

INTROGEN THERAPEUTICS INC

Form 10-Q

November 09, 2007

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

Form 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2007.

or

**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

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

74-2704230

*(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 No

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

Large accelerated filer Accelerated filer Non-accelerated filer

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

As of November 7, 2007 the registrant had 43,878,099 shares of its common stock, \$0.001 par value per share, issued and outstanding.

**INTROGEN THERAPEUTICS, INC.
QUARTERLY REPORT ON FORM 10-Q
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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, 2006	September 30, 2007 (Unaudited)
ASSETS		
Current Assets:		
Cash and cash equivalents	\$ 25,578	\$ 9,404
Short-term investments	15,767	12,504
Total cash, cash equivalents and short-term investments	41,345	21,908
Marketable securities	6,957	16,162
Prepaid expense and other current assets	397	243
Total current assets	48,699	38,313
Property and equipment, net of accumulated depreciation of \$13,976 and \$14,764	5,172	4,436
Other assets	290	272
Total assets	\$ 54,161	\$ 43,021
 LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	\$ 2,384	\$ 1,563
Accrued liabilities and other	4,817	3,433
Deferred revenue and other	624	624
Current portion of notes payable	917	637
Total current liabilities	8,742	6,257
Notes payable, net of current portion	7,448	7,180
Deferred revenue and other, long-term	923	290
Total liabilities	17,113	13,727
Non-controlling and minority interests in consolidated subsidiaries		
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 2006 and 2007, respectively	44	44

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Common stock, \$.001 par value per share; 100,000 shares authorized; shares issued and outstanding of 43,591 in 2006 and 43,845 in 2007		
Additional paid-in capital	205,350	209,311
Accumulated deficit	(172,260)	(193,172)
Accumulated other comprehensive gain	3,914	13,111
Total stockholders' equity	37,048	29,294
Total liabilities and stockholders' equity	\$ 54,161	\$ 43,021

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		Nine Months Ended	
	September 30,		September 30,	
	2006	2007	2006	2007
Contract services, grant and other revenue	\$ 733	\$ 139	\$ 1,056	\$ 543
Operating costs and expense:				
Research and development, including share-based compensation of \$267 and \$180 for the three months ended September 30, 2006 and 2007 and \$737 and \$799 for the nine months ended September 30, 2006 and 2007	4,256	5,074	14,198	13,012
General and administrative, including share-based compensation of \$928 and \$946 for the three months ended September 30, 2006 and 2007 and \$4,256 and \$3,086 for the nine months ended September 30, 2006 and 2007	2,546	2,980	9,615	9,780
Total operating costs and expense	6,802	8,054	23,813	22,792
Loss from operations	(6,069)	(7,915)	(22,757)	(22,249)
Interest income	226	281	792	1,096
Interest expense	(176)	(169)	(507)	(514)
Other income	281	257	824	755
Loss before non-controlling and minority interests in consolidated subsidiaries	(5,738)	(7,546)	(21,648)	(20,912)
Non-controlling and minority interests in consolidated subsidiaries				
Net loss	\$ (5,738)	\$ (7,546)	\$ (21,648)	\$ (20,912)
Net loss per share, basic and diluted	\$ (0.15)	\$ (0.17)	\$ (0.58)	\$ (0.48)
Shares used in computing basic and diluted net loss per share	37,245	43,845	37,213	43,768

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)

	Nine Months Ended September 30,	
	2006	2007
Cash flows from operating activities:		
Net loss	\$ (21,648)	\$ (20,912)
Adjustments to reconcile net loss to net cash used in operating activities:		
Non-controlling and minority interests in consolidated subsidiaries		
Depreciation	1,098	788
Share-based compensation	4,995	3,885
Amortization of grant rights acquired	133	
Changes in assets and liabilities:		
(Increase) decrease in other assets	23	172
Increase (decrease) in accounts payable	(5)	(821)
Increase (decrease) in accrued liabilities	(247)	117
Increase (decrease) in deferred revenue and other	(672)	(633)
 Net cash used in operating activities	 (16,323)	 (17,404)
Cash flows from investing activities:		
Purchases of property and equipment	(102)	(52)
Purchases of short-term investments	(25,070)	(29,589)
Maturities of short-term investments	27,080	32,852
 Net cash provided by investing activities	 1,908	 3,211
Cash flows from financing activities:		
Payment of offering costs related to sale of common stock		(1,571)
Proceeds from exercise of options for common stock	37	145
Proceeds from notes payable	377	157
Principal payments under notes payable	(624)	(704)
 Net cash used in financing activities	 (210)	 (1,973)
 Effect of exchange rate changes on cash	 15	 (8)
 Net decrease in cash	 (14,610)	 (16,174)
Cash and cash equivalents, beginning of period	28,090	25,578
 Cash and cash equivalents, end of period	 \$ 13,480	 \$ 9,404
Supplemental disclosure of cash flow information:		
Cash paid for interest	\$ 474	\$ 491
	\$ 28	\$

