INTROGEN THERAPEUTICS INC
Form 10-Q
August 16, 2004

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

FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2004

or

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

For the transition period from to .

Commission file number 000-21291

INTROGEN THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

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

301 Congress Avenue, Suite 1850
Austin, Texas 78701
(Address of principal executive offices, including zip code)

(512) 708-9310
(Registrant s telephone number, including area code)

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

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

As of August 12, 2004, the registrant had 26,623,379 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. Condensed Consolidated Financial Statements.

INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES

CONDENSED CONSOLIDATED BALANCE SHEETS

(Amounts in thousands, except per share amounts)

	December 31, 2003	June 30, 2004
		(Unaudited)
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 36,397	$ 15,017
Short-term investments		10,977
Total cash, cash equivalents and short-term investments	36,397	25,994
Prepaid expenses and other current assets	302	437
Total current assets	36,699	26,431
Property and equipment, net of accumulated depreciation of $9,661 and $10,309, respectively	7,502	6,976
Other assets	282	383
Total assets	$ 44,483	$ 33,790
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	$ 2,054	$ 2,460
Accrued liabilities	2,535	3,768
Deferred revenues from affiliate	16	5
Current portion of capital lease obligations and notes payable	1,003	302
Total current liabilities	5,608	6,535
Capital lease obligations, net of current portion	172	120
Notes payable, net of current portion	6,542	7,556

Deferred revenue, long-term	876	1,007
Total liabilities	$ 13,198	$ 15,218
Commitments and contingencies		
Stockholders Equity:		
Series A non-voting convertible preferred stock, $.001 par value per share, 100 shares authorized, 100 shares issued and outstanding	1	1
Common stock, $.001 par value per share, 100,000 shares authorized, 26,539 and 26,623 shares issued and outstanding, respectively	27	27
Additional paid-in capital	124,270	124,598
Deferred compensation	(44)	(87)
Accumulated deficit	(92,969)	(105,967)
Total stockholders equity	31,285	18,572
Total liabilities and stockholders equity	$ 44,483	$ 33,790

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 June 30,		Six Months Ended June 30,	
	2003	2004	2003	2004
Contract services, grant and other revenue	$ 143	$ 273	$ 293	$ 382
Costs and expenses:				
Research and development	2,957	5,948	7,299	10,243
General and administrative	1,808	2,147	3,195	3,591
Total operating expenses	4,765	8,095	10,494	13,834
Loss from operations	(4,622)	(7,822)	(10,201)	(13,452)
Interest income	475	59	536	126
Interest expense	(161)	(94)	(330)	(228)
Other income	254	306	502	556
Net loss	$ (4,054)	$ (7,551)	$ (9,493)	$(12,998)
Net loss per share, basic and diluted	$ (0.19)	$ (0.28)	$ (0.44)	$ (0.49)
Shares used in computing basic and diluted net loss per share	21,851	26,607	21,679	26,587

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)

	Six Months Ended June 30,	
	2003	**2004**
Cash flows from operating activities:		
Net loss	$ (9,493)	$(12,998)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	739	647
Compensation related to issuance of stock options	1,041	14
Changes in assets and liabilities:		
Decrease (increase) in other assets	406	(236)
Increase in accounts payable and accrued liabilities	235	1,640
Increase in deferred revenue	98	119
Net cash used in operating activities	(6,974)	(10,814)
Cash flows from investing activities:		
Purchases of property and equipment, net of retirements	10	(120)
Purchases of short-term investments		(27,428)
Maturities of short-term investments		16,451
Net cash (used in) provided by investing activities	10	(11,097)
Cash flows from financing activities:		
Proceeds from sale of common stock, including stock option exercises	10,823	270
Borrowings under capital lease obligations and notes payable	141	668
Principal payments under notes payable and capital lease obligations	(811)	(407)
Net cash provided by financing activities	10,153	531
Net increase (decrease) in cash	3,189	(21,380)
Cash and cash equivalents, beginning of period	23,467	36,397

Cash and cash equivalents, end of period	$26,656	$ 15,017
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 330	$ 228
Total cash, cash equivalents and short term investments	$19,101	$ 25,994

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

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INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES

UNAUDITED NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

1. Business

See Management s Discussion and Analysis of Financial Condition and Results of Operations below for a discussion of our business.

We have not yet generated any significant revenues from unaffiliated third parties, nor is there any assurance of future product revenues. Our research and development activities involve a high degree of risk and uncertainty, and our ability to successfully develop, manufacture and market our proprietary products is dependent upon many factors. These factors include, but are not limited to, the need for 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 associated with them, there can be no assurance of our future success.

2. Basis of Presentation

The accompanying condensed consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States for interim financial information and pursuant to the rules and regulations of the Securities and Exchange Commission (SEC). These financial statements do not include all of the information and footnotes required under generally accepted accounting principles in the United States for complete financial statements. In the opinion of management, all accounting entries considered necessary for a fair presentation have been made in preparing these financial statements. Operating results for the three and six month periods ended June 30, 2004 are not necessarily indicative of the results that may be expected for the entire fiscal year. For further information, refer to the consolidated financial statements and related footnotes as of December 31, 2003, and for the year then ended, included in our Annual Report on Form 10-K, filed with the SEC on March 5, 2004.

3. Net Loss Per Share

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

4. Stock Based Compensation

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

equal to the fair value of our stock on the date of grant, no compensation expense is recorded.

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

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	Three Months Ended June 30,		Six Months Ended June 30,	
	2003	2004	2003	2004
Net loss, as reported	$(4,054)	$(7,551)	$ (9,493)	$(12,998)
Add: Stock-based director and employee compensation expense included in reported net loss determined using the intrinsic value method	556		843	46
Deduct: Stock-based director and employee compensation expense determined using the fair value method	(2,190)	(714)	(2,568)	(1,528)
Pro forma net loss	(5,688)	(8,265)	(11,218)	(14,480)
Earnings per share:				
Basic and diluted, as reported	$ (0.19)	$ (0.28)	$ (0.44)	$ (0.49)
Basic and diluted, pro forma	$ (0.26)	$ (0.31)	$ (0.52)	$ (0.55)

5. Investment in VirRx, Inc.

We have an agreement with VirRx, Inc. to purchase shares of VirRx s Series A Preferred Stock for $150,000 on the first day of each fiscal quarter through January 1, 2006. We purchased $150,000 and $300,000 of this stock for cash during the three- and six-month periods ended June 30, 2004, respectively. We recorded these purchases as research and development expense. VirRx is required to use the proceeds from these stock sales in accordance with the terms of a collaboration and license agreement between VirRx and us for the development of VirRx s technologies. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice, which would also terminate the requirement for us to make any additional stock purchases. In accordance with the provisions of Financial Accounting Standards Board Interpretation 46, Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51, VirRx is not consolidated in our financial statements. For additional discussion of our agreements with VirRx, see Note 6 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2003, filed with the SEC on March 5, 2004.

6. Notes Payable

During the quarter ended June 30, 2004, we amended the mortgage note payable related to our facilities. The original $6.0 million principal balance of our note payable was increased to $7.8 million. The proceeds from this increase were used to pay in full the principal and interest outstanding on our note payable with an original principal balance of approximately $3.3 million, which resulted in that note being retired. In addition to this note retirement, the proceeds from this loan amendment were used to pay the costs related to this transaction and to add $668,000 to our cash and cash equivalents.

