INTROGEN THERAPEUTICS INC
Form 10-Q
May 10, 2006

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

Form 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2006.

or

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

For the transition period from to .

Commission file number 000-21291

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

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

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

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

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

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

As of May 8, 2006, the registrant had 37,195,053 shares of its common stock, $0.001 par value per share, issued and outstanding.

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PART I
FINANCIAL INFORMATION

Item 1. Financial Statements

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

	December 31, 2005	March 31, 2006 (Unaudited)
ASSETS		
Current Assets:		
Cash and cash equivalents	$ 28,090	$ 6,537
Short term investments	5,032	20,841
Total cash, cash equivalents and short term investments	33,122	27,378
Marketable securities	2,892	2,764
Prepaid expense and other current assets	297	282
Total current assets	36,311	30,424
Property and equipment, net of accumulated depreciation of $12,588 and $12,946, respectively	6,181	5,859
Grant rights acquired	163	
Other assets	326	321
Total assets	$ 42,981	$ 36,604
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	$ 2,258	$ 2,481
Accrued liabilities	3,296	2,938
Deferred revenue	472	513
Current portion of notes payable	756	730
Total current liabilities	6,782	6,662
Notes payable, net of current portion	7,784	7,683
Deferred revenue, long-term	1,404	1,358
Total liabilities	15,970	15,703
Commitments and Contingencies (Note 8)		
Stockholders Equity:		
Preferred stock, $.001 par value per share; 5,000 shares authorized; 4,900 shares issuable; 100 and zero Series A shares issued and outstanding in 2005 and 2006, respectively		
Common stock, $.001 par value per share; 100,000 shares authorized; 37,147 and 37,195 shares issued and outstanding in 2005 and 2006, respectively	37	37
Additional paid-in capital	170,675	172,844

Deferred compensation	(68)	
Accumulated deficit	(143,459)	(151,678)
Accumulated other comprehensive loss	(174)	(302)
Total stockholders equity	27,011	20,901
Total liabilities and stockholders equity	$ 42,981	$ 36,604

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

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

	Three Months Ended March 31,	
	2005	2006
	(Unaudited)	
Contract services, grant and other revenue	$ 509	$ 225
Operating costs and expense:		
Research and development, including share-based compensation of zero and $217 in 2005 and 2006, respectively	5,239	5,046
General and administrative, including share-based compensation of $88 and $2,021 in 2005 and 2006, respectively	1,810	3,796
Total operating costs and expense	7,049	8,842
Loss from operations	(6,540)	(8,617)
Interest income	184	299
Interest expense	(150)	(156)
Other income	275	255
Net loss	$ (6,231)	$ (8,219)
Net loss per share, basic and diluted	$ (0.20)	$ (0.22)
Shares used in computing basic and diluted net loss per share	30,741	37,180

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

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

	Three Months Ended March 31,	
	2005	2006
	(Unaudited)	
Cash flows from operating activities:		
Net loss	$ (6,231)	$ (8,219)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	400	358
Share-based compensation	88	2,238
Amortization of grant rights acquired	237	133
Changes in assets and liabilities:		
Increase (decrease) in other assets	(25)	20
Increase (decrease) in accounts payable	(139)	223
Increase (decrease) in accrued liabilities	(358)	(357)
Increase (decrease) in deferred revenue	153	(6)
Net cash used in operating activities	(5,875)	(5,610)
Cash flows from investing activities:		
Purchases of property and equipment	(97)	(36)
Purchases of short-term investments	(14,046)	(15,809)
Maturities of short-term investments	5,964	
Net cash used in investing activities	(8,179)	(15,845)
Cash flows from financing activities:		
Proceeds from exercise of stock options	346	29
Proceeds from notes payable	265	97
Principal payments under notes payable	(171)	(224)
Net cash provided by (used in) financing activities	440	(98)
Net decrease in cash and cash equivalents	(13,614)	(21,553)
Cash and cash equivalents, beginning of period	30,187	28,090
Cash and cash equivalents, end of period	$ 16,573	$ 6,537
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 133	$ 148
Non-cash unrealized loss on marketable securities	$	$ 128

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

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

1. Formation and Business of the Company

See Management s Discussion and Analysis of Financial Condition and Results of Operations (Part I, Item 2) below for a discussion of our business.

