INTROGEN THERAPEUTICS INC
Form 10-Q
August 14, 2003

Table of Contents

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

# FORM 10-Q

(Mark One)

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

For the quarterly period ended June 30, 2003

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 x 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 x

As of August 11, 2003, the registrant had 23,646,002 shares of its common stock, $0.001 par value per share, issued and outstanding.

**TABLE OF CONTENTS**

**Table of Contents**

INTROGEN THERAPEUTICS, INC.

QUARTERLY REPORT ON FORM 10-Q

TABLE OF CONTENTS

Table of Contents

**PART I**
**FINANCIAL INFORMATION**

**Item 1. Condensed Consolidated Financial Statements.**

INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES

CONDENSED CONSOLIDATED BALANCE SHEETS
(Amounts in thousands)

| | December 31, 2002 | June 30, 2003 |
|---|---|---|
| | | (Unaudited) |
| ASSETS | | |
| Current Assets: | | |
| Cash and cash equivalents | $ 23,467 | $ 26,656 |
| Prepaid expenses and other current assets | 812 | 409 |
| Total current assets | 24,279 | 27,065 |
| Property and equipment, net of accumulated depreciation of $8,228 and $8,974, respectively | 8,742 | 7,994 |
| Other assets | 295 | 292 |
| Total assets | $ 33,316 | $ 35,351 |
| LIABILITIES AND STOCKHOLDERS EQUITY | | |
| Current Liabilities: | | |
| Accounts payable | $ 1,774 | $ 1,399 |
| Accrued liabilities | 1,997 | 2,607 |
| Deferred revenues from affiliate | 69 | 35 |
| Current portion of capital lease obligations and notes payable | 1,587 | 1,331 |
| Total current liabilities | 5,427 | 5,372 |
| Capital lease obligations, net of current portion | 125 | 85 |
| Notes payable, net of current portion | 7,310 | 6,937 |
| Deferred revenue, long-term | 619 | 751 |
| Total liabilities | 13,481 | 13,145 |
| Commitments and contingencies | | |
| Stockholders Equity: | | |
| Series A non-voting convertible preferred stock, $.001 par value, 100 shares authorized, 100 shares issued and outstanding | 1 | 1 |
| Common stock, $.001 par value; 50,000 shares authorized, 21,446 and 23,646 shares issued and outstanding, respectively | 21 | 24 |
| Additional paid-in capital | 94,430 | 105,651 |
| Deferred compensation | (974) | (334) |
| Accumulated deficit | (73,643) | (83,136) |
| Total stockholders equity | 19,835 | 22,206 |

| | | |
|---|---|---|
| Total liabilities and stockholders equity | $ 33,316 | $ 35,351 |

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

Table of Contents

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, | |
|---|---|---|---|---|
| | 2002 | 2003 | 2002 | 2003 |
| Contract services, grant and other revenue | $ 322 | $ 143 | $ 551 | $ 293 |
| Costs and expenses: | | | | |
| Research and development | 5,805 | 2,957 | 12,504 | 7,299 |
| General and administrative | 1,679 | 1,808 | 3,434 | 3,195 |
| Total operating expenses | 7,484 | 4,765 | 15,938 | 10,494 |
| Loss from operations | (7,162) | (4,622) | (15,387) | (10,201) |
| Interest income | 166 | 475 | 357 | 536 |
| Interest expense | (203) | (161) | (422) | (330) |
| Other income | 332 | 254 | 649 | 502 |
| Net loss | $ (6,867) | $ (4,054) | $ (14,803) | $ (9,493) |
| Net loss per share, basic and diluted | $ (0.32) | $ (0.19) | $ (0.69) | $ (0.44) |
| Shares used in computing basic and diluted net loss per share | 21,463 | 21,851 | 21,457 | 21,679 |

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

**Table of Contents**

INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(Amounts in thousands)

