section 10A(i)(2) of the Exchange Act, as added by Section 202 of the Sarbanes-Oxley Act of 2002, we are responsible for disclosing the non-audit services approved by the Audit Committee to be performed by Ernst & Young LLP, our independent auditors. Non-audit services are defined as services other than those provided in connection with an audit or a review of our financial statements. The services approved by the Audit Committee are each considered by the Audit Committee to be services closely related to the financial audit process. Each of the services was pre-approved by the Audit Committee.

The Audit Committee has pre-approved additional engagements of Ernst & Young LLP for the non-audit services of preparation of state and federal tax returns.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates, foreign currency exchange rates and equity prices. Our risks, risk management strategies and sensitivity analyses estimating the effects of changes in fair values for each of these exposures at March 31, 2008 are outlined below. Actual results may differ materially from our sensitivity analyses based on changes in the timing and amount of interest rate, foreign currency exchange rate and equity price movements and our actual exposures.

Our market risk profile has not changed significantly from that described in our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 17, 2008.

Interest Rate Risk

Our exposure to market risk for changes in interest rates relates primarily to our fixed rate long-term debt and short-term investments in investment grade securities, which consist primarily of federal government obligations. Investments are classified as held-to-maturity and are carried at amortized cost. We do not hedge interest rate exposure or invest in derivative securities.

We have performed sensitivity analyses as of March 31, 2008 and December 31, 2007 using a modeling technique that measures the change in our interest income arising from a hypothetical 100-basis point decrease in the levels of interest rates across the entire yield curve, with all other variables held constant. The analyses cover our fixed rate long-term debt and short-term investments. The analyses use actual maturities for our fixed rate long-term debt and short-term investments. The discount rates we used were based on the market interest rates in effect at March 31, 2008 and December 31, 2007. The sensitivity analyses indicated a hypothetical 100-basis point decrease in the interest rates of our cash, cash equivalents and short-term investments as of March 31, 2008 would decrease our interest income by approximately $165,000 per year and approximately $41,250 per quarter, compared to a decrease in our interest income of approximately $149,000 per year and approximately $37,260 per quarter as of December 31, 2007.

At March 31, 2008, the fair value of our fixed-rate debt approximated its carrying value based upon discounted future cash flows using current market prices.

Foreign Currency Exchange Rate Risk

Substantially all of our revenue and expenses are denominated in U.S. dollars, and therefore our results of operations are not subject to foreign currency risk. However, we may continue to expand our operations globally and receive payments and incur expenses that are denominated in foreign currencies, which may increase our exposure to foreign currency exchange fluctuations.

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Item 4. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. Our management evaluated, with the participation of our Chief Executive Officer and our Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms and are effective in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and our Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosures.

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

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PART II
OTHER INFORMATION

Item 1. Legal Proceedings

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

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

Item 1A. Risk Factors

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

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

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

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

We have completed or are conducting clinical trials of our lead product candidate, ADVEXIN therapy, which is based on the p53 tumor suppressor, for the treatment of various cancers. Current or future clinical trials may demonstrate ADVEXIN therapy is neither safe nor effective.

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

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

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

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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, EMEA or other regulatory approval. Pre-clinical and clinical data can be interpreted in many different ways, and the FDA, EMEA or other foreign regulatory officials could interpret differently data we consider promising, which could halt or delay our clinical trials or prevent regulatory approval.

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. The FDA s approval for marketing of other competing products before ADVEXIN therapy is approved could terminate this Fast Track designation for ADVEXIN therapy. Similarly, we may encounter delays in the regulatory approval process due to additional information requirements from the EMEA, unintentional omissions in our Marketing Authorization Application filed with the EMEA, or other delays in the EMEA s review process. We may encounter delays or rejections in the regulatory approval process because of additional government regulation from future legislation or administrative action or changes in FDA or EMEA policy during the period of product development, clinical trials and FDA and EMEA regulatory review.

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-approval studies could cause the product to be withdrawn from the market by the FDA on an expedited basis.