Cash paid for taxes for the issuance of common stock in connection with the grant of common stock

Supplemental disclosure of non-cash investing and financing activities:

Grant rights acquired in asset acquisition	\$	30	\$	
Non-cash unrealized gain (loss) on marketable securities	\$	(513)	\$	9,205
Issuance of common stock in connection with the grant of stock	\$	251	\$	210
Construction allowance for leasehold improvements	\$	194	\$	

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. Formation and Business of the Company

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, interest income, and 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.

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, 2006 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 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 and nine month periods ended September 30, 2007, are not necessarily indicative of the results that may be expected for the entire fiscal year.

Our significant accounting policies are described in Note 2 to the Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2006, filed with the SEC on March 8, 2007.

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 generally accepted accounting principles. Accordingly, the subsidiaries accounts are included in these consolidated financial statements. We record a non-controlling or minority interest for the portion of those subsidiaries we do not own to the extent such minority interest constitutes a liability in our financial statements. If those subsidiaries have an accumulated net loss, the minority interest is zero. See footnote 3 regarding new subsidiaries.

See footnote 5 regarding our adoption of and accounting policies related to Statement of Financial Accounting Standard (SFAS) Interpretation No. 48, Accounting for Uncertainty in Income Taxes an interpretation of SFAS Statement No. 109 (FIN 48),

Table of Contents**3. Consolidated Subsidiaries**

During the nine months ended September 30, 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. For the three and nine months ended September 30, 2007, we recorded grant income of zero and \$213,000, respectively, all of which is related to grants held by IRI. We have contractual relationships with IRI under which we may perform research and development services for them in the future.

In May 2007, we established the following subsidiaries:

Introgen Global Limited (IGL), owned 100% by Introgen;

Gendux Pharmaceuticals Limited (GPL), owned 85% by IGL; and

Gendux Molecular Limited (GML), owned 100% by GPL.

These subsidiaries were formed to develop and commercialize targeted molecular medicines in European markets. We have licensed certain technologies to IGL and anticipate that it might further sublicense certain technologies to GPL and/or GML.

Introgen originally owned 85% of GPL, but on September 5, 2007, Introgen transferred its ownership of GPL to its wholly-owned subsidiary, IGL. The 15% of GPL not owned by IGL is owned by certain of Introgen's directors, officers, employees and key medical consultants in the form of 150,000 shares of restricted common stock (also called ordinary shares) granted to them as approved by our Board of Directors. The restricted common stock of GPL is designed to provide performance incentives similar in nature to a stock option plan. This stock is subject to transfer and other restrictions. These restrictions are subject to release under a vesting schedules that are contingent upon continued service by the stockholder to Introgen and/or GPL. This stock is voted by Introgen under proxy from the stockholders. This stock had a nominal value at the time it was issued such that the share-based compensation related to those shares at that time was not material.

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 September 30,		Nine Months Ended September 30,	
	2006	2007	2006	2007
Net loss	\$ (5,738)	\$ (7,546)	\$ (21,648)	\$ (20,912)
Foreign currency translation adjustments	1	6	15	(8)
Unrealized gain (loss) on marketable securities	478	(3,530)	(513)	9,205
Total other comprehensive income (loss)	\$ (5,259)	\$ (11,070)	\$ (22,146)	\$ (11,715)

5. Accounting for Uncertainty in Income Taxes

We adopted FIN 48 as of January 1, 2007. FIN 48 applies to all tax positions accounted for under SFAS No. 109. FIN 48 refers to tax positions as positions taken in a previously filed tax return or positions expected to be taken in a future tax return which are reflected in measuring current or deferred income tax assets and liabilities reported in the financial statements. FIN 48 further clarifies a tax position to include, but not be limited to, the following:

An allocation or a shift of income between taxing jurisdictions;

The characterization of income or a decision to exclude reporting taxable income in a tax return;

A decision to classify a transaction, entity, or other position in a tax return as tax exempt.