(UNAUDITED)

| | Six Months Ended June 30, | |
|---|---|---|
| | **2002** | **2003** |
| Cash flows from operating activities: | | |
| Net loss | $ (14,803) | $ (9,493) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation | 959 | 739 |
| Compensation related to issuance of stock options | 741 | 1,041 |
| Changes in assets and liabilities: | | |
| Decrease (increase) in accounts receivable | 63 | 45 |
| Decrease (increase) in other assets | 107 | 361 |
| Increase (decrease) in accounts payable and accrued liabilities | 1,281 | 235 |
| Increase (decrease) in deferred revenue | 414 | 98 |
| Net cash used in operating activities | (11,238) | (6,974) |
| Cash flows from investing activities: | | |
| Purchases of property and equipment, net of retirements | (76) | 10 |
| Purchases of short-term investments | (37,878) | |
| Maturities of short-term investments | 23,389 | |
| Net cash provided (used in) by investing activities | (14,565) | 10 |
| Cash flows from financing activities: | | |
| Proceeds from sale of common stock | 10 | 10,823 |
| Borrowings under capital lease obligations and notes payable | | 141 |
| Principal payments under capital lease obligations and notes payable | (728) | (811) |
| Net cash provided by (used in) financing activities | (718) | 10,153 |
| Net increase (decrease) in cash | (26,521) | 3,189 |
| Cash, beginning of period | 37,397 | 23,467 |
| Cash, end of period | $ 10,876 | $ 26,656 |
| Supplemental disclosure of cash flow information: | | |
| Cash paid for interest | $ 415 | $ 330 |

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

Table of Contents

**INTROGEN THERAPEUTICS, INC. AND SUBSIDIARIES**

**UNAUDITED NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

**1. Business**

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

We have not 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. 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 well as those factors set forth below under Factors Affecting Future Operating Results. As a result of the aforementioned 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 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) and, accordingly, 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, 2003, are not necessarily indicative of the results that may be expected for the year ending December 31, 2003. For further information, refer to the consolidated financial statements and footnotes thereto as of December 31, 2002, and for the year then ended, included in our Annual Report on Form 10-K as filed with the SEC on March 31, 2003.

**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**

For stock options granted to our directors and employees, we record compensation using the intrinsic value method allowed by Statement of Financial Accounting Standards (SFAS) No. 123, Accounting for Stock-Based Compensation, and as set forth 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. Under this method, for stock options granted to our directors and employees, we record compensation expense based on the excess of the market value of our stock over the exercise price of the stock option on the date of the stock option grant. If the exercise price of the stock option is equal to or less than the market value of our stock on the date of grant, we do not record compensation expense. For stock options granted to persons other than our directors and employees, we record compensation expense based on the fair value method and the Black-Scholes option pricing model. Under both methods, if the compensation expense relates to a stock option that vests over future periods, we defer that expense and amortize that deferral over the vesting period of the stock option, which is generally four years.

For stock options granted to our directors and employees, we have estimated the fair value of options granted 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 3.6 percent to 6.1 percent, expected stock option lives of seven to ten years, no expected dividends and volatility factors ranging from 58.0 percent to 110.8 percent. Had compensation expense for stock options granted to our directors and employees been determined using the Black-Scholes option pricing model allowed under SFAS No. 123, our net loss would have been increased to the following pro forma amounts (in thousands, except per share information):

Table of Contents

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2002 | 2003 | 2002 | 2003 |
| Net loss, as reported | $ (6,867) | $ (4,054) | $ (14,803) | $ (9,493) |
| Add: Stock-based director and employee compensation expense included in reported net loss determined using the intrinsic value method | 352 | 556 | 741 | 843 |
| Deduct: Stock-based director and employee compensation expense determined using the fair value method | (599) | (2,190) | (1,094) | (2,568) |
| Pro forma net loss | (7,114) | (5,688) | (15,156) | (11,218) |
| Earnings per share: | | | | |
| Basic and diluted, as reported | $ (0.32) | $ (0.19) | $ (0.69) | $ (0.44) |
| Basic and diluted, pro forma | $ (0.33) | $ (0.26) | $ (0.71) | $ (0.52) |

**5. Investment in VirRx, Inc.**

We have an agreement with VirRx, Inc. (VirRx) to purchase $150,000 of VirRx Series A Preferred Stock on the first day of each quarter through January 1, 2006. We purchased $150,000 and $300,000 of this stock for cash during the three and six months ended June 30, 2003, respectively. 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 our requirement 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, 2002, filed with the SEC on March 31, 2003.

**6. Sale of Common Stock**

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.

**7. Recently Issued Accounting Standards**

In January 2003, the Financial Accounting Standards Board (FASB) issued Interpretation 46, *Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51*, (FIN 46). FIN 46 requires the consolidation of entities in which an enterprise absorbs a majority of another entity s expected losses, receives a majority of the entity s expected residual returns, or both, as a result of ownership, contractual or other interests in the entity. Currently, entities are generally consolidated by an enterprise when it has a controlling financial interest through ownership of a majority voting interest in the entity. The consolidation requirements of FIN 46 apply to variable interest entities created after January 31, 2003. The consolidation requirements apply to older entities in the first fiscal year or interim period beginning after June 15, 2003. The Company is still evaluating the potential impact, if any, that the adoption of FIN 46 may have.