The amended mortgage note payable bears interest at 6.25%. The note is payable in monthly installments of $56,400 until May 2006. At that time, we may extend the note to a November 2009 maturity date. Upon such extension, the interest rate is modified to the lesser of (1) 2.5% above the five-year U.S. Treasury Bond Note rate or (2) 8.5%, and principal and interest on the note become payable in equal monthly installments based on a 225-month amortization period. The principal balance outstanding on the note s extended maturity date is payable in full at that time.

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. The 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, as amended. These forward-looking statements are based on our current expectations and entail various risks and uncertainties. Our actual results could differ materially from those projected in the forward-looking statements as a result of various factors, including those set forth below under Risk Factors.

Product Development Overview

Introgen Therapeutics, Inc. was incorporated in Delaware in 1993. We are a biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for the treatment of cancer and other diseases.

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

We believe using genes that do not integrate into the patient s genome and are cleared from the body after administration in order to induce the production of biopharmaceutical proteins is an emerging field presenting a new approach for treating many cancers without the toxic side effects common to traditional therapies. We have developed significant expertise in identifying therapeutic genes, which are genes that may be used to treat disease, and in using what we believe are safe and effective delivery systems to transport these genes to the cancer cells. We believe we are able to treat a number of cancers in a way that kills cancer cells without harming normal cells.

ADVEXIN® Therapy (p53)

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

We are conducting two multi-national, multi-site Phase 3 clinical trials of ADVEXIN therapy, both by itself and in combination with chemotherapy, in recurrent squamous cell cancer of the head and neck. Multi-national, multi-site Phase 2 clinical trials of ADVEXIN therapy in 217 patients with recurrent squamous cell cancer of the head and neck treated previously with surgery, radiation or chemotherapy indicated treatment with ADVEXIN therapy provided tumor growth control, including shrinkage and eradication of some tumors, and was well tolerated. Monotherapy data from these Phase 2 clinical trials indicate ADVEXIN therapy compares favorably with Erbitux® in a number of areas, including tumor growth control and survival.

The design of our two Phase 3 clinical trials has been reviewed by the Food and Drug Administration (FDA) under a protocol assessment. We have received Fast Track designation for ADVEXIN therapy from the FDA. By designating ADVEXIN therapy as a Fast Track product, the FDA will take actions to expedite the evaluation and review of the ADVEXIN therapy marketing application. ADVEXIN therapy for head and neck cancer is also designated as an Orphan Drug under the Orphan Drug Act, which may give us seven years of marketing exclusivity for ADVEXIN therapy for this indication if ADVEXIN therapy is approved by the FDA.

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

A Phase 2 clinical trial of ADVEXIN therapy combined with systemic chemotherapy for the treatment of breast cancer;

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

A completed Phase 2 clinical trial of ADVEXIN therapy administered as a complement with radiation therapy in non-small cell lung cancer;

A Phase 1/early Phase 2 clinical trial of ADVEXIN therapy for the treatment of advanced, unresectable squamous cell esophageal cancer;

A Phase 1/early Phase 2 clinical trial in which ADVEXIN therapy is being administered to prevent precancerous oral lesions from developing into cancerous lesions;

A Phase 1 clinical trial of ADVEXIN therapy in prostate cancer; and

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A Phase 1 clinical trial of ADVEXIN therapy in bronchoalveolar cancer.

To date, clinical investigators at sites in North America, Europe and Japan have treated over 500 patients with ADVEXIN therapy, establishing a large safety database.

A growing body of data suggests ADVEXIN therapy has clinical activity in a variety of cancer indications. Safety data from our clinical trials suggests 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 or radiation does not appear to increase the frequency or severity of side effects normally associated with these treatment regimens.

Recent pre-clinical studies provide new insight into the molecular pathways by which the p53 gene, the active component of ADVEXIN therapy, kills tumor cells. These pre-clinical studies were undertaken to provide additional molecular data supporting the activity observed during the clinical development of ADVEXIN therapy and to provide additional information regarding the specific pathways that mediate the observed clinical effects of ADVEXIN therapy. The studies were conducted by our collaborators at Okayama University in Japan and at The University of Texas M. D. Anderson Cancer Center and were published in a 2004 issue of *Molecular Cancer Therapeutics*. Other pre-clinical data suggest the enhanced therapeutic effects of a combination of ADVEXIN and Erbitux therapies in an animal model of human non-small cell lung cancer.

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

INGN 241 (mda-7)

Our second product candidate, INGN 241, uses the mda-7 gene, a promising tumor suppressor gene. We believe the mda-7 gene has broad potential to induce apoptosis, or cell death, in many types of cancer. We have combined the mda-7 gene with our adenoviral gene delivery system to form INGN 241. Our pre-clinical studies 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 growth of normal cells. It appears mda-7 functions via a novel mechanism of tumor suppression because INGN 241 kills cancer cells, even if other tumor suppressor genes, including p53, are not functioning properly.

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

We have completed enrollment of a Phase 1/early Phase 2 clinical trial using INGN 241 to evaluate safety, mechanism of action and efficacy in approximately 25 patients with solid tumors. This trial indicated that in patients with solid tumors, INGN 241 was well tolerated, was biologically active and displayed minimal toxicity associated with its use. As a successor to this work, we have initiated a Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma to further determine if intratumoral injection of INGN 241 can exert regional and systemic

biological activity, with secondary objectives that include analysis of toxicity, tumor response and induction of specific immunity against the melanoma tumors. This Phase 2 clinical trial is designed to enroll up to 25 patients. We have a Small Business Technology Transfer grant from the National Cancer Institute that will provide over $1.8 million of funding for work on this clinical trial.

Pre-clinical studies in INGN 241 in breast cancer cell lines 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 above that seen with either agent alone. In these studies, we noted that while Herceptin exhibited no activity on Her-2/neu negative cells, the combination with INGN 241 did induce cell death in these cells. The results of other pre-clinical studies published in *Molecular Therapy* indicate inhibition of tumor growth by INGN 241 in combination with radiotherapy.

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INGN 225 (p53 immunotherapy)

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

INGN 401 (FUS-1)

Pre-clinical studies have shown gene delivery of FUS-1, which we exclusively license from M. D. Anderson Cancer Center, significantly inhibits the growth of tumors and greatly reduces the metastatic spread of lung cancer in animals when delivered to tumor cells via either an adenoviral or a non-viral delivery system. Results from some of these pre-clinical studies have been published in *Cancer Research*. A Phase 1 clinical trial is ongoing at M. D. Anderson Cancer Center testing INGN 401 in patients with advanced non-small cell lung cancer who have previously been treated with chemotherapy.

Other Programs

We are conducting research on additional genes, including BAK, which hold promise as therapeutic candidates. BAK is a pro-apoptotic gene that kills cancer cells. We are working with our collaborators at M. D. Anderson Cancer Center to identify and develop both viral and non-viral vectors containing this gene. We have exclusive rights to use the BAK gene under a license with Tanox, Inc., the rights of which were previously held by LXR Biotechnology, Inc.