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

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data and promotional activities for such product, will be subject to continual review and periodic inspections by the FDA, EMEA 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

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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 March 31, 2008, we had an accumulated deficit of approximately $205.1 million. We expect to incur substantial additional operating expense and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities continue. As we expand our operations and develop systems to support commercialization of our product candidates, these losses, among other things, have had, and are expected to continue to have, an adverse impact on our total assets, stockholders equity and working capital.

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

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

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

We expect we will fund our operations through at least March 31, 2009, and perhaps longer, 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 be required 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, EMEA or other foreign regulatory approval of ADVEXIN therapy;
- higher than expected costs of developing the processes and systems to support FDA, EMEA or other foreign regulatory approval of ADVEXIN therapy;

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

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

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

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

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

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

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

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

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

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

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

products successfully.

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

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

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

We report to the FDA, EMEA 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.

No recombinant DNA therapy products of the types being developed by us have been approved by the FDA for sale in the United States or by the EMEA for sale in Europe. The commercial success of our products will depend in part on public acceptance of the use of these types of recombinant DNA products, which are a new type of disease treatment for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that these types of recombinant DNA products are unsafe, and these treatment methodologies may not gain the acceptance of the public or the medical community. Negative public reaction to these types of recombinant DNA products could also result in greater government regulation and stricter clinical trial oversight.

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

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

the size of the patient population;

the nature of the clinical protocol requirements;

the diversion of patients to other trials or marketed therapies;

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

the proximity of patients to clinical sites; and

the patient eligibility criteria for the study.

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

an NDA for regulatory approval of our product candidates or we may be forced to terminate or abandon the study.

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

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

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

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

Our ability to develop and protect a competitive position based on our biotechnological innovations, innovations involving molecular therapies, recombinant DNA therapeutic agents, viruses for delivering targeted molecular therapies to cells, formulations, delivery systems not involving viruses, and the like, is particularly uncertain. Due to the unpredictability of the biotechnological sciences, the PTO, as well as patent offices in other jurisdictions, has often required patent applications concerning biotechnology-related inventions to be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting their scope of protection against competitive challenges. Similarly, courts have invalidated or significantly narrowed many key patents in the biotechnology industry. Thus, even if we are able to obtain patents covering commercially significant innovations, our patents may not be upheld or our patents may be substantially narrowed.

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

Schering-Plough filed with the European Patent Office, or EPO, an opposition against our European patent directed to combination therapy with p53 and conventional chemotherapy and/or radiation. An opposition is an administrative

proceeding instituted by a third party and conducted by the EPO to determine whether a patent should be maintained or revoked, in part or in whole, based on evidence brought forth by the party opposing the patent. In February 2006, the Technical Board of Appeals of the EPO held a final oral proceeding concerning Schering-Plough s opposition and determined our patent should be maintained as amended. No further appeal by Schering-Plough is possible.

We rely on trade secrets law to protect technology where we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. In addition, we generally require employees, academic collaborators and consultants to enter into confidentiality agreements. Despite these measures, we may not be able to adequately protect our trade secrets or other proprietary information. We are a party to various license agreements that give us rights to use specified technologies in our research and

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development processes. If we are not able to continue to license this technology on commercially reasonable terms, our product development and research may be delayed. In addition, in the case of technologies that we have licensed, we do not have the ability to make the final decisions on how the patent application process is managed, and accordingly are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology. Our research collaborators and scientific advisors have rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be diminished.

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

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

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

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

We have recently been involved in patent opposition proceedings before the EPO, in which we have sought to have the EPO revoke three different European patents owned or controlled by Canji/Schering-Plough. These European patents relate to the use of p53, or the use of tumor suppressors, in the preparation of therapeutic products. In one opposition involving a Canji European patent directed to the use of a recombinant tumor suppressor, the EPO revoked

the European patent in its entirety in a final, non-appealable decision. In the second opposition, involving a patent that is directed to therapeutic and other applications of the p53 and that is owned by Johns Hopkins and, we understand, controlled by Schering-Plough, the EPO recently revoked the patent in its entirety. The patent owner appealed this decision and the final hearing before the EPO Technical Board of Appeals was held in June 2005, at which time the Technical Board of Appeals confirmed the final revocation of all claims of this patent relevant to clinical therapeutic applications of p53. In a third case involving the use of p53, the European patent at issue was initially upheld, but finally revoked in a hearing held in late April 2004.