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FIN 48 provides that a tax benefit may be reflected in the financial statements only if it is more likely than not that a company will be able to sustain the tax return position, based on its technical merits. If a tax benefit meets this criterion, it should be measured and recognized based on the largest amount of benefit that is cumulatively greater than 50% likely to be realized. This approach is a change from previous practice under which a tax benefit could be recognized only if it was probable a tax position could be sustained.

FIN 48 requires we make qualitative and quantitative disclosures, including a discussion of reasonably possible changes that might occur in unrecognized tax benefits over the next twelve months, a description of open tax years by major jurisdictions and a roll-forward of all unrecognized tax benefits, presented as a reconciliation of the beginning and ending balances of the unrecognized tax benefits on an aggregated basis.

We and certain of our subsidiaries file income tax returns in the U.S. federal jurisdiction, various state jurisdictions, and certain foreign jurisdictions. Generally, we are no longer subject to examinations for U.S. federal income taxes for years prior to 2003 and for state income taxes for years prior to 2002. Examinations for foreign income taxes for previous years remain open, but tax considerations in those jurisdictions are not material to us.

The adoption of FIN 48 did not have a material impact on our financial statements or disclosures. As of January 1, 2007 and September 30, 2007, we did not recognize any assets or liabilities for unrecognized tax benefits relative to uncertain tax positions. We anticipate no significant increase or decrease to gross unrecognized tax benefits will be recorded during the next twelve months. Any interest or penalties resulting from examinations will continue to be recognized as a component of the income tax provision. However, since there are no unrecognized tax benefits as a result of tax positions taken, we have no accrued interest and penalties.

6. 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		Nine Months Ended	
September 30,		September 30,	
2006	2007	2006	2007
16,675	0	61,501	206,723

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:

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.

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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, cell cycle control, cell growth control and gene regulation, including the regulation of angiogenic and immune factors. Our products work by acting as templates for the transient *in vivo* production of proteins that have pharmacological properties. The resultant proteins engage disease-related molecular targets or receptors to produce specific therapeutic effects.

We believe the use of targeted molecular therapies to induce the production of biopharmaceutical proteins represents a new approach for treating many cancers while avoiding the toxic side effects common to traditional therapies. We have developed significant expertise in developing targeted therapies that may be used to treat disease and in using what we believe are safe and effective delivery systems to transport these agents to the cancer cells. We believe we 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 under these clinical trials. We produce ADVEXIN therapy and other product candidates in manufacturing facilities we own and operate using production methods we developed. We hold a number of patents or patents pending on certain product candidates and manufacturing processes used to produce certain product candidates.

We have not yet generated any significant revenue from unaffiliated third parties nor is there any assurance of future product revenue. 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.

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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 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:

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, 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.

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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.

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). In September 2006, the European Medicines Agency (EMA) 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 an agreement with EMA to file for marketing approval for ADVEXIN therapy under the EMA's Exceptional Circumstances (EC) provisions. The application will be for the use of ADVEXIN therapy for the treatment of Li-Fraumeni Syndrome. Exceptional circumstances provisions are designed to facilitate access to needed treatments for certain Orphan Medicinal Products. A Marketing Authorization Application filed with the EMA under these provisions can be reviewed on an expedited basis. This EC registration approach is designed by EMA to be more streamlined than EMA's Conditional Approval procedures, which are similar to the FDA's Accelerated Approval regulations.

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

We have two ongoing 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 independently 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 ongoing Phase 3 clinical trials of ADVEXIN therapy. Under this Fast Track designation, the FDA will take actions to expedite the evaluation and review of the Biologics License Application (BLA) for ADVEXIN therapy.