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

As a supplement to our gene-induced protein therapy product programs, we are evaluating mebendazole, our first small molecule candidate, which we refer to as INGN 601, for treatment of cancer and other hyperproliferative diseases. The use of the mebendazole compound is approved by the FDA for the oral treatment of parasitic diseases. Pre-clinical studies suggest mebendazole may also be an effective treatment of cancer. The results of pre-clinical studies involving mebendazole and lung cancer have been published in *Clinical Cancer Research* and *Molecular Cancer Therapeutics.* We are working with M. D. Anderson Cancer Center to further evaluate this molecule as a cancer treatment.

We are investigating vector technologies for delivering gene-based products into targeted cells. Through our strategic collaboration with VirRx, Inc., we are developing INGN 007, a replication-competent viral therapy that over-expresses an adenoviral gene and thereby causes rapid disruption of tumor cells in which the adenovirus replicates. Pre-clinical testing indicates INGN 007 can eradicate human tumors in animal models. We anticipate pursuing clinical confirmation of this therapeutic candidate. We are also evaluating whether this replicating viral

construct could form the basis of a self-amplifying delivery system, which could complement our existing replication-disabled, adenoviral gene delivery system in selected therapeutic scenarios. We are working also with VirRx to develop another novel oncolytic adenovirus, designated INGN 009, which has been engineered to kill cancer cells through viral replication and which has been designed to kill cells carrying a mutation common in many colon cancers. The results of several pre-clinical studies indicate these viral therapies can be modified so their activity is targeted to tumor cells. In addition, their anti-cancer effects can be enhanced to produce proteins that kill cancer cells.

Data from pre-clinical studies indicate a proprietary, non-viral gene delivery system we control results in prolonged expression of delivered genes in mice implanted with human lung tumors. Repeated injections of the non-viral vector produce enhanced effects in animals bearing tumors. We believe our non-viral formulation may produce robust and persistent gene expression in cancer patients, which in turn may lead to enhanced clinical effects.

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Manufacturing and Process Development

We own and operate a state-of-the-art, validated manufacturing facility we believe complies with the FDA s current Good Manufacturing Practices requirements, commonly known as CGMP requirements. We produce ADVEXIN therapy in this facility for use in our Phase 1, 2 and 3 clinical trials. The design and processes of this facility have been reviewed with the FDA. The validation of our manufacturing processes is ongoing. We plan to use this facility for our market launch of ADVEXIN therapy. To date, we have produced over 20 batches of ADVEXIN therapy clinical material, including all clinical material used in the Phase 1, 2 and 3 clinical trials for this product candidate. In addition, we have entered into agreements with third parties under which we have provided process development and manufacturing services related to products they are developing. We are outfitting a separate, second facility for continued production of INGN 241 for use in our clinical trials of that product candidate.

Patents and Intellectual Property

We place substantial emphasis on developing and maintaining a strong intellectual property program. We own or exclusively control numerous patents and pending patent applications in the United States and elsewhere covering ADVEXIN therapy and INGN 241 (mda-7) therapy in particular, adenoviral p53 and adenoviral mda-7 in general, clinical applications of adenoviral and other forms of p53 and mda-7, and adenoviral production. Certain of our patents are licensed from The University of Texas System, Columbia University and Aventis Pharmaceuticals, Inc. The patents directed to clinical applications of p53 broadly cover the use of p53 in combination with standard chemotherapy and clinical therapy with adenoviral p53 in general. Our adenoviral production patent position is of particular potential commercial importance in that it covers most methods currently in use by us and others for commercial scale adenoviral production and purification processes. We have recently been successful in having two of three European patents held by our competitors finally revoked by the technical board of appeals of the European Patent Office, with no possibility of further appeal, with the one remaining European patent revoked but still subject to appeal by the patent holder. In addition to our p53 and mda-7 intellectual property position, we own or have exclusively licensed rights in a number of other patents and applications directed to the clinical application of various other tumor suppressor genes.

Recent notable intellectual property activity includes the issuance of the following United States patents:

No. 6,726,907, which broadly covers purified adenoviral compositions or preparations without limitation as to the type of adenovirus, the use or application of the adenovirus and how the adenovirus is produced. This patent complements and broadens a previously issued patent in our intellectual property portfolio directed to processes for purifying adenoviruses. This patent was issued directly to us.

No. 6,740,320, which broadly covers adenoviral p53 constructs for use in therapeutic applications and is not limited to our ADVEXIN therapy adenoviral p53 product. This patent extends our patent coverage for ADVEXIN therapy to the year 2021, not taking into account possible patent extensions. We believe this patent establishes our control of ADVEXIN therapy specifically and pharmaceutical adenoviral p53 products in general. This patent was issued to the Board of Regents of the University of Texas System and is exclusively licensed to us.

No. 6,689,600, which covers our technology for producing long-term, storage-stable adenovirus. This patent addresses the need for formulations that permit the long-term storage of adenoviral therapeutics under regular refrigerated conditions. We believe the storage-stable formulations described in this patent may eventually replace formulations currently in use by the adenovirus industry by providing conveniences and efficiencies in storage, distribution, pharmacy handling and clinical administration. This patent was issued directly to us.

No. 6,720,408, which directly covers the mda-7/IL-24 tumor suppressor gene. This gene forms the genetic basis of our INGN 241 product. This patent, which was issued to the trustees of Columbia University, is exclusively licensed to us for gene therapy applications through an agreement with Corixa Corporation.

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 June 30, 2004, we had an accumulated deficit of $106.0 million. We anticipate we will incur losses in the future that may be greater than losses incurred in prior periods. At June 30, 2004, we had cash, cash equivalents and short-term investments of $26.0 million. During the six months ended June 30, 2004, we used

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$11.1 million of cash to conduct our business. We expect to incur substantial additional operating expenses and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities increase and as we expand our operations and develop systems to support commercialization of our product candidates. These losses, among other things, have caused and may cause our total assets, stockholders equity and working capital to decrease. Currently, we earn revenue or income from federal research grants, contract services and process development activities, the lease of a portion of our facilities to M. D. Anderson Cancer Center and interest income on cash placed in short-term, investment grade securities. In order to fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed, or on terms favorable to us or our stockholders.

In June 2003, we sold 2.0 million shares of our common stock for an aggregate purchase price of $11.5 million to selected institutional investors through a private placement pursuant to Regulation D promulgated under the Securities Act of 1933, as amended. Our net proceeds from this transaction, after related fees and expenses, were $10.8 million. In connection with this sale, we issued warrants to purchase 400,000 shares of our common stock at $7.89 per share. These warrants are exercisable at any time by the warrant holders through June 2008. Beginning in June 2005, we may force the exercise of these warrants if the average closing market price of our common stock during any 20 consecutive trading days is greater than $15.78 per share. The shares of common stock issued and issuable upon the exercise of the warrants issued in this transaction were registered on a registration statement on Form S-3, effective August 7, 2003 (Commission File No. 333-107028).

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

We have a Small Business Technology Transfer grant from the National Cancer Institute to support our Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma. This grant will provide over $1.8 million of funding during the course of this clinical trial to evaluate the efficacy and biologic activity of INGN 241 in this indication.