**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. 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 Factors Affecting Future Operating Results.

Table of Contents

**Overview**

Introgen Therapeutics, Inc. was incorporated in Delaware on June 17, 1993. We are a leading developer of biopharmaceutical products using non-integrating gene agents designed to induce therapeutic protein expression for the treatment of cancer and other diseases. Our drug discovery and development programs have resulted in innovative approaches by which physicians may use genes to initiate therapeutic protein production. Genes provide instructions for the manufacture of proteins in a cell. In the Introgen approach, genes are used as the means of introducing into the target cancer cells the necessary amounts of normal cancer fighting proteins that act to overpower the cancer cell. Thus, rather than acting to repair or replace aberrant or missing genes and thereby creating a permanent, long-term change to the patient s genome, our products work in a different manner by targeting genes formulated to act as pharmacologic agents to engage molecular targets. The resultant proteins engage their normal molecular targets or receptors to produce a specific therapeutic effect. Our lead product candidate, ADVEXIN® therapy, combines the p53 gene with an adenoviral gene delivery system that 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 pivotal Phase 3 clinical trials of ADVEXIN therapy, both by itself and in combination with chemotherapy, in advanced squamous cell cancer of the head and neck. Pivotal Phase 3 clinical trials are efficacy trials, which are usually followed by the filing of an application with the United States Food and Drug Administration (FDA) to market the product being tested.

We have completed a Phase 2 clinical trial of ADVEXIN therapy administered as a complement with radiation therapy in non-small cell lung cancer. Phase 2 trials are efficacy trials. This Phase 2 trial showed that approximately 60 percent of patients primary tumors regressed or disappeared after the combination therapy, as assessed by both biopsies and by CT scans three months after treatment. Moreover, ADVEXIN therapy administration did not appear to increase the side effects caused by radiation treatment. These data were published in the January 2003 issue of the journal *Clinical Cancer Research*. We are reviewing future development plans for this indication.

We are conducting a Phase 2 clinical trial of ADVEXIN therapy combined with systemic chemotherapy for the treatment of breast cancer. Interim results of this trial were published in June 2003 at the annual meeting of the American Society of Clinical Oncology. These results indicated that in patients with locally advanced breast cancer, ADVEXIN therapy can be safely combined with a two-drug standard chemotherapy regimen and that 90 percent of the patients had objective responses to the therapy.

We are conducting a Phase 1-2 clinical trial of ADVEXIN therapy for the treatment of advanced unresectable squamous cell esophageal cancer. The study protocol was developed and is sponsored by investigators at Chiba University in Japan. Preliminary results from this trial indicate ADVEXIN therapy can be safely administered and that a positive biological effect resulted from the expression of the p53 protein. These results were published in June 2003 at the meeting of the American Society of Clinical Oncology. Of the first eight patients evaluated to date, one patient was observed to have minor tumor regression following ADVEXIN therapy injections.

We are conducting Phase 1 clinical trials, or safety trials, of ADVEXIN therapy in other types of cancer. In a Phase 1 trial for the treatment of bronchoalveolar cancer, a form of non-small cell lung cancer, in which ADVEXIN therapy is administered directly into the airway leading to the diseased lung, we noted the therapy was well-tolerated in all 26 patients treated, that there was an improved ability to breathe in 20 percent of the patients who were able to be evaluated and that the disease stabilized and did not continue to grow in a majority of those patients. This trial was conducted under our Cooperative Research and Development Agreement with the National Cancer Institute (NCI).

We and the NCI will conduct a Phase 1-2 clinical trial in which ADVEXIN therapy will be administered in the form of an oral rinse or mouthwash. This trial will be the first to investigate the cancer prevention effect of ADVEXIN therapy on oral lesions that have a high risk of developing into cancer. Currently, there are no treatments for such cancer prevention approved by the FDA.

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 patient s particular immune cell known as a dendritic cell. Recently published research in *Current Opinion in Drug Discovery & Development* concluded that ADVEXIN therapy can be used with a patient s isolated dendritic cells as an antigen delivery and immune enhancing therapeutic strategy. Preclinical testing has shown that the immune system can recognize and kill tumors after treatment with ADVEXIN therapy stimulated dendritic cells. We believe ADVEXIN therapy applied in this manner could have broad utility as a prophylaxis for cancer progression in patients with

**Table of Contents**

solid cancers. A Phase 1 trial has been initiated to treat patients with small-cell lung cancer using INGN 225 after treatment with standard chemotherapy.