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

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

2. Basis of Presentation

The accompanying condensed consolidated financial statements have been prepared in accordance with United States generally accepted accounting principles 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 United States generally accepted accounting principles for complete financial statements. In management s opinion, all accounting entries considered necessary for a fair presentation have been made in preparing these financial statements, and such entries are normal in nature. Operating results for the three month period ended March 31, 2006 are not necessarily indicative of the results that may be expected for the entire fiscal year.

3. Significant Accounting Policies

Our significant accounting policies are described in Note 2 to the consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, filed with the SEC on March 16, 2006. Those accounting policies remain in effect except to the extent described in the following notes.

Share-Based Compensation

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

Prior to January 1, 2006, we applied Accounting Principles Board Opinion No. 25 (APB No. 25), Accounting for Stock Issued to Employees and related interpretations for determining compensation expense related to our stock option grants. Under that principle, we measured compensation expense for stock options issued to our directors and employees using the intrinsic value of the stock option at date of grant, which generally resulted in us recording no compensation expense since the intrinsic value of those stock options was typically zero at the date of grant due to the exercise price of those stock options being equal to the fair value of our shares on the date of grant. Compensation expense for stock options issued to all other persons was measured using the fair value of the stock option at the date of grant determined under the Black-Scholes option pricing model, which generally resulted in us recording a compensation expense.

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

We implemented SFAS No. 123R using the modified prospective transition method. Under this method, prior periods are not restated.

4. Stock Options

The 2000 Stock Option Plan (Stock Option Plan) was initiated in October 2000. All stock option grants since that time have been under this plan. The Stock Option Plan provides for the granting of options, either incentive or non-statutory, or stock purchase rights to our employees, directors and consultants to purchase shares of our common stock. Option awards are generally granted with an exercise price equal to the fair value of the Company's stock at the date of grant. The awards generally cliff vest 25% per year over a four year period and have contractual terms of ten years. The Stock Option Plan provides for annual increases each January 1 in the number of shares available for issuance in an amount equal to the lesser of 1.6 million shares, 5% of the outstanding shares on the date of the annual increase, or a lesser amount as may be determined by the Board of Directors. At March 31, 2006, there were approximately 2.4 million shares of common stock reserved for future grants under this plan. In the event of a merger, reorganization or change in our controlling ownership, options granted under the Stock Option Plan (1) may be assumed or substituted with substantially equivalent options by the successor corporation and (2) become fully vested and immediately exercisable regardless of whether or not they are assumed or substituted by the successor corporation. The Stock Option Plan terminates in 2010 and may be amended or terminated by the Board of Directors.

Prior to October 2000, stock options were granted under our 1995 Stock Plan. We no longer issue options under this plan. In the event of a merger, reorganization or change in our controlling ownership, all options outstanding under this plan become fully vested and immediately exercisable unless the successor corporation assumes or substitutes other options in their place. No shares of common stock were reserved for future grants under this plan at March 31, 2006.

Our accounting policy for stock options is described in Note 3 under Share-Based Compensation. Had we recognized share-based compensation expense in our financial statements for the three months ended March 31, 2005 determined using the fair value method for all stock options (as allowed by SFAS No. 123), our net loss would have been increased to the following pro forma amounts (in thousands, except per share information):

		Three Months Ended March 31, 2005
Net loss, as reported	$	(6,231)
Add: Share-based employee compensation expense included in reported net loss		
Deduct: Total share-based employee compensation expense determined under fair value based method for all awards		(750)
Pro forma net loss	$	(6,981)
Loss per share:		
Basic and Diluted as reported	$	(0.20)
Basic and Diluted pro forma	$	(0.23)

These pro forma disclosures are not applicable to the three months ended March 31, 2006, because share-based compensation expense for all stock options vesting during that period is recognized in our financial statements for that

period. Our adoption of SFAS No. 123R increased research and development expense by $217,000 and general and administrative expense by $2.0 million for the three months ended March 31, 2006.

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Activity under our option plans is as follows:

	Options Outstanding	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value (000 s)
Balance, December 31, 2005	5,978,369	$ 4.49	n/a	n/a
Granted	265,200	5.47	n/a	n/a
Exercised	(44,826)	0.64	n/a	n/a
Cancelled	(3,075)	5.60	n/a	n/a
Balance, March 31, 2006	6,195,668	4.56	6.76	$ 6,822
Exercisable at March 31, 2006	3,963,709	3.86	5.96	$ 6,179

Additional information of note related to our stock options includes:

The weighted average fair value of options granted during the three months ended March 31, 2006 was $3.96.