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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 the past decade, approximately 14 cancer drugs were initially approved based upon submissions of Phase 2 clinical data. A number of the Phase 2 trials supporting these approvals employed single-arm studies involving relatively small patient populations. Virtually all of those drugs relied on surrogate endpoints for approval and a substantial number of the products were for orphan drug indications.

We conducted a series of meetings with the FDA to develop and implement the filing strategy for the BLA for ADVEXIN therapy. As a result of these meetings, we are developing and pursuing an initial rolling BLA filing strategy 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 concurred that preliminary evaluation of this data suggests a level of efficacy consistent with the standard for the initiation of a rolling BLA. This submission process is also known as Submission Of a Partial Application or SOPA.

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. In conjunction with the new data, the new analyses, and other newly employed biological techniques, 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 approach will improve efficacy by identifying the patients most likely to benefit from Advexin therapy.

We submitted a 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 is Phase 2 clinical data utilizing surrogate endpoints, the rolling BLA could be evaluated under the provisions of Subpart H for Accelerated Approval. In order to fully explore all of the review and approval possibilities for ADVEXIN therapy, the FDA has requested we submit 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 ongoing Phase 3 trials. Given that we have two ongoing 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.

We have 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. We have employed several biomarker and response criteria to evaluate ADVEXIN efficiency as described below.

We are conducting the efficacy analysis of one of our ADVEXIN Phase 3 studies. This analysis involves comparing ADVEXIN therapy to methotrexate for the treatment of recurrent head and neck cancer. The prospective 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 in recurrent head and neck cancer.

During the remainder of 2007, we plan to:

Complete the efficacy analyses of one or both of our two ongoing Phase 3 clinical trials for recurrent head and neck cancer;

Submit Phase 3 clinical data to the FDA and EMEA in support of our ADVEXIN registration program; and

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

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We have noted a positive correlation between ADVEXIN therapy clinical activity and abnormal p53 protein levels in multiple patients with different types of cancer. We are continuing to analyze patient tissue samples, protein expression and other biomarker data obtained from previously conducted clinical trials investigating the use of ADVEXIN therapy in various solid cancers. We plan to include relevant data from this research in our submissions to regulatory agencies.

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. 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. A molecular biomarker predictive of ADVEXIN therapy activity is abnormal p53 pathway function detected in tumor tissues by a routine immunohistochemistry laboratory test. The population we identified as benefiting from ADVEXIN therapy includes patients who are less likely to respond to standard therapies such as chemotherapies and radiation.

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 the following paragraphs. In the subset of patients with tumor samples available for evaluation, there was a statistically significant correlation between the abnormal p53 biomarker and tumor response after treatment with ADVEXIN. In 54 cancer patients evaluated, tumor response after ADVEXIN monotherapy was observed in 35 percent of patients with the abnormal p53 biomarker, and all tumor responses occurred in the abnormal p53 biomarker group. The association of tumor response with the abnormal p53 biomarker was statistically significant ($p = 0.0013$). The p53 biomarker is typically abnormal in over half of solid tumor cancers.

In an analysis of 112 patients in the Phase 2 trial of recurrent head and neck cancer treated with the ADVEXIN therapy dose proposed for regulatory approval, the percentages of patients with tumor responses defined by reductions in bi-dimensional tumor area on CT scan of 50 percent, 25 percent, 10 percent or stable disease for more than 2 treatment cycles were 6 percent, 7 percent, 12 percent and 22 percent, respectively. Median survival for these responder populations were 41, 17, 15 and 10 months, respectively. There was a statistically significant increase in median survival for each of the responder populations compared to the 6 month median survival of the non-responders (tumor reduction of less than 10% and p less than 0.0016). Spontaneous tumor remissions generally are not observed in recurrent head and neck cancer.

The predictive abnormal p53 biomarker was associated with a statistically significant increase in tumor responses to ADVEXIN therapy in recurrent head and neck cancer. A reduction in tumor size was observed in 38 percent of patients with the abnormal p53 protein biomarker compared to none (zero percent) of the patients with p53 protein normal tumors. The increased tumor response associated with the abnormal p53 biomarker was statistically significant ($p = 0.05$). In addition, the abnormal p53 protein was a predictive biomarker for increased survival following ADVEXIN treatment. Median survival of patients with abnormal p53 was 11.6 months, compared to 3.5 months for patients with normal p53 ($p = 0.0007$). These biomarker analyses were conducted with pre-treatment samples from 28 patients on a completely blinded basis by an independent laboratory that was not aware of the clinical results of the

study.