To date, clinical investigators at clinical sites in North America, Europe and Japan have treated hundreds of patients with ADVEXIN therapy, establishing a large safety database. We hold the worldwide rights for pre-clinical and clinical development, manufacturing, marketing and commercialization of ADVEXIN therapy. ADVEXIN therapy for head and neck cancer is designated as an orphan drug under the Orphan Drug Act, which gives us seven years of marketing exclusivity for ADVEXIN therapy if approved by the FDA.

We are developing additional gene-induced therapeutic protein agents that we believe may be effective in treating certain cancers. These additional therapeutic protein agents include those based on several genes, including the mda-7, FUS-1 and BAK genes, as well as additional vector technologies for delivering the gene-based products efficiently into target cells.

Our INGN 241 product candidate, which combines the mda-7 gene with our adenoviral vector system, is undergoing safety and efficacy testing in a Phase 1-2 clinical trial, with one of the objectives also being to determine if this technology displays anti-tumor activity. This trial has demonstrated that in patients with solid tumors, INGN 241 is well tolerated, is biologically active, displays minimal toxicity associated with its use and can lead to tumor regression. Preclinical studies have demonstrated that INGN 241 works to kill tumor cells directly and simultaneously stimulates the immune system, known as cytokine activity, to kill metastatic tumor cells through multiple mechanisms in a variety of cancers. These studies have shown that the mda-7 protein produced by INGN 241 may play an important role in controlling the growth of tumors, which resulted in the designation of mda-7 as interleukin-24, or IL-24. Preclinical studies also suggest INGN 241 can be effectively combined with radiation therapy and may be useful in enhancing the effects of such therapy.

Preclinical studies have shown that gene delivery of FUS-1, our INGN 401 product candidate, which we exclusively license from The University of Texas M. D. Anderson Cancer Center, using either adenoviral or non-viral gene transfer, significantly inhibits the growth of tumors and greatly reduces the metastatic spread of lung cancer in animals. A Phase 1 trial is ongoing for INGN 401 in patients with advanced non-small cell lung cancer who have previously been treated with chemotherapy.

We are investigating other 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 causes rapid disruption of tumor cells in which the adenovirus replicates. Preclinical testing indicates that INGN 007 over-expresses a gene that allows the vector to saturate the entire tumor and to eradicate cancer in animal models. We anticipate pursuing clinical confirmation as to whether this self-amplifying delivery system can complement our existing adenoviral gene delivery system, which is replication disabled, in selected therapeutic scenarios.

We believe our research and development expertise gained from our gene-induced protein therapies for cancer is also applicable to other diseases that, like cancer, result from cellular dysfunction and uncontrolled cell growth. As a result, we are conducting research in collaboration with medical institutions to understand the safety and effectiveness of our gene-induced protein therapy product candidates in the treatment of diseases such as rheumatoid arthritis. In addition, we have developed a variety of technologies, which we refer to as enabling technologies, for administering gene-based products to patients and enhancing the effects of these products. We also have specialized manufacturing expertise and a manufacturing facility to support our continued product development and commercialization efforts.

As a supplement to our gene-induced therapeutic protein programs, we are evaluating the development of mebendazole, our first small molecule product candidate, which we refer to as INGN 601. The use of the mebendazole compound is approved by the FDA for the oral treatment of parasitic diseases. Pre-clinical studies suggest that mebendazole may also be an effective treatment of cancer. The results of pre-clinical studies involving mebendazole and lung cancer are published in the January 2003 edition of *Molecular Cancer Therapeutics*. We are working with The University of Texas M. D. Anderson Cancer Center to further evaluate development of this molecule as a cancer treatment.

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 that cover 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

**Table of Contents**

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 certain European patents held by our competitors revoked by the European Patent Office, subject to appeal by the patent holders. In addition to our p53 and mda-7 intellectual property position, we also 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.

We own and operate a manufacturing facility that we believe complies with the FDA s current Good Manufacturing Practices requirements, commonly known as CGMP requirements. We have produced ADVEXIN therapy in this facility for use in our Phase 1, 2 and 3 clinical trials. The design of the facility and the processes operated in the facility have been reviewed with the FDA. Our work to validate our manufacturing processes in accordance with FDA regulations is ongoing. We plan to use this facility for our market launch of ADVEXIN therapy. We have produced over 20 batches of ADVEXIN therapy clinical material, including all clinical material used in our Phase 2 and Phase 3 clinical trials. 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 have also produced INGN 241 in a separate facility for use in our Phase 1-2 clinical trials.