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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. The related 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.

The market for therapeutic and commercial products is intensely competitive, rapidly evolving and subject to rapid technological change. We compete with pharmaceutical and biotechnology companies, including Canji and Genvec, which are pursuing forms of treatment similar to ours for the diseases ADVEXIN therapy and our other product candidates target. We are aware that Canji, with its parent Schering-Plough, has in the past been involved in research and/or development of adenoviral p53 products and has numerous patents and patent applications relating to adenoviral p53 therapy. We understand Schering-Plough has stopped its adenoviral p53 clinical trials, and it is unknown whether these parties are continuing their adenoviral p53 research and/or development efforts. We are also aware that a Chinese pharmaceutical company, Benda Pharmaceutical, Inc. (formerly SiBiono GeneTech), 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. We do not know if monetary damages could be recovered from Benda Pharmaceutical, Inc. 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. Geopolitical developments, including trade and tariff disputes between the government of China and the United States Department of Commerce could add additional uncertainty to any effort to enforce patents, recover damages, if any, or engage in the sales and marketing of patented or non-patented products in China. We are aware that ImClone and Bristol Myers Squibb have obtained marketing approval for a monoclonal antibody product (Erbitux) for the treatment of certain kinds of recurrent head and neck cancer. We also may face competition from companies that may develop internally or acquire competing technology from universities and other research institutions. As these companies develop or acquire their technologies, they may develop competitive positions that may prevent or limit our product commercialization efforts.

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

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

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

they are more effective than alternative treatments;

their side effects are acceptable to patients and doctors;

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

we produce and sell them at a profit; and

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

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

ADVEXIN therapy, our lead product candidate, will, if approved by the FDA, initially be targeted for the treatment of recurrent head and neck cancer, a disease with an annual incidence of approximately 40,000 patients in the United States. We are simultaneously pursuing approval of ADVEXIN therapy in Europe for the treatment of recurrent head and neck cancer where the annual incidence is equal to and perhaps greater than the US incidence of this disease. Also in Europe, we are seeking approval from the EMEA to market ADVEXIN therapy for Li Fraumeni Syndrome, a rare, inherited disorder. 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 obtain adequate reimbursement from governments or third-party payors for any products that we may develop or if we are unable to obtain acceptable prices for those products, they may not be purchased or used and our revenues and prospects for profitability will suffer.

Our future revenues and profits will depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third-party payors, both in the United States and in other markets. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor s determination that use of a product is:

a covered benefit under its health plan;

safe, effective and medically necessary;

appropriate for the specific patient;

cost-effective; and

neither experimental nor investigational.

Obtaining reimbursement approval for a product from each government or other third-party payor is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to each payor. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement. Even when a payor determines that a product is eligible for reimbursement, the payor may impose coverage limitations that preclude payment for some uses that are approved by the FDA, EMEA or other foreign authorities. In addition, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent.

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Governments outside the United States may impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Legislation has been introduced into the United States Congress that, if enacted, would permit more widespread re-importation of drugs from foreign countries into the United States, which may include re-importation from foreign countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could decrease the price we receive for any approved products which, in turn, could adversely affect our operating results and our overall financial condition.

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

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

Before we can begin commercially manufacturing ADVEXIN therapy, INGN 241 or any other product candidate, we must obtain regulatory approval of our manufacturing facilities and processes. Manufacturing of our product candidates for clinical and commercial purposes must comply with the FDA s CGMP requirements in the United States and European Good Manufacturing Practices in Europe. These requirements govern quality control and documentation policies and procedures. In complying with these 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 certain inspections by regulatory authorities in the United States and Europe to obtain marketing approval in those countries.