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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.

We have an agreement with EMEA to file for marketing approval for ADVEXIN therapy under the EMEA's Exceptional Circumstances provisions. The application will be for the use of ADVEXIN therapy for the treatment of Li-Fraumeni Syndrome. Exceptional circumstances 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 have made 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

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median survival of less than ten months was observed for patients who did not respond to standard treatments. Six patients, or 60%, were still alive one year after beginning ADVEXIN therapy. This clinical trial was performed at Chiba University in Japan.

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.

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 and at The University of Texas M. D. Anderson Cancer Center and were published in *Molecular Cancer Therapeutics*.

Other data suggest the enhanced therapeutic effects of a combination of ADVEXIN and Erbitux® therapies in an animal model of human non-small cell lung cancer. Other pre-clinical studies conducted by our collaborators at Wayne State University, the Karmanos Cancer Institute located in Detroit, Michigan and the University of California-Irvine, as published in *The Laryngoscope*, show that the combination of ADVEXIN therapy and docetaxel resulted in increased levels of programmed cell death in head and neck tumor cells.

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 later stage clinical trials using INGN 241 in patients with metastatic melanoma. We are conducting a Phase 3 clinical trial using INGN 241 in combination with radiation therapy for solid tumors.

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Data from our Phase 1/early Phase 2 clinical trial of INGN 241 in patients with solid tumors demonstrate that direct injection of INGN 241 induced programmed cell death in 100% of the tumors treated, even in patients who had failed prior therapy with other anti-cancer drugs. Clinical responses were observed in 44% of the treated lesions, including complete and partial responses 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.

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® (Bortezomib), 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- κ B, enhanced the tumor killing effects of INGN 241 in cell culture and in preclinical

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models of human tumors. Researchers at Introgen and The University of Texas M. D. Anderson Cancer Center conducted these 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 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 Immunopharmacology*. 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. We originally licensed aspects of this technology from Corixa Corporation (Corixa), which was subsequently acquired by GlaxoSmithKline, which in turn assigned its interest in this license to Columbia University. 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® (bortezomib).

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*

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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.

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 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.

Moffitt Cancer Center plans to conduct a Phase 2 randomized, controlled study of INGN 225 involving as many as 80 patients. 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.

INGN 234 (p53 topical)

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

We have entered into an alliance agreement with Colgate-Palmolive to develop and potentially market oral healthcare products. See 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 ongoing 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.

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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.

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 completed our Investigation 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.

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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 LXR Biotechnology, Inc. (LXR), with the LXR rights being subsequently sold to Tanox, Inc. (Tanox).

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.

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. In addition, our peptide nanoparticles can include special targeting molecules to further enhance cellular uptake and to improve therapeutic efficacy.

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.

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Additional Enabling Technologies

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

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

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

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

Manufacturing and Process Development

Commercialization of a targeted molecular therapy product requires process methodologies, formulations and quality release assays 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

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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.

Under an agreement with VirRx, we purchased \$2,475,000 of VirRx's Series A Preferred Stock for cash, of which we purchased zero during the three months ended September 30, 2007 and September 30, 2006, respectively, and zero and \$150,000 during the nine months ended September 30, 2007 and September 30, 2006, respectively. We are not obligated to make any additional such purchases at this time. We recorded these purchases as research and development expense.

Provided the agreement with VirRx remains in place, we are required to make additional milestone stock purchases, either for cash or through the issuance of our common stock, upon the completion of Phase 1, 2 and 3 clinical trials involving technologies licensed under this agreement. We are required to make a \$5.0 million cash milestone payment to VirRx, for which we 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 have already made cash milestone payments, we may receive a credit of 50% of the Phase 2 clinical trial milestone payments and 25% of the Phase 3 clinical trial milestone payments against this \$5.0 million cash milestone payment.

The additional milestone stock purchases and cash payment are not 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.