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, 2003, we had an accumulated deficit of approximately $83.1 million. We anticipate that we will incur losses in the future that may be greater than losses incurred in prior periods. At June 30, 2003, we had cash and cash equivalents of $26.7 million. During the six months ended June 30, 2003, we used $7.0 million of cash for operating activities. While we implemented measures during the six months ended June 30, 2003 to reduce the amount of cash used in our operating activities, our cash usage rate could increase in future periods as we continue our ADVEXIN therapy clinical trials, prepare regulatory documentation for product application submissions to the FDA and conduct our research and development of various other technologies,. Currently, we earn revenue 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. We may 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 have been registered on a registration statement on Form S-3, effective August 7, 2003 (Commission File No. 333-107028).

**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 and Cash Equivalents.* Our cash and cash equivalents 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 becomes impaired or the investment is downgraded.

*Research and Development Costs.* In conducting our clinical trials of ADVEXIN therapy and other product candidates, we procure services from numerous third-party vendors. The cost of these services constitutes a significant portion of the cost of these trials and of our research and development 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

Table of Contents

forth in our contracts with these vendors, the period of time over which the vendor will render the services and the rate of enrollment of patients in our clinical trials. Using these estimates, we record expenses and accrued liabilities in each accounting period that we believe fairly represent our obligations to these vendors. Actual results could differ from these estimates, resulting in increases or decreases in the amount of expense recorded and the related accrual.

**Results of Operations**

**Comparison of the Quarters Ended June 30, 2003 and June 30, 2002**

**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 earn contract research services revenue from Aventis Pharmaceuticals Products, Inc., one of our stockholders, under an agreement through which Aventis provides 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 $143,000 for the quarter ended June 30, 2003, compared to $322,000 for the quarter ended June 30, 2002, a decrease of 56%. This decrease was primarily due to a decline in the level of our contract manufacturing activity due to the completion of work under services agreements with certain third parties subsequent to June 30, 2002.

**Costs and Expenses**

*Research and Development.* Research and development expenses, excluding compensation related to the issuance of stock options of $58,000 for the quarter ended June 30, 2003 and $107,000 for the quarter ended June 30, 2002, were $2.9 million for the quarter ended June 30, 2003, compared to $5.7 million for the quarter ended March 31, 2002, a decrease of 49%. This decrease was primarily due to cost control programs implemented during the first quarter of 2003 to reduce the rate at which we use cash for operations.

*General and Administrative.* General and administrative expenses, excluding compensation related to the issuance of stock options of $692,000 for the quarter ended June 30, 2003 and $244,000 for the quarter ended June 30, 2002, were $1.1 million for the quarter ended June 30, 2003, compared to $1.4 million for the quarter ended June 30, 2002, a decrease of 21%. This decrease was primarily due to cost control programs implemented during the first quarter of 2003 to reduce the rate at which we use cash for operations.

*Compensation Related to the Issuance of Stock Options.* Compensation related to the issuance of stock options was $750,000 for the quarter ended June 30, 2003, compared with $351,000 for the quarter ended June 30, 2002, an increase of 114%. This increase was due to stock options granted in June 2003 to (1) certain members of our Board of Directors for which some of the options have exercise prices below the market value of our common stock at the date of grant and were fully vested upon issuance, and (2) our corporate secretary, who is not a director or employee and for whom options grants are subject to fair value accounting. This increase was offset by a lower expense related to stock options granted in previous periods as deferred compensation related to those options became fully amortized. The amount of 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 or are issued to individuals or entities other than employees or directors and 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 Expenses and Other Income**

Interest income was $475,000 for the quarter ended June 30, 2003, compared to $166,000 for the quarter ended June 30, 2002, an increase of 186%. 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, which decreased 70% from the amount for the quarter ended June 30, 2002, due to our lower average cash and cash equivalents balances during 2003 and declining interest rates.

Interest expense was $161,000 for the quarter ended June 30, 2003, compared with $203,000 for the quarter ended June 30, 2002, a decrease of 21%. This decrease was due to lower principal amounts upon which interest was incurred in 2003 compared to 2002 as a result of continuing debt service payments on notes payable and capital lease obligations.

Other income was $254,000 for the quarter ended June 30, 2003, compared to $332,000 for the quarter ended June 30, 2002, a