During the quarter ended June 30, 2004, we amended the mortgage note payable related to our facilities. The original $6.0 million principal balance of our note payable was increased to $7.8 million. The proceeds from this increase were used to pay in full the principal and interest outstanding on our note payable with an original principal balance of approximately $3.3 million, which resulted in that note being retired. In addition to this note retirement, the proceeds from this loan amendment were used to pay the costs related to this transaction and to add $668,000 to our cash and cash equivalents. The amended mortgage note payable bears interest at 6.25%. The note is payable in monthly installments of $56,400 until May 2006. At that time, we may extend the note to a November 2009 maturity date. Upon such extension, the interest rate is modified to the lesser of (1) 2.5% above the five-year U.S. Treasury Bond Note rate or (2) 8.5%, and principal and interest on the note become payable in equal monthly installments based on a 225-month amortization period. The principal balance outstanding on the note s extended maturity date is payable in full at that time.

In June 2004, our stockholders approved an amendment to our certificate of incorporation to increase the number of our authorized common shares from 50,000,000 shares to 100,000,000 shares.

Summary of Significant 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 revenues and expenses during the reporting period. Actual results could differ from those estimates.

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

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becomes impaired or the investment is downgraded.

Research and Development Expenses. 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 expenses 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 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. Our experience has been our estimates have reasonably reflected the expenses we actually incur.

Results of Operations

Comparison of the Quarters Ended June 30, 2004 and June 30, 2003

Revenues

Contract Services, Grant and Other Revenue. We earned contract services revenues from third parties under agreements to provide manufacturing process development services and to produce products for them. We earned contract research services revenue from Aventis Pharmaceuticals Products, Inc. (Aventis), one of our stockholders, under an agreement through which Aventis provided funding for the conduct of a Phase 2 clinical trial of ADVEXIN therapy in breast cancer. We earned grant revenue under research grants from U.S. Government agencies. Total contract services, grant and other revenue was $273,000 for the quarter ended June 30, 2004, compared to $143,000 for the quarter ended June 30, 2003, a increase of 91%. This increase was primarily due to increased grant funding under our Small Business Technology Transfer grant from the National Cancer Institute to support our Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma as a result of our increased activity related to that research.

Costs and Expenses

Research and Development. Research and development expenses were $5.9 million for the quarter ended June 30, 2004, compared to $3.0 million for the quarter ended June 30, 2003, an increase of 97%. These expenses included compensation expense related to stock options of zero in 2004 and $58,000 in 2003. Research and development expenses increased as a result of increased activity related to the preparation of the Biologics License Application (BLA) for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work.

General and Administrative. General and administrative expenses were $2.1 million for the quarter ended June 30, 2004, compared to $1.8 million for the quarter ended June 30, 2003, an increase of 17%. These expenses included compensation expense related to stock options of $8,000 in 2004 and $692,000 in 2003. General and administrative expenses increased primarily due to increased activity related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work. Also, in the 2004 period, we expensed approximately $381,000 of costs, the expensing of $244,000 of which was previously deferred in earlier periods, which were incurred with respect to securities offering activities for the sale of our common stock, which offering was not completed.

Compensation Related to the Issuance of Stock Options. Compensation related to the granting of stock options was $8,000 for the quarter ended June 30, 2004, compared to $750,000 for the quarter ended June 30, 2003, a decrease of 99%. This compensation for the 2003 period arose primarily as a result of:

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

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

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

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This compensation expense decreased in the 2004 period because:

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

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

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

The amount of stock option compensation expense to be recorded in future periods may increase if additional options are issued at a price below the market price of common stock at the date of grant, the market value of our stock increases or additional options are granted to individuals or entities other than employees or directors. This compensation expense may decrease if unvested options for which deferred compensation has been recorded are subsequently forfeited or as previously recorded deferred compensation becomes fully amortized.

Interest Income, Interest Expense and Other Income

Interest income was $59,000 for the quarter ended June 30, 2004, compared to $475,000 for the quarter ended June 30, 2003, a decrease of 88%. Included in the 2003 amount is $425,000 we received from the settlement of litigation related to a decline in the market value of certain commercial paper we held as an investment during the quarter ended March 31, 2001. Excluding the amount from this settlement, interest income for the quarter ended June 30, 2003, was $50,000. Interest income in 2004 increased compared to interest income in 2003, exclusive of the litigation settlement, due to higher average cash balances during the 2004 period as a result of the proceeds received from the sales of our common stock in June 2003 and December 2003.

Interest expense was $94,000 for the quarter ended June 30, 2004, compared with $161,000 for the quarter ended June 30, 2003, a decrease of 42%. This decrease was primarily due to (1) our capital leases becoming fully paid during periods subsequent to June 30, 2003, and (2) lower notes payable principal amounts upon which interest was incurred in 2004 compared to 2003 as a result of continuing principal debt service payments on those notes payable.

Other income was $306,000 for the quarter ended June 30, 2004, compared to $254,000 for the quarter ended June 30, 2003, an increase of 20%. This increase was primarily due to increased recovery of facilities operating expenses from tenants to whom we sublease space in our facilities.

Comparison of the Six Months Ended June 30, 2004 and June 30, 2003

Revenues

Contract Services, Grant and Other Revenue. We earn contract services revenues from third parties under agreements to provide manufacturing process development services and to produce products for them. We earned contract research services revenue from Aventis under an agreement through which Aventis provided funding for the conduct of a Phase 2 clinical trial of ADVEXIN therapy in breast cancer. We earn grant revenue under research grants from U.S. Government agencies. Total contract services, grant and other revenue was $382,000 for the six months ended June 30, 2004, compared to $293,000 for the six months ended June 30, 2003, an increase of 30%. This increase was primarily due to increased grant funding under our Small Business Technology Transfer grant from the National Cancer Institute to support our Phase 2 clinical trial of INGN 241 in patients with metastatic melanoma as a result of increased activity related to that research.

Costs and Expenses

Research and Development. Research and development expenses were $10.2 million for the six months ended June 30, 2004, compared to $7.3 million for the six months ended June 30, 2003, and increase of 40%. These expenses included compensation expense related to stock options of $44,000 in 2004 and $122,000 in 2003. Research and development expenses increased as a result of increased activity related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work.

General and Administrative. General and administrative expenses were $3.6 million for the six months ended June 30, 2004, compared to $3.2 million for the six months ended June 30, 2003, an increase of 12%. These expenses included compensation

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expense related to stock options of $47,000 in 2004 and $914,000 in 2003. General and administrative expenses increased primarily due to increased activity related to the preparation of the BLA for ADVEXIN therapy for filing with the FDA, which resulted in us hiring more employees and engaging additional consultants to perform this work. Also, in the 2004 period, we expensed $381,000 of costs incurred with respect to securities offering activities for the sale of our common stock, which offering was not completed.

Compensation Related to the Issuance of Stock Options. Compensation related to the issuance of stock options was $91,000 for the six months ended June 30, 2004, compared to $1.0 million for the six months ended June 30, 2003, a decrease of 91%. This compensation for the 2003 period arose primarily as a result of:

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

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

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

This compensation expense decreased in the 2004 period because:

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

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

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

The amount of stock option compensation expense to be recorded in future periods may increase if additional options are issued at a price below the market price of common stock at the date of grant, the market value of our stock increases or additional options are granted to individuals or entities other than employees or directors. This compensation expense may decrease if unvested options for which deferred compensation has been recorded are subsequently forfeited or as previously recorded deferred compensation becomes fully amortized.