Our current manufacturing facilities have not yet been subject to a Pre-Approval Inspection by the FDA, EMEA or other foreign regulatory authorities. Failure to pass Pre-Approval Inspections may significantly delay approval of our products. If we fail to comply with these requirements, we would be subject to possible regulatory action and may be limited in the jurisdictions in which we are permitted to sell our products. Further, the FDA, EMEA and other 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

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infringes other patents. The defense and prosecution of intellectual property suits and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

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

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

If product liability lawsuits are brought against us, we may incur substantial expenses and 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;

a diversion of our management and key personnel away from our core business;

injury to our reputation, significant media attention and potential harm to our market position;

withdrawal of clinical trial volunteers;

substantial delay in or withdrawal of FDA, EMEA or other foreign regulatory authority approval;

costs of investigation and litigation; and

substantial monetary awards to plaintiffs.

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

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

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

Our stock price may fluctuate substantially.

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

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

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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 our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 17, 2008. 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.

Our research and development efforts may not result in additional product candidates being discovered on anticipated timelines, if at all, which could limit our ability to generate revenues.

Our research and development programs, other than our programs for ADVEXIN therapy, are at preclinical stages. Additional product candidates that we may develop will require significant research, development, preclinical studies and clinical trials, regulatory approval and commitment of resources before any commercialization may occur. We cannot predict whether our research will lead to the discovery of any additional product candidates that could generate revenues for us.

Recently enacted legislation may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, market and distribute our existing products.

On September 27, 2007, the President signed into law the FDA Amendments Act, or FDAAA. This new legislation grants significant new powers to the FDA, many of which are aimed at improving drug safety and assuring the safety of drug products after approval. Under the FDAAA, companies that violate the new law are subject to substantial civil monetary penalties. While we expect the FDAAA to have a significant impact on the pharmaceutical industry, the FDA has not yet implemented many of its provisions and the extent of the impact is not yet known. The new requirements and changes imposed by the FDAAA may make it more difficult, and more costly, to obtain and maintain approval of new pharmaceutical products and to produce, market and distribute existing products.

In addition, the FDA s regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post-approval activities. It is impossible to predict whether additional legislative changes will be enacted,

or FDA regulations, guidance or interpretations changed, or what the impact of such changes, if any, may be.

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

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

potential exposure to unknown liabilities of acquired companies;

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

diversion of management time and attention and other resources;

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

the incurrence of amortization expense; and

possible dilution to our stockholders.

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

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, EMEA and other foreign regulatory authority requirements and for the advancement of our product candidates toward FDA, EMEA and other foreign regulatory authority approval. Our manufacturing staff is responsible for designing and conducting our manufacturing processes in accordance with the FDA s CGMP requirements. The quality and reputation of our scientific, clinical, regulatory and manufacturing staff, especially the senior staff, and their success in performing their responsibilities, are a basis on which we attract potential funding sources and collaborators. In addition, our Chief Executive Officer and other executive officers are involved in a broad range of critical activities, including providing strategic and operational guidance. The loss of these individuals, or our inability to retain or recruit other key management and scientific, clinical, regulatory, manufacturing and other personnel, may delay or prevent us from achieving our business objectives. We face intense competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

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

A change in accounting standards or practices or a change in existing taxation rules or practices can have a significant effect on our reported results and may even affect our reporting of transactions completed before the change is effective. New accounting pronouncements and taxation rules and varying interpretations of accounting pronouncements and taxation practice have occurred and may occur in the future. Changes to existing rules or the questioning of current practices may adversely affect our reported financial results or the way we conduct our business. For example, Statement of Financial Accounting Standards (SFAS) No. 123R, Share-Based Payment, became effective for us on January 1, 2006. This statement requires that employee share-based compensation be measured based on its fair value on the grant date and treated as an expense that is reflected in the financial statements over the related service period. SFAS No. 123R has had a significant impact on our results of operations for the three months ended March 31, 2008. Using the Black-Scholes option pricing model to compute share-based compensation

expense as we do requires extensive use of accounting judgment and financial estimates. Items requiring estimation include the expected term optionholders will retain their vested stock options before exercising them, the estimated volatility of our common stock price over the expected term of a stock option and the number of stock options that will be forfeited prior to the completion of their vesting requirements. Application of

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alternative assumptions could result in significantly different share-based compensation amounts being recorded in our financial statements. We anticipate that SFAS No. 123R will continue to have a significant impact on our results of operations.

