CYTOGEN CORP
Form 10-K
March 16, 2006
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-K

FOR ANNUAL AND TRANSITION REPORTS

PURSUANT TO SECTIONS 13 OR 15(d) OF THE

SECURITIES EXCHANGE ACT OF 1934

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2005

OR

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to _____

Commission File Number 000-14879

CYTOGEN CORPORATION

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**22-2322400**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
650 College Road East, Suite 3100 Princeton, New Jersey	**08540**

(Address of Principal Executive Offices) **(Zip Code)**

Registrant s telephone number, including area code: (609) 750-8200

Securities registered pursuant to Section 12(b) of the Act: None

Securities registered pursuant to Section 12(g) of the Act:

Common Stock, $0.01 par value per share

(Title of Class)

Preferred Stock Purchase Rights, $0.01 par value per share

(Title of Class)

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x

Indicate by check mark whether the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

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 ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer.

Large Accelerated Filer ¨ Accelerated Filer x Non- Accelerated Filer ¨

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

The aggregate market value of the registrant s voting shares of Common Stock held by non-affiliates of the registrant on June 30, 2005, based on $5.23 per share, the last reported sale price on the NASDAQ National Market on that date, was $72,623,393.

The number of shares of Common Stock, $.01 par value, of the registrant outstanding as of March 1, 2006 was 22,473,762 shares.

The following documents are incorporated by reference into this Annual Report on Form 10-K: Portions of the registrant s definitive Proxy Statement for its 2006 Annual Meeting of Stockholders are incorporated by reference into Part III hereof.

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PART I

Item 1. Business

OVERVIEW

Founded in 1980, Cytogen Corporation of Princeton, NJ is a biopharmaceutical company dedicated to improving the lives of patients with cancer by acquiring, developing and commercializing innovative molecules targeting the sites and stages of cancer progression. Our marketed products include QUADRAMET® (samarium Sm-153 lexidronam injection) and PROSTASCINT® (capromab pendetide) kit for the preparation of Indium In-111 capromab pendetide in the United States. We also have exclusive United States marketing rights to COMBIDEX® (ferumoxtran-10) for all applications, and the exclusive right to market and sell ferumoxytol (formerly Code 7228) for oncology applications in the United States. We are also developing therapeutics targeting prostate-specific membrane antigen (PSMA), a protein highly expressed on the surface of prostate cancer cells and the neovasculature of solid tumors.

In February 2006, we executed a binding letter of intent with Savient Pharmaceuticals, Inc. to negotiate a definitive agreement granting us exclusive marketing rights for SOLTAMOX (tamoxifen citrate) in the United States. SOLTAMOX is an oral liquid hormonal therapy approved for marketing in the United States. Consummation of the transaction is subject to a number of conditions, including satisfactory completion of due diligence by us and negotiation and execution of definitive licensing and supply agreements.

Our proprietary and licensed products, product candidates and technologies are as follows:

Marketed Products:

Product	Description	Status
QUADRAMET (samarium Sm-153 lexidronam injection)	Targeted oncology product indicated for the relief of pain due to metastatic bone disease arising from prostate, breast, multiple myeloma and other types of cancer	Developed by Cytogen based upon technology licensed from The Dow Chemical Company Marketed in the United States by Cytogen as of August 1, 2003, and previously by Berlex Laboratories from May 1999 until July 2003
PROSTASCINT (capromab pendetide) kit for the preparation of Indium In-111 capromab pendetide	The first and only commercial monoclonal antibody-based agent targeting prostate-specific membrane antigen (PSMA) to image the extent and spread of prostate cancer	Developed and marketed by Cytogen in the United States

Product Candidates and Pipeline:

Product	Description	Status
SOLTAMOX	The first oral liquid hormonal therapy for the treatment of breast cancer in adjuvant and metastatic settings and to reduce the risk of breast cancer in women with ductal carcinoma *in situ* or with high risk of breast cancer	Developed by Savient Pharmaceuticals, Inc. Letter of intent executed for exclusive license to Cytogen for marketing in the United States