Interest Income, Interest Expense and Other Income

Interest income was $126,000 for the six months ended June 30, 2004, compared to $536,000 for the six months ended June 30, 2003, a decrease of 76%. Included in the 2003 amount is $425,000 we received from the settlement of litigation related to a decline in the market value of certain commercial paper we held as an investment during the quarter ended March 31, 2001. Excluding the amount from this settlement, interest income for the six months ended June 30, 2003, was $111,000. Interest income in 2004 increased compared to interest income in 2003, exclusive of the litigation settlement, due to higher average cash balances during the 2004 period as a result of the proceeds received from the sales of our common stock in June 2003 and December 2003.

Interest expense was $228,000 for the six months ended June 30, 2004, compared with $330,000 for the six months ended June 30, 2003, a decrease of 31%. This decrease was primarily due to (1) our capital leases becoming substantially fully paid during periods subsequent to June 30, 2003, and (2) lower notes payable principal amounts upon which interest was incurred in 2004 compared to 2003 as a result of continuing debt service payments on those notes payable.

Other income was $556,000 for the six months ended June 30, 2004, compared to $502,000 for the six months ended June 30, 2003, an increase of 11%. This increase was primarily due to increased recovery of facilities operating expenses from tenants to whom we sublease space in our facilities.

Liquidity and Capital Resources

We have incurred annual operating losses since our inception, and at June 30, 2004, we had an accumulated deficit of $106.0 million. From inception through June 30, 2004, we have financed our operations using $49.7 million of collaborative research and

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development payments from Aventis, $32.2 million of net proceeds from our initial public offering in October 2000, $39.4 million of private equity sales to Aventis, $26.0 million of private equity sales, net of offering costs, to others, $18.5 million of equity sales in a registered direct offering under an existing shelf registration in December 2003, $7.5 million of sales of ADVEXIN therapy product to Aventis for use in later-stage clinical trials, $9.9 million in mortgage financing from banks for our facilities, $4.5 million in leases from commercial leasing companies to acquire equipment pledged as collateral for those leases and $13.5 million from contract services, grants, interest and other income.

At June 30, 2004, we had cash, cash equivalents and short-term investments of $26.0 million, compared to $36.4 million at December 31, 2003. Cash and cash equivalents constituted $15.0 million and $36.4 million of these amounts at June 30, 2004, and December 31, 2003, respectively. The decrease in cash, cash equivalents and short-term investments at June 30, 2004, as compared to December 31, 2003 was due to the use of $11.1 million to conduct our business during the six months ended June 30, 2004, offset by the receipt of $668,000 in proceeds from the refinancing of the mortgage note payable on our facilities. We expect to continue to focus our activities primarily on conducting Phase 3 and other clinical trials, conducting data analysis, preparing regulatory documentation submissions to the FDA and conducting pre-marketing activities for ADVEXIN therapy. We expect to continue our research and development of various other gene-based technologies. If ADVEXIN therapy or any of our other product candidates are approved for commercial sale by the FDA, we expect to conduct activities supporting the marketing, sales, production and distribution of those products, either ourselves or in collaboration with other parties. The majority of our expenditures over the next two years will most likely be for these activities as they relate to ADVEXIN therapy. These activities may increase the rate at which we use cash in the future as compared to the cash we used for operating activities during the six months ended June 30, 2004. We believe our existing working capital can fund our operations for the next 12 to 15 months, although we may have to make adjustments to the scope of operations to achieve that objective and unforeseen events could shorten that time period. Our existing resources may not be sufficient to support the commercial introduction of any of our product candidates. In order to fund our operating losses, we will need to raise additional funds through public or private equity offerings, debt financings or additional corporate collaboration and licensing arrangements. We do not know whether such additional financing will be available when needed, or on terms favorable to us or our stockholders.

Net cash used in operating activities was $10.8 million for the six months ended June 30, 2004 compared to $7.0 million for the six months ended June 30, 2003. This increase was due to a larger net loss during the 2004 period compared to the 2003 period, which was (1) increased by an increase in other assets during the 2004 period, compared to a decrease in other assets during the 2003 period, due primarily to the expensing during the 2004 period of $381,000 of costs incurred with respect to securities offering activities for the sale of our common stock, which offering was not completed, and (2) decreased by:

Lower depreciation during the 2004 period compared to the 2003 period as accelerated depreciation methods result in lower depreciation charges as property and equipment ages;

Lower compensation related to stock options in the 2004 period compared to the 2003 period for the reasons discussed above under Costs and Expenses Compensation Related to the Issuance of Stock Options;

A larger increase in accounts payable and accrued liabilities in the 2004 period compared to the 2003 period due to a higher level of operating activity and expenses resulting in increased liabilities to be paid in the future; and

An increase in deferred revenue that was comparable between periods due to no change of significance related to the tenants to whom we sublease space in our facility.

Net cash used in investing activities was $11.1 million for the six months ended June 30, 2004 compared to $10,000 of net cash provided by investing activities for the six months ended June 30, 2003. This increase was

primarily due to our resumption during the first quarter of 2004 of investments in financial instruments with original maturities in excess of three months, primarily as a result of cash from the sale of shares of our common stock in December 2003 being available for such investments. While we have no obligations at this time to purchase significant amounts of additional property or equipment, our needs may change. It may be necessary for us to purchase larger amounts of property and equipment to support our clinical programs and other research, development and manufacturing activities. We may need to obtain debt or lease financing to facilitate such purchases. If that financing is not available, we may need to use our existing resources to fund those purchases, which could result in a reduction in the cash and cash equivalents available to fund operating activities.

Net cash provided by financing activities was $531,000 for the six months ended June 30, 2004, compared to $10.2 million for the six months ended June 30, 2003. The 2003 period included the net proceeds from the sale of 2.0 million shares of our common stock in June 2003, as discussed above under Financial Overview, for which there was no comparable transaction in the 2004 period. Borrowings under capital lease obligations and notes payable were higher during the 2004 period compared to the 2003 period as a result of proceeds received during the 2004 period from the refinancing of the mortgage note payable related to our

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facilities as discussed above under Financial Overview. Principal payments under capital lease obligations and notes payable were lower in the 2004 period compared to the 2003 period as a significant portion of our capital lease obligations were paid in full during the 2004 period.

We have an agreement with VirRx, Inc. (VirRx) that was entered into in 2002, to purchase shares of VirRx s Series A Preferred Stock for $150,000 on the first day of each fiscal quarter through January 1, 2006. We purchased $150,000 and $300,000 of this stock for cash during the three- and six-month periods ended June 30, 2004, respectively. We recorded these purchases as research and development expense. VirRx is required to use the proceeds from these stock sales in accordance with the terms of a collaboration and license agreement between VirRx and us for the development of VirRx s technologies. We may unilaterally terminate this collaboration and license agreement with 90 days prior notice, which would also terminate the requirement for us to make any additional stock purchases. For additional discussion of our agreements with VirRx, see Note 6 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2003, filed with the SEC on March 5, 2004.