Silence Therapeutics plc

We own approximately 6.3% of the issued share capital of Silence Therapeutics plc (formerly SR Pharma plc). We purchased these shares for approximately \$3.0 million in July 2005. The shares we own had a quoted market value of \$16.2 million at September 30, 2007 and \$13.7 million at November 5, 2007. Silence Therapeutics is a European biotechnology company publicly traded on the Alternative Investment Market of the London Stock Exchange (LSE) that is developing oncology and other products.

Academic and Other Collaborations

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

The University of Texas M. D. Anderson Cancer Center

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

We have exclusive license agreements with The Board of Regents of the University of Texas System and M. D. Anderson Cancer Center covering many of the core technologies and products we are developing, including technology used for ADVEXIN therapy and other product candidate programs. These license agreements generally terminate on the date of expiration of the last to expire patents covered by these agreements (or earlier if no patent rights are applicable), and are terminable upon either party's breach, upon notice on a patent by patent basis or should we become insolvent.

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To maintain the exclusivity of these licenses, we are required to conduct ongoing research and development of, and/or use commercially reasonable efforts to, commercialize these technologies. We have agreed to pay M. D. Anderson Cancer Center royalties on sales of products utilizing these technologies. We are obligated to reimburse M. D. Anderson Cancer Center's costs that may be incurred in connection with obtaining patents related to the licensed technologies. Our strategy for product development is designed to take advantage of the significant multidisciplinary resources available at M. D. Anderson Cancer Center. These efforts have resulted in our becoming a significant corporate sponsor of activities at M. D. Anderson Cancer Center in recent years and have yielded to us exclusive patent and licensing rights to numerous technologies.

National Cancer Institute

We have 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 will pay 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 The University of Texas 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 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 Phase 1/2 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.

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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 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

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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, the 3p21.3 family (FUS-1) and anti-sense K-ras. We have exclusively licensed or optioned rights in a number of issued United States patents covering the use of the mda-7 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.

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.

Benzimidazole Small Molecule Cancer Therapy

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

Trade Secrets

We rely on trade secrets law to protect technology where we believe patent protection is not appropriate or obtainable. 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.

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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 September 30, 2007, we had an accumulated deficit of \$193.2 million. We anticipate we will incur losses in the future that may be greater than losses incurred in prior periods. At September 30, 2007, we had cash, cash equivalents and short-term investments of \$21.9 million, compared to \$41.3 million at December 31, 2006.

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

	Nine Months Ended September 30,	
	2006	2007
Operating activities	\$16,323	\$17,404
Purchases of property and equipment	102	52
Principal payments on notes payable	624	704
Payment of offering costs related to previous sales of common stock		1,571

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

	Nine Months Ended September 30,	
	2006	2007
Proceeds from notes payable	\$377	\$157
Proceeds from stock option exercises	37	145

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. In order to fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed or on terms favorable to us or our stockholders.

In November and December 2006, we sold approximately 6.3 million shares of our common stock in direct equity offerings pursuant to a shelf registration statement for an aggregate purchase price of approximately \$30.0 million. Our net proceeds from these transactions, after related expenses payable in cash, were approximately \$27.6 million. These expenses include approximately \$2.1 million of fees to the placement agent for this transaction, of which \$1.5 million were paid in January 2007 and \$601,000 are payable in equal installments over 24 months through December 2008. Warrants were issued to the placement agent to purchase up to 73,199 shares of our common stock at a price of \$5.03 per share, exercisable beginning November 2008, and 326,801 shares of our common stock at a price of \$4.75 per share, exercisable beginning December 2008. These warrants will expire in December 2015.

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 the Introgen. 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 other persons generally vest 25% on each annual anniversary of the option grant date such that they are fully vested after four years.

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Our outstanding stock options have an exercise price equal to the market price of our common stock on their date of grant. At September 30, 2007, 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
5,627,945	2,582,929	8,210,874	\$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 September 30, 2006		Nine Months Ended September 30, 2007	
16,675	0	61,501	206,723

Restricted Stock

In connection with the formation of GPL, 150,000 shares of restricted common stock (also called ordinary shares) of that entity were granted to certain of Introgen's directors, officers, employees and key medical consultants as approved by our Board of Directors. The restricted common stock of GPL is designed to provide performance incentives similar in nature to a stock option plan. This stock is subject to transfer and other restrictions. These restrictions are subject to release under vesting schedules that are contingent upon continued service by the stockholder to Introgen and/or GPL. This stock is voted by Introgen under proxy from the stockholders. This stock had a nominal value at the time it was issued such that the share-based compensation related to those shares at that time was not material.