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

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

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

Our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock beneficially own shares representing more than 50% of our outstanding capital stock. As a result, these stockholders, if they act together, will be able to exercise a controlling influence over matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions, such as mergers, consolidations and sales of all or substantially all of our assets, and will have significant control over our management and policies. The interests of this group of stockholders may not always coincide with our corporate interests or the interests of other stockholders. This significant concentration of stock ownership could also result in the entrenchment of our management and adversely affect the price of our common stock.

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

Dr. John N. Kapoor, a member of our Board of Directors, is also associated with EJ Financial, a healthcare investment firm that is wholly owned by him. We have paid EJ Financial $175,000 per year under a consulting agreement 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. Effective December 31, 2007, this consulting agreement ended by mutual agreement between EJ Financial and us. Accordingly we no longer make payments under this agreement.

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

We have relationships with Jack A. Roth, M.D., a beneficial owner of our common stock, and M. D. Anderson Cancer Center, both of whom are affiliated with The Board of Regents of the University of Texas System, one of our stockholders. For more information concerning these relationships, see our Notes to Consolidated Financial Statements beginning on page F-8 of our Annual Report on Form 10-K for the year ended December 31, 2007, filed with the SEC on March 17, 2008.

In the three months ended March 31, 2007, we became an owner of 49% of the outstanding stock of Introgen Research Institute (IRI). The other 51% of IRI is owned by our corporate Secretary, who is also an Introgen stockholder. We transferred to IRI an NIH grant originally awarded to us. IRI will be responsible for the remaining research contemplated by that grant and will receive future funding, if any, from the NIH under that grant. We have contractual relationships with IRI under which we may perform research and development services for them in the future.

We have an agreement with Mr. Robert W. Pearson, who became a member of our Board of Directors in April 2008. Under this agreement, he will provide certain business development services to us in connection with potential co-development, collaborative, marketing partnership or certain other potential strategic transactions. In consideration for his services, upon the consummation of

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such a transaction, we will pay him a fee equal to one-half of one percent (0.5%) of certain monetary benefits received by our stockholders or us. The maximum fee he can receive is $3,000,000. The fee we pay him will be reduced by expenses or other expenditures made or contemplated under such a transaction. This fee is not payable for funding we receive that we are expected to expend for research and development programs, full time equivalent payments to employees, loans, collaborative programs, business partnerships or strategic transactions, or otherwise. Transactions between our affiliates and us, whether now existing or created in the future, are excluded from this agreement. This agreement may be terminated at any time by written notice from us or this board member. In the event of such termination, the fee shall be paid with respect to a transaction produced through services performed by this board member before termination if the transaction is closed within two years after the date of termination of the agreement.

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

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

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

None.

Item 5. Other Information

None.

Item 6. Exhibits

Exhibit Number	Description of Document
3.2(1)	Amended and Restated Bylaws of Introgen, Inc., effective as of April 11, 2008
10.64	Letter Agreement with Robert W. Pearson dated as of January 30, 2008
31.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to Rule 13a-14(a) and Rule 15d-14(a) of the Exchange Act
32.1	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

(1) Incorporated by reference to the same-numbered exhibit filed with our Current Report on Form 8-K, filed with the SEC on April 17, 2008.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934 the Registrant has duly caused this Quarterly Report on Form 10-Q to be signed on its behalf by the undersigned thereunto duly authorized.

INTROGEN THERAPEUTICS, INC.

May 12, 2008

By: /s/ James W. Albrecht, Jr.
James W. Albrecht, Jr.
On behalf of the Registrant and as Chief Financial Officer
(Principal Financial and Accounting Officer)

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