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

Total debt service and lease payments for July 1, 2004 through December 31, 2004	$ 409
Total debt service and lease payments due during the year ending December 31:	
2005	797
2006	745
2007	675
2008	675
Thereafter	10,855
Total debt service and lease payments	14,156
Less portion representing interest	(6,178)
Total principal balance at June 30, 2004	7,978
Principal balance presented on the June 30, 2004 balance sheet as liabilities in these categories:	
Current portion of obligations under capital leases and notes payable	302
Capital lease obligations, net of current portion	120
Notes payable, net of current portion	7,556
Total principal balance at June 30, 2004	$ 7,978

We have a fixed rent obligation under a ground lease for the land on which we built our facilities. Since this is an operating lease, there is no liability reflected on our balance sheet for this item, which is in accordance with generally accepted accounting principles. We make total annual payments of $144,000 under this lease which will continue until the expiration of the initial term of this lease in September 2026. Future annual rental payments due under all operating leases are as follows (in thousands):

July 1, 2004 through December 31, 2004	$ 164
Year ending December 31:	

2005	206
2006	144
2007	144
2008	144
Thereafter	2,562
Total minimum lease payments under operating leases	$3,364

See Financial Overview for discussion of the modification of our mortgage note payable during the three months ended June 30, 2004.

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

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

We have a consulting agreement with Jack A. Roth, M.D., Chairman of the Department of Thoracic Surgery and Director of the Keck Center for Gene Therapy at The University of Texas M. D. Anderson Cancer Center. Dr. Roth is the primary inventor of the technology upon which our ADVEXIN therapy is based and numerous other technologies we utilize. We licensed Dr. Roth s inventions from M. D. Anderson Cancer Center. Dr. Roth is our Chief Medical Advisor and chairman of our scientific advisory board. His duties involve the regular interaction and consultation with our scientists and others on our behalf. As compensation for his services and responsibilities, this consulting agreement provides for payments to Dr. Roth of $200,000 per annum through the end of its term on September 30, 2009, with such future payments subject to adjustment for inflation. We may terminate this agreement at our option upon one year s advance notice. If we had terminated this agreement as of June 30, 2004, we would have been obligated to make final payments totaling $200,000. Dr. Roth is one of our stockholders.

We sublease a portion of our facilities to M. D. Anderson Cancer Center under a lease with a non-cancelable term expiring in 2009. M. D. Anderson Cancer Center is obligated to pay us rent of approximately $76,000 per month until February 2006 and approximately $13,000 per month thereafter.

Risk Factors

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

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

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

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

We have completed three Phase 2 clinical trials and are conducting two Phase 3 clinical trials of our lead product candidate, ADVEXIN therapy, for the treatment of head and neck cancer. In addition, we have completed a Phase 2

clinical trial of ADVEXIN therapy for the treatment of non-small cell lung cancer and are conducting a Phase 2 clinical trial of ADVEXIN therapy for the treatment of breast cancer. We also are conducting or have conducted several Phase 1 and Phase 2 clinical trials of ADVEXIN therapy for other types of cancer. Current or future clinical trials may demonstrate ADVEXIN therapy is neither safe nor effective.

While we have completed enrollment of patients with metastatic melanoma in a Phase 1/early Phase 2 clinical trial of INGN 241, a product candidate based on the mda-7 gene, and have initiated a follow-on Phase 2 clinical trial of INGN 241 for the same indication, our most significant clinical trial activity and experience has been with ADVEXIN therapy. We will need to continue conducting significant research and animal testing, referred to as pre-clinical testing, to support performing clinical trials for our other product candidates. It will take us many years to complete pre-clinical testing and clinical trials, and failure could occur at any stage of testing. Current or future clinical trials may demonstrate INGN 241 or our other product candidates are neither safe

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nor effective.

Any delays or difficulties we encounter in our pre-clinical research and clinical trials, in particular the Phase 3 clinical trials of ADVEXIN therapy for the treatment of head and neck cancer, may delay or preclude regulatory approval. Our product development costs will increase if we experience delays in testing or regulatory approvals or if we need to perform more or larger clinical trials than planned. Any delay or preclusion could also delay or preclude the commercialization of ADVEXIN therapy or any other product candidates. In addition, we or the FDA might delay or halt any of our clinical trials of a product candidate at any time for various reasons, including:

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

the presence of unforeseen adverse side effects of a product candidate, including its delivery system;

a longer than expected time required to determine whether or not a product candidate is effective;

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

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

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

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

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

Despite the FDA s designation of ADVEXIN therapy as a Fast Track product, we may encounter delays in the regulatory approval process due to additional information requirements from the FDA, unintentional omissions in our BLA for ADVEXIN therapy, or other delays in the FDA s review process. We may encounter delays or rejections in the regulatory approval process because of additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review.

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

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

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

For marketing drugs and biologics outside the United States, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country and may require additional testing. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approval on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other

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countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or to obtain required approvals could impair our ability to develop these markets and could have a material adverse effect on our results of operations and financial condition.

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

We have generated operating losses since we began operations in June 1993. As of June 30, 2004, we had an accumulated deficit of approximately $106.0 million. We expect to incur substantial additional operating expenses and losses over the next several years as our research, development, pre-clinical testing and clinical trial activities increase. As we expand our operations and develop systems to support commercialization of our product candidates, these losses, among other things, have had, and are expected to continue to have, an adverse impact on our total assets, stockholders equity and working capital.

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

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

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

We expect we will fund our operations over approximately the next 12 to 15 months with our current working capital, which we accumulated primarily from sale of equity securities, income from contract services and research grants, debt financing of equipment acquisitions, the lease of a portion of our facilities to M. D. Anderson Cancer Center and interest on invested funds. We may need to raise additional capital sooner, however, under various circumstances, including if we experience:

an acceleration of the number, size or complexity of our clinical trials;

slower than expected progress in developing ADVEXIN therapy, INGN 241 or other product candidates;

higher than expected costs to obtain regulatory approvals;

higher than expected costs to pursue our intellectual property strategy;

higher than expected costs to further develop and scale up our manufacturing capability;

higher than expected costs to develop our sales and marketing capability;

faster than expected rate of progress and cost of our research and development and clinical trial activities;

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

higher than expected costs of preparing an application for FDA approval of ADVEXIN therapy;

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

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

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

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products;

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

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

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

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

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

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

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

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

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

response by the FDA to such clinical trials, may impede the timing of our clinical trials, delay or prevent us from obtaining regulatory approval or negatively influence public perception of our product candidates, which could harm our business and results of operations and depress the value of our stock.

For example, in 2002, the FDA placed a clinical hold on gene therapy clinical trials using retroviral vectors to transduce hematopoietic stem cells after two participants in such a trial for the X-linked form of severe combined immune deficiency disease (X-SCID), being conducted in Europe, developed what appeared to be a leukemia-like illness. This clinical hold requires a case-by-case review of the use of retroviral vectors in these European trials before consideration of the removal of this clinical hold for these trials. We do not use retroviral vectors in our ongoing clinical trials and are not developing products using the production

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process used in those clinical trials. We have received no communications from the FDA to indicate this clinical hold will affect our clinical trials. We anticipate no future negative effects on our clinical trials from this event, but we cannot assure you the FDA or any other regulatory authority will not issue a clinical hold with respect to any of our clinical trials in the future. In accordance with our pharmacovigilance procedures and regulatory procedures, we monitor every patient in our clinical trials for safety and report all side effects to the FDA and the National Institutes of Health, or NIH.