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. At September 30, 2007, we had warrants outstanding and obligations to issue warrants 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. The exercise price of these warrants was adjusted downward to \$4.60 per share in connection with the sale of shares of our common stock in November 2006.

Investment in Silence Therapeutics plc

As of September 30, 2007, we owned approximately 6.3% of the issued share capital of Silence Therapeutics plc. The shares we own had a fair market value of approximately \$16.2 million at September 30, 2007 and \$13.7 million at November 5, 2007. We paid approximately \$3.0 million for these shares. Silence Therapeutics is a European biotechnology company publicly traded on the Alternative Investment Market of the LSE that is developing oncology and other products.

London Stock Exchange

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

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In March 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 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. The amount of future grant funding, if any, available to IRI 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, the success in obtaining additional grants in the future and compliance with statutes and regulations governing such grants. For the three and nine months ended September 30, 2007, we recorded grant income of zero and \$213,000 related to grants held by IRI.

In May 2007, we established the following subsidiaries:

Introgen Global Limited (IGL), owned 100% by Introgen;

Gendux Pharmaceuticals Limited (GPL), owned 85% by IGL; and

Gendux Molecular Limited (GML), owned 100% by GPL.

These subsidiaries were formed to develop and commercialize targeted molecular medicines in European markets. We have licensed certain technologies to IGL and anticipate that it might further sublicense certain technologies to GPL and/or GML.

Introgen originally owned 85% of GPL, but on September 5, 2007, Introgen transferred its ownership of GPL to its wholly-owned subsidiary, IGL. The 15% of GPL not owned by IGL is owned by certain of Introgen's directors, officers, employees and key medical consultants in the form of 150,000 shares of restricted common stock (also called ordinary shares) granted to them as approved by our Board of Directors. The restricted common stock of GPL is designed to provide performance incentives similar in nature to a stock option plan. This stock is subject to transfer and other restrictions. These restrictions are subject to release under vesting schedules that are contingent upon continued service by the stockholder to Introgen and/or GPL. This stock is voted by Introgen under proxy from the stockholders. This stock had a nominal value at the time it was issued such that the share-based compensation related to those shares at that time was not material.

We account for Introgen Therapeutic Inc.'s investment in these subsidiaries in accordance with the relevant provisions of generally accepted accounting principles, and specifically FIN 46(R), Consolidation of Variable Interest Entities (as amended). Accordingly, the subsidiaries' accounts are included in these consolidated financial statements. We record a non-controlling or minority interest for the portion of these subsidiaries we do not own to the extent such minority interest constitutes a liability in our financial statements. If those subsidiaries have an accumulated net loss, the minority interest is zero.

Critical Accounting Policies

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

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

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

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Revenue Recognition. We recognize revenue as follows:

Contract services revenue is recognized when the related services are completed and delivered to the customer. We record deferred revenue for cash received for which the related work has not been completed and/or the related expense has not been incurred.

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

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

Research and Development Costs. In conducting our clinical trials of ADVEXIN therapy and other product candidates, we procure services from numerous third-party vendors. The cost of these services constitutes a significant portion of the cost of these trials and of our research and development expense in general. These vendors do not necessarily provide us billings for their services on a regular basis and, accordingly, are often not a timely source of information to determine the costs we have incurred relative to their services for any given accounting period. As a result, we make significant accounting estimates as to the amount of costs we have incurred relative to these vendors in each accounting period.

These estimates are based on numerous factors, including, among others, costs set forth in our contracts with these vendors, the period of time over which the vendor will render the services and the rate of enrollment of patients in our clinical trials. Using these estimates, we record expenses and accrued liabilities in each accounting period that we believe fairly represent our obligations to these vendors. Actual results could differ from these estimates, resulting in increases or decreases in the amount of expense recorded and the related accrual. We have consistently applied these estimation procedures in the past and plan to continue applying such procedures in the same manner during the foreseeable future. Our experience has been that our estimates have reasonably reflected the expense we actually incur.