The aggregate intrinsic value of stock options at exercise, represented in the table above, was $207,000 for the three months ended March 31, 2006.

The total unrecognized share-based compensation expense related to unvested stock options and subject to recognition in future periods was approximately $8.1 million as of March 31, 2006. This amount relates to approximately 2.2 million shares with a per share weighted average fair value of $5.14. We anticipate this expense to be recognized over a weighted average period of approximately 1 year.

We applied the following assumptions on a weighted average basis in computing the fair value of stock options at their date of grant using the Black-Scholes option pricing model:

	Three Months Ended March 31,	
	2005	2006
Expected volatility	91.80%	90.41%
Risk free interest rate	4.12%	4.31%
Expected dividend yield	0.00%	0.00%
Expected life, in years	10.00	5.07

Specifics regarding these assumptions include:

The expected volatility is calculated using the daily historical volatility of our common stock since our initial public offering in October 2000, which approximates the expected life of the option grants.

The risk-free interest rate is based on the U.S. treasury yield curve for a seven-year term and the ten-year zero coupon treasury bill rate for the three months ended March 31, 2006 and 2005, respectively.

As allowed by Staff Accounting Bulletin No. 107, we have elected to apply the shortcut approach in developing our estimate of expected term for plain vanilla stock options by using the mid-point between the vesting date and contractual termination date.

We periodically evaluate and revise, as necessary, the assumptions used to calculate the fair value of our stock options in response to changing market conditions and experience.

5. Intangible Assets

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

	December 31, 2005			March 31, 2006			
	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount	Gross Carrying Amount	Adjustment To Carrying Amount	Accumulated Amortization	Net Carrying Amount
Asset acquisition:							
Acquired grant rights (22 month amortization period)	$ 1,741	$ (1,578)	$ 163	$ 1,741	$ (30)	$ (1,711)	$
Ending balance	$ 1,741	$ (1,578)	$ 163	$ 1,741	$ (30)	$ (1,711)	$

Research and development expense includes amortization of intangibles of $133,000 and $237,000 for the three months ended March 31, 2006 and March 31, 2005, respectively. During the three months ended March 31, 2006, the acquired grant rights were reduced by $30,000 as a result of the final contractual settlement of the purchase of Magnum. During the three months ended December 31, 2005, we changed our estimate of the useful life of the acquired grant rights from 22 months to 17 months. The effect of

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this change was to increase amortization expense in 2005 and decrease amortization expense in 2006 by $470,000. Estimated annual amortization expense for fiscal year 2006 is $133,000 and zero thereafter.

6. Investment in VirRx, Inc.

Under an agreement with VirRx, Inc. (VirRx), we purchased $150,000 of their Series A Preferred Stock in the three month period ended March 31, 2006 and the three month period ended March 31, 2005. We record these purchases as research and development expense. We are no longer required to make periodic purchases of their Series A Preferred Stock under this agreement but may be required to make additional stock purchases in the event VirRx reaches certain specified milestones as described below in Management s Discussion and Analysis of Financial Condition and Results of Operations Business and Collaborative Arrangements VirRx, Inc. 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 upon 90 days prior written notice. In accordance with the provisions of Financial Accounting Standards Board Interpretation 46R, 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 9 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, filed with the SEC on March 16, 2006.

7. Investment in SR Pharma plc

In July 2005, we purchased approximately 8.3% of the issued share capital of SR Pharma plc (SR Pharma) for approximately $3.0 million. SR Pharma is a European biotechnology company publicly traded on the Alternative Investment Market of the London Stock Exchange (LSE) that is developing oncology and other products. This investment is classified as marketable securities on our balance sheet. Marketable securities are classified as available-for-sale and are presented at fair value with any unrealized gains or losses included in other comprehensive income (loss).

8. Mortgage Note Payable

We have a mortgage note payable to a bank related to our facilities that had an outstanding principal balance of $7,427,000 and $7,482,000 at March 31, 2006 and December 31, 2005, respectively. In April 2006, we exercised our option to extend the note payable to a November 2009 maturity date, at which time the remaining outstanding principal balance is payable in full. As a result, the interest rate changed from 6.25% to 7.35% and our monthly installments of principal and interest changed from approximately $56,000 per month to approximately $61,000 per month. Our facilities are pledged as security for the mortgage note payable.