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

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

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

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

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

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

Our commercial success will depend in part on obtaining patent protection for our products and other technologies and successfully defending these patents against third-party challenges. Our patent position, like that of other biotechnology and pharmaceutical companies, is highly uncertain. One uncertainty is the United States Patent and Trademark Office, or PTO, or the courts, may deny or significantly narrow claims made under patents issued to us or patent applications we file. This is particularly true for patent applications or patents that concern biotechnology and pharmaceutical technologies, such as ours, since the PTO and the courts often consider these technologies to involve unpredictable sciences. Another uncertainty is any patents that may be issued or licensed to us may not provide any competitive advantage to us because they may not effectively preclude others from developing and marketing products like ours. Also, our patents may be successfully challenged, invalidated or circumvented in the future. In

addition, our competitors, many of which have substantial resources and have made significant investments in competing technologies, may seek to apply for and obtain patents that will prevent, limit or interfere with our ability to make, use and sell our potential products either in the United States or in international markets.

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

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

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

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

The biotechnology and pharmaceutical industry has been characterized by extensive litigation regarding patents and other intellectual property rights, and companies have employed intellectual property litigation to gain a competitive advantage. We are aware of a number of issued patents and patent applications related to gene therapy, the treatment of cancer and the use of the p53 and other tumor suppressor genes. Schering-Plough Corporation, including its subsidiary Canji, Inc., controls various United States patent applications and a European patent and applications, some of which are directed to therapy using the p53 gene, and others to adenoviruses containing the p53 gene, or adenoviral p53, and to methods for carrying out therapy using adenoviral p53. Adenoviral p53 technology underlies our ADVEXIN therapy product candidate. In addition, Canji controls an issued United States patent and its international counterparts, including a recently revoked European patent, involving a method of treating mammalian cancer cells lacking normal p53 protein by introducing a p53 gene into the cancer cell. Furthermore, we are aware of a United States patent directed to replication-deficient recombinant adenoviral vectors apparently controlled by Transgene SA. While we believe the claims of the Canji p53 patents or the Transgene adenoviral vector patent are invalid or not infringed by our products, Transgene, Canji or Schering-Plough could assert a claim against us.

One of the foregoing patent applications directed to p53 therapy, which we understand is owned by The Johns Hopkins University and controlled by Schering-Plough, is involved in a PTO interference proceeding with a patent owned by Canji. We further understand this Johns Hopkins application is the United States counterpart to the European patent recently revoked in its entirety by the EPO (see below). We have now learned that priority of invention in this interference has been awarded by the PTO to the Johns Hopkins application, and the Canji patent has been found unpatentable. We cannot at present assess whether any patent might ultimately issue on the Johns Hopkins application or the potential impact, if any, of this PTO ruling on our business. If this application issues as a patent, Schering-Plough or Johns Hopkins may assert that our ADVEXIN therapy, which uses p53 therapy, infringes the claims of such patent. While we believe we would have an invalidity defense against such an assertion, in the United States an issued patent enjoys a presumption of validity, which can be overcome only through clear and convincing evidence. We cannot assure you such a defense would prevail.

We may also become subject to infringement claims or litigation arising out of other patents and pending applications of our

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competitors, if they issue, or additional interference proceedings declared by the PTO to determine the priority of inventions. The defense and prosecution of intellectual property suits, PTO interference proceedings and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain. Litigation may be necessary to enforce our issued patents, to protect our trade secrets and know-how or to determine the enforceability, scope and validity of the proprietary rights of others. An adverse determination in litigation or interference proceedings to which we may become a party could subject us to significant liabilities, require us to obtain licenses from third parties, or restrict or prevent us from selling our products in certain markets. Although patent and intellectual property disputes are often settled through licensing or similar arrangements, costs associated with such arrangements may be substantial and could include ongoing royalties. Furthermore, the necessary licenses may not be available to us on satisfactory terms, if at all. In particular, if we were found to infringe a valid claim of the Transgene adenoviral vector United States patent, Canji p53 issued United States patent or a claim that may issue from a currently pending application, such as the Johns Hopkins application discussed above or other patents that might issue with similar claims, our business could be materially harmed.

We have recently been involved in patent opposition proceedings before the EPO, in which we have sought to have the EPO revoke three different European patents owned or controlled by Canji/Schering-Plough. These European patents relate to the use of a p53 gene, or the use of tumor suppressor genes, in the preparation of therapeutic products. In one opposition involving a European patent directed to the use of a tumor suppressor gene, the EPO revoked the European patent in its entirety in a final, non-appealable decision. In the second opposition, involving a patent that is directed to therapeutic and other applications of the p53 gene and that is owned by Johns Hopkins and, we understand, controlled by Schering-Plough, the EPO recently revoked the patent in its entirety. The patent owner has appealed this decision. In a third case involving the use of a p53 gene, the European patent at issue was initially upheld, but finally revoked in a hearing held in late April 2004. That revocation is also final, and non-appealable. If we do not ultimately prevail in the one remaining appeal involving the revoked Johns Hopkins patent, our competitors could seek to assert their rights by means of litigation to limit or stop European commercial activities involving our potential products. If our competitors are successful in any such litigation, it could have a significant detrimental effect on our ability to commercialize our potential commercial products in Europe.

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

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

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

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

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

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

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

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

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

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

they are more effective than alternative treatments;

their side effects are acceptable to patients and doctors;

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

we produce and sell them at a profit; and

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

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

ADVEXIN therapy, our lead product candidate for the treatment of recurrent squamous cell cancer of the head and neck, targets diseases with small patient populations. As a result, our per-patient prices must be relatively high in

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

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

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

Before we can begin commercially manufacturing ADVEXIN therapy, INGN 241 or any other product candidate, we must obtain regulatory approval of our manufacturing facilities and process. Manufacturing of our product candidates for clinical and commercial purposes must comply with the FDA s CGMP requirements, and foreign regulatory requirements. The CGMP requirements govern quality control and documentation policies and procedures. In complying with CGMP and foreign regulatory requirements, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure the product meets applicable specifications and other requirements. We must also pass a FDA inspection prior to FDA approval.

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

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

Canji controls a United States patent and the corresponding international applications, including a European counterpart, relating to the purification of viral or adenoviral compositions. While we believe our manufacturing process does not infringe this patent, Canji could still assert a claim against us. We may also become subject to infringement claims or litigation if our manufacturing process infringes upon other patents. The defense and prosecution of intellectual property suits and related legal and administrative proceedings are costly and time-consuming to pursue, and their outcome is uncertain.

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

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

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

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The testing and marketing of medical products is subject to an inherent risk of product liability claims. Regardless of their merit or eventual outcome, product liability claims may result in:

decreased demand for our product candidates;

injury to our reputation and significant media attention;

withdrawal of clinical trial volunteers;

substantial delay in FDA approval;

costs of litigation; and

substantial monetary awards to plaintiffs.

We currently maintain product liability insurance with coverage of $5.0 million per occurrence with a $15.0 million annual aggregate limit. This coverage may not be sufficient to protect us fully against product liability claims. We intend to expand our product liability insurance coverage beyond clinical trials to include the sale of commercial products if we obtain marketing approval for any of our product candidates. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against product liability claims could prevent or limit the commercialization of our products.