Share-Based Compensation. Effective January 1, 2006, we adopted SFAS No. 123R, Accounting For Share-Based Compensation. From that date forward, we record share-based compensation expense based upon fair value for all stock options issued to all persons to the extent such options vest on January 1, 2006 or later. That expense is determined under the fair value method using the Black-Scholes option pricing model. We record that expense ratably over the period the stock options vest.

The Black-Scholes option pricing model we use to compute share-based compensation expense requires extensive use of accounting judgment and financial estimates. Items requiring estimation include the expected term option holders will retain their vested stock options before exercising them, the estimated volatility of our common stock price over the expected term of a stock option, and the number of stock options that will be forfeited prior to the completion of their vesting requirements. Application of alternative assumptions could result in significantly different share-based compensation amounts being recorded in our financial statements.

Recently Issued Accounting Pronouncements

In June 2006, the Financial Accounting Standards Board (FASB) issued Interpretation No. 48, Accounting for Uncertainty in Income Taxes, an interpretation of FASB Statement No. 109 (FIN 48). FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006. We have adopted FIN 48 beginning January 1, 2007, which did not have a material impact on our financial position and results of operations.

In June 2007, the FASB ratified the consensus reached by the FASB Emerging Issues Task Force on Issue No. 07-3, Accounting for Advance Payments for Goods or Services to Be Used in Future Research and Development Activities (EITF 07-3). EITF 07-3 requires entities to defer income statement recognition of nonrefundable advance

payments for research and development activities, such as up-front nonrefundable payments to contract research organizations, if the contracted party has not yet performed activities related to the up-front payment. Amounts deferred are to be recognized by the contracting company as expense when the research and

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development activities are performed. The application of EITF 07-3 is effective for interim or annual reporting periods in fiscal years beginning after December 15, 2007. Earlier application of EITF 07-3 is not permitted. Companies are required to report the effects of applying EITF 07-3 prospectively for new contracts entered into after the effective date of EITF 07-3. We do not expect the application of EITF 07-3 to have a material effect on our consolidated results of operations and financial condition.

In September 2006, the FASB issued Statement of Financial Accounting Standards No. 157, *Fair Value Measurements*, which defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles (GAAP), and expands disclosures about fair value measurements. In February 2007, the FASB issued Statement of Financial Accounting Standards No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*, which permits entities to choose to measure many financial instruments and certain other items at fair value with the objective of improving financial reporting by providing entities with the opportunity to mitigate volatility in reported earnings caused by measuring related assets and liabilities differently without having to apply complex hedge accounting provisions. Both these statements are effective as of the beginning of an entity's first fiscal year that begins after November 15, 2007. The nature of our business and the items reflected in our financial statements are such that we believe these statements will have little or no effect on our financial statements in the foreseeable future.

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 September 30, 2007 and September 30, 2006* and *Comparison of Nine Months Ended September 30, 2007 and September 30, 2006*

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

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

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.

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 or foreign regulatory authority requirements or encounter delays or difficulties in clinical trials for our product candidates, we may not obtain regulatory approval of some or all of our product candidates on a timely basis, if at all ;

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

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 will generally 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. As we obtain more financing to support these activities, we expect our interest expense and other expenses associated with obtaining debt and equity capital to increase in the future. 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 September 30, 2007 and September 30, 2006

The following comparisons are for the three months ended September 30, 2007 and September 30, 2006. References to the 2007 period refer to the three months ended September 30, 2007 and references to the 2006 period refer to the three months ended September 30, 2006. All dollar amounts are in thousands unless noted otherwise.

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	Three Months Ended September 30,	
	2006	2007
Contract services, grant and other revenue	\$ 733	\$ 139
Percent increase (decrease) from previous period	N/A	(81)%

The change in contract services, grant and other revenue for the 2007 period compared to the 2006 period was a result of :

Decreased contract manufacturing process development and product production services revenue as a result of the completion of certain such work previously in process that was not replaced with additional such work.

Increased contract services revenue from clinical trials management work we performed for third parties.

Research and Development Expense

	Three Months Ended September 30,	
	2006	2007
Pre-clinical stage programs expense	\$ 201	\$ 474
Clinical stage programs expense	3,049	3,683
General research and development expense	1,006	917