9. Stockholders Equity

Stock Sales

In November 2005, we sold approximately 3.6 million shares of our common stock in a direct equity sale to Colgate-Palmolive pursuant to a shelf registration statement for an aggregate purchase price of approximately $20.0 million. Our net proceeds from this transaction, after related fees and expense, were approximately $19.6 million. For additional discussion of our agreements with Colgate-Palmolive, see Note 9 to our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2005, filed with the SEC on March 16, 2006.

Conversion of Preferred Stock to Common Stock

In 2001, we sold 100,000 shares of $0.001 par value, Series A Non-Voting Convertible Preferred Stock to Aventis Pharmaceutical Products, Inc. (Aventis), which is now Sanofi-Aventis, for $25.0 million. In June 2005, these 100,000 issued and outstanding shares of our Series A non-voting convertible preferred stock were converted into 2,343,721 shares of our common stock. Following the conversion, these shares of preferred stock were cancelled and are no longer issuable. We received no cash or other consideration in connection with this conversion.

Under a voting agreement related to these shares, Aventis must vote all of the shares of ours it holds in the same manner as the shares voted by a majority of the other stockholders on any corporate action put to a vote of our stockholders. This voting requirement terminates at the earliest of June 2011 or the sale of these shares pursuant to an effective registration statement on the open market or to an Aventis non-affiliate, as defined in the voting agreement.

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Pursuant to a demand registration made by Aventis in accordance with the terms of a registration rights agreement related to these shares, in November 2005 we filed a Registration Statement on Form S-3 (File No. 333-129687) to facilitate the public resale of up to 4,322,369 shares of our common stock held by Aventis, which includes the converted shares. This registration statement has been declared effective by the SEC and Aventis may resell these shares from time to time in the open market pursuant to the registration statement. We will not receive any of the proceeds from the sale of the shares held by Aventis. As of March 31, 2006, Aventis held approximately 4.2 million shares of our common stock subject to the voting agreement.

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

10. Accumulated Other Comprehensive Income or Loss

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

	Three Months Ended March 31,	
	2005	2006
Net loss	$ (6,231)	$ (8,219)
Foreign currency translation adjustments		
Unrealized gain (loss) on marketable securities		(128)
Total comprehensive loss	$ (6,231)	$ (8,347)

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, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). 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 Part II, Item 1A. 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 molecular therapies for the treatment of cancer and other diseases. We are developing product candidates to treat a wide range of cancers using tumor suppressors, cytokines and other targeted molecular therapies. These agents are designed to increase production of normal cancer-fighting proteins that act to overpower cancerous cells, stimulate immune activity and enhance conventional cancer therapies.

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

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

kills cancer cells without harming normal cells.

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The Introgen Strategy

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

Develop and Commercialize ADVEXIN therapy, INGN 225 and INGN 241 for Multiple Cancer Indications. We plan to continue our development programs to commercialize our ADVEXIN therapy using the p53 tumor suppressor and our INGN 241 product using the mda-7 tumor suppressor, also know as interleukin 24 (IL-24), in multiple cancer indications.

Develop Our Portfolio of Targeted Molecular Therapies and Other Drug Products. Utilizing our significant research, clinical, regulatory and manufacturing expertise, we are evaluating development of additional molecular therapies for various cancers, such as INGN 225, a highly specific cancer immunotherapy, INGN 234, an oral rinse or mouthwash formulation containing the p53 tumor suppressor, INGN 401, using the FUS-1 tumor suppressor, and INGN 007, a replication-competent viral therapy. We have established an efficient process for evaluating new drug candidates and advancing them from pre-clinical to clinical development. We have identified and licensed multiple technologies, which we intend to combine with our adenoviral and non-viral vector systems and which we believe are attractive development targets for the treatment of various cancers. We are also evaluating the development of mebendazole (INGN 601), our first small molecule product candidate. We intend to evaluate additional opportunities to in-license or acquire new technologies.

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

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

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

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

ADVEXIN® Therapy (p53)

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

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

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

We have received Fast Track designation for ADVEXIN therapy from the FDA under its protocol assessment program as a result of the FDA s agreement with the design of our two ongoing Phase 3 clinical trials of ADVEXIN therapy. Under this Fast Track designation, the FDA will take actions to expedite the evaluation and review of the Biologics License Application (BLA) for

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ADVEXIN therapy. We plan to pursue with the FDA an Accelerated Approval of ADVEXIN therapy, which is one alternative provided under a Fast Track designation.