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

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

Our stock price may fluctuate substantially.

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

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

announcement of technological innovations by us or our competitors;

developments concerning proprietary rights, including patent and litigation matters;

publicity regarding actual or potential results with respect to products under development by us or by our competitors;

regulatory developments;

the announcement of new products by us or our competitors;

quarterly variations in our or our competitors results of operations;

failure to achieve operating results projected by securities analysts;

changes in earnings estimates or recommendations by securities analysts;

developments in our industry; and

general market conditions and other factors.

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In addition, stock prices for many companies in the technology and emerging growth sectors have experienced wide fluctuations that have often been unrelated to the operating performance of such companies.

If we do not progress in our programs as anticipated, our stock price could decrease.

For planning purposes, we estimate the timing of a variety of clinical, regulatory and other milestones, such as when a certain product candidate will enter clinical development, when a clinical trial will be completed or when an application for regulatory approval will be filed. Some of our estimates are included in this Quarterly Report on Form 10-Q. Our estimates are based on present facts and a variety of assumptions. Many of the underlying assumptions are outside of our control. If milestones are not achieved when we expect them to be, investors could be disappointed, and our stock price may decrease.

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

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

potential exposure to unknown liabilities of acquired companies;

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

diversion of management time and attention and other resources;

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

the incurrence of amortization expenses; and

possible dilution to our stockholders.

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

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

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

from other companies, universities, public and private research institutions, government entities and other organizations.

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

Dr. John N. Kapoor, the Chairman of our Board of Directors, is also associated with EJ Financial Enterprises, Inc., a health care investment firm which is wholly owned by him, and therefore may have conflicts of interest in allocating his time among us

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and his other business activities, and he may have legal obligations to multiple entities. We have entered into a consulting agreement with EJ Financial. The consulting agreement provides we will pay EJ Financial $175,000 per year for certain management consulting services, which is based on anticipated time spent by EJ Financial personnel on our affairs. EJ Financial is also involved in the management of health care companies in various fields, and Dr. Kapoor is involved in various capacities with the management and operation of these companies. In addition, EJ Financial is involved with other companies in the cancer field. Although these companies are pursuing different therapeutic approaches for the treatment of cancer, discoveries made by one or more of these companies could render our products less competitive or obsolete.

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

We are in negotiations with Dr. Robert Sobol, our Senior Vice President, Medical and Scientific Affairs, to acquire a company of which he is the sole shareholder. The specific terms of the proposed transaction have not been finalized, but the purchase price is likely to be between $1.0 million and $2.0 million to be paid in shares of our common stock valued at approximately $6.50 per share. We believe the technology which is owned by Dr. Sobol s company will be a valuable addition to our intellectual property portfolio. We have endeavored to conduct the negotiations at arm s length. This transaction has been approved by the Audit Committee of our Board of Directors (Audit Committee).

We have relationships with Jack A. Roth, M.D., and M. D. Anderson Cancer Center, both of whom are affiliated with The Board of Regents of the University of Texas System, one of our stockholders. For more information concerning these relationships, see the notes to our consolidated financial statements and the footnotes thereto as of December 31, 2003, and for the year then ended, included in our Annual Report on Form 10-K, as filed with the SEC on March 5, 2004.

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

Item 3. Quantitative and Qualitative Disclosures about Market Risk.

Our exposure to market risk for changes in interest rates relates primarily to our fixed rate long-term debt and short-term investments in investment grade securities, which consist primarily of federal and state government obligations, commercial paper and corporate bonds. Investments are classified as held-to-maturity and are carried at amortized costs. We do not hedge interest rate exposure or invest in derivative securities. Based on our cash, cash equivalent and short-term investment balances at June 30, 2004, a hypothetical 100-basis point decrease in the interest rates we earn on those investments would decrease our interest income by approximately $260,000 per year and approximately $65,000 per quarter.

At June 30, 2004, the fair value of our fixed-rate debt approximated its carrying value based upon discounted future cash flows using current market prices.

Item 4. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures. Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Quarterly Report on Form 10-Q. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded our disclosure controls and procedures are effective to ensure

that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms.

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

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PART II

OTHER INFORMATION

Item 1. Legal Proceedings.

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

We do not believe the outcome of any present litigation, or all litigation in the aggregate, other than our opposition of the one remaining European patent controlled by Canji discussed under Risk Factors, will have a material effect on our business. You can read the discussion of our opposition of this patent under Risk Factors.

Item 2. Changes in Securities and Use of Proceeds.

None.

Item 3. Defaults Upon Senior Securities.

None.

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

(a) We held our Annual Meeting of Stockholders (Annual Meeting) on June 18, 2004.

(b) At the Annual Meeting, our stockholders elected William H. Cunningham, Ph.D. and S. Malcolm Gillis, Ph.D. as Class I directors, each to serve a term of three years. In addition, the term of office continued for the following directors: Charles E. Long and Mahendra G. Shah, Ph.D. as Class II directors and John N. Kapoor, Ph.D. and David G. Nance as Class III directors.

(c) Our stockholders voted on the following matters at the Annual Meeting:

1. The amendment to our Certificate of Incorporation to increase the authorized number of shares of common stock to a new total of 100,000,000 shares;

2. The election of two Class I directors to our Board of Directors, each to serve a term of three years; and

3. The ratification of the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2004.

Our stockholders approved the amendment to our Certificate of Incorporation to increase the authorized number of shares of common stock to a new total of 100,000,000 shares as follows:

24,270,566 votes for approval; 744,696 votes against; and 62,463 abstentions.

Votes were cast for the election of William H. Cunningham, Ph.D. and S. Malcolm Gillis, Ph.D. as Class I directors as follows:

Director:	Votes For:	Votes Withheld:
William H. Cunningham, Ph.D.	24,657,464	420,261
S. Malcolm Gillis, Ph.D.	24,654,317	423,408

The ratification of the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2003 was approved as follows:

24,948,488 votes for approval; 59,889 votes against; and 69,348 abstentions.

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Item 5. Other Information.

Pursuant to Section 10A(i)(2) of the Securities Exchange Act of 1934, as added by Section 202 of the Sarbanes-Oxley Act of 2002, we are responsible for disclosing the approval of non-audit services approved by the Audit Committee to be performed by Ernst & Young LLP, our independent auditors. Non-audit services are defined as services other than those provided in connection with an audit or a review of our financial statements. Except as set forth below, the services approved by the Audit Committee are each considered by the Audit Committee to be audit-related services closely related to the financial audit process. Each of the services was pre-approved by the Audit Committee.

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

Item 6. Exhibits and Reports on Form 8-K.

(a) Exhibits

3.1(c)	Amendment to Certificate of Incorporation, filed with the Secretary of State of Delaware on August 6, 2004.
10.7(f)	Modification Agreement effective April 1, 2004 by TMX Realty Corporation and Texas State Bank (formerly known as Riverway Bank), and other related agreements.
31.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 17 C.F.R. 240.13a-14 or 17 C.F.R. 240.15d-14, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

(b) Reports on Form 8-K

In connection with our earnings press release for the quarter ended March 31, 2004, we filed a Current Report on Form 8-K on May 11, 2004.

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SIGNATURES

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

INTROGEN THERAPEUTICS, INC.

August 16, 2004

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

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EXHIBIT INDEX

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