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

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

Accordingly, we have submitted a SOPA Request to the FDA Division of Cell and Gene Therapy proposing a rolling BLA for ADVEXIN therapy for the treatment of recurrent head and neck cancer, based primarily on data from our Phase 2 clinical trials. We have further proposed to the FDA that, since the basis of the proposed rolling BLA is Phase 2 clinical data utilizing surrogate endpoints, the rolling BLA could be evaluated under the provisions of Subpart H for Accelerated Approval. In order to fully explore all of the review and approval possibilities for ADVEXIN therapy, the FDA has requested we submit existing new data and analyses from the Phase 2 ADVEXIN therapy clinical trials for recurrent head and neck cancer and consider conducting interim efficacy analyses on one or both of our ongoing Phase 3 trials. Given that we have two ongoing Phase 3 clinical trials in head and neck cancer as discussed further below, we and the FDA are evaluating the most effective use of the data from these Phase 2 and 3 clinical trials in the review and approval of ADVEXIN therapy. Regulatory approval approaches may allow Accelerated Approval on the basis of Phase 2 clinical data with subsequent confirmatory data being provided by the Phase 3 clinical studies or, alternatively, a full approval based on data from Phase 2 and certain Phase 3 clinical trials. We will also be exploring with the FDA whether its recently announced Critical Path Initiative, which permits new product evaluation on the basis of specifically targeted (i.e., by prognostic or biologic parameters) clinical trials and/or patient populations, can be used in the ADVEXIN therapy approval process.

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

We have conducted multi-national, multi-site Phase 2 clinical trials of ADVEXIN therapy in 217 patients with recurrent squamous cell cancer of the head and neck treated previously with surgery, radiation or chemotherapy. In the combined analysis of these trials, the overall tumor growth control rate was 59%. Tumor growth control rate represents the percentage of treated tumors where there was disappearance of the tumor, shrinkage of the tumor or the

absence of additional tumor growth beyond 25% of pre-treatment measurements. In approximately 10% of the treated lesions there was either complete tumor regression or a reduction of tumor size greater than or equal to 50% of the pre-treatment size. Subpopulations of patients participating in these trials had certain defining prognostic, medical and biological characteristics that represent refined targeting of ADVEXIN therapy. Analysis of the data from these patient subpopulations showed objective response rates of up to 29%. These findings, along with other data, are planned for presentation at future scientific meetings and for future publication in a peer-reviewed medical journal.

We performed a Phase 2 clinical trial of ADVEXIN therapy combined with neoadjuvant chemotherapy and surgery in women with locally advanced breast cancer. After at least 35 months of follow-up, 92% of the treated patients were alive and 83% had survived

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without evidence of disease recurrence. Objective clinical responses were seen following the combined therapy in all of the patients with a median of 80% reduction in tumor size. Following tumor shrinkage, complete tumor removal by subsequent surgery was achieved in 100% of the patients. The results of the therapy with the addition of ADVEXIN are better than what would be expected from neoadjuvant chemotherapy treatment alone. Neoadjuvant treatments are administered prior to surgery and represent a novel and increasingly applied approach to making surgical tumor resections less invasive, improving outcomes and facilitating breast conservation. These data were announced during the 2005 San Antonio Breast Cancer Symposium.

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

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

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

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

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

We have completed other clinical trials of Advexin, including Phase 1 studies in prostate cancer and bronchoalveolar carcinoma. To date, clinical investigators at sites in North America, Europe and Japan have treated over 500 patients with ADVEXIN therapy, establishing a large safety database. Findings from several of our clinical trials have been published in *Clinical Cancer Research* and *Proceedings of the American Society for Clinical Oncology* as well as presented at numerous conferences, including the San Antonio Breast Cancer Conference and various meetings of the American Society of Clinical Oncology, the American Association for Cancer Research and the American Society of Gene Therapy.

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

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

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

Cancer Institute located in Detroit, Michigan and the University of California-Irvine, as published in *The Laryngoscope,* show that the combination of ADVEXIN therapy and docetaxel resulted in increased levels of programmed cell death in head and neck tumor cells. Two lung cancer patients, who were part of our ADVEXIN therapy studies program and who had recently celebrated their five-year survival anniversary, were featured in *Conquest* magazine, a publication of M. D. Anderson Cancer Center. In addition,

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a patient with recurrent head and neck cancer who achieved a complete tumor remission on ADVEXIN therapy continues to be disease-free over seven years later while receiving repeated ADVEXIN treatments.

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

INGN 241 (mda-7)

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