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Product	Description	Status
COMBIDEX (ferumoxtran-10)	Investigational functional molecular imaging agent consisting of iron oxide nanoparticles used in conjunction with magnetic resonance imaging to aid in the differentiation of cancerous from normal lymph nodes	Developed by Advanced Magnetics, Inc. and exclusively licensed by Cytogen for marketing in the United States
		Under review by FDA
		Received an approvable letter in June 2000; On March 3, 2005, FDA advisory committee voted to not recommend approval of proposed broad indication; Received an approvable letter on March 24, 2005, subject to certain conditions
Therapeutic 7E11-C5 monoclonal antibody	Targeted oncology product in which proprietary MeO-DOTA bifunctional chelant technology will be used to radiolabel Cytogen s PSMA targeting 7E11-C5 antibody with Lu-177	Phase I
		Developed by Cytogen using bifunctional chelant technology licensed from The Dow Chemical Company
rs-PSMA protein vaccine	An *in vivo* vaccine consisting of recombinant soluble PSMA combined with an immune stimulant to induce an immune response	Phase I trial completed*
PSMA viral vector vaccine	An *in vivo* vaccine that utilizes viral vectors designed to deliver the PSMA gene to immune system cells in order to generate potent and specific immune response	Preclinical*
PSMA monoclonal antibodies	Novel fully-human monoclonal antibodies that bind to the three-dimensional structure of PSMA as presented on cancer cells, initially being pursued for toxin-linked approaches	Preclinical*

* Jointly developed with Progenics Pharmaceuticals, Inc. via our joint venture, PSMA Development Company LLC

We market QUADRAMET and PROSTASCINT in the United States through our staff of in-house specialty sales, technical and marketing representatives, directly to medical oncologists, radiation oncologists, nuclear medicine physicians, radiologists and urologists.

We were incorporated in Delaware on March 3, 1980 under the name Hybridex, Inc. and changed our name to Cytogen Corporation on April 1, 1980. Our executive offices are located at 650 College Road East, Suite 3100, Princeton, New Jersey, 08540 and our telephone number is 609-750-8200.

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QUADRAMET®, PROSTASCINT® and ONCOSCINT® are registered United States trademarks of Cytogen Corporation. All other trade names, trademarks or servicemarks appearing in this Annual Report on Form 10-K are the property of their respective owners, and not the property of Cytogen Corporation or any of our subsidiaries.

We also maintain a website at www.cytogen.com, which is not a part of this Annual Report on Form 10-K. References to our website in this Annual Report on Form 10-K are intended as an inactive textual reference only. We provide an internet link on our website to the documents that we file with the Securities and Exchange Commission s website, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to such reports filed pursuant to Section 13(a) or 15(d) of the Exchange Act. These documents are posted as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Alternatively, we will provide electronic or paper copies of our filings free of charge upon request.

MARKETED PRODUCTS AND PRODUCT CANDIDATES PENDING APPROVAL

THERAPEUTICS

QUADRAMET

Overview

QUADRAMET is an oncology product that pairs the targeting ability of a small molecule, bone-seeking phosphonate (EDTMP) with the therapeutic potential of radiation (samarium Sm-153). QUADRAMET is prescribed as a pain therapy for patients when cancer has spread to the bone. The skeleton is one of the most common organs to be affected by metastatic cancer. Skeletal invasion by prostate, breast, multiple myeloma, and other cancers often creates an imbalance between the normal process of bone destruction and formation. QUADRAMET selectively targets such sites of imbalance, thereby delivering radioactivity directly to areas of the skeleton that have been invaded by metastatic tumor.

QUADRAMET has demonstrated a range of characteristics that may be advantageous for the treatment of pain arising from metastatic bone disease. In clinical trials, QUADRAMET demonstrated significant reductions in pain scores compared with placebo. Patients may experience pain relief within the first week lasting a median of 16 weeks, with maximal relief generally occurring at three to four weeks after injection. Patients who experience a reduction in pain may be encouraged to decrease their use of opioid analgesics.

QUADRAMET is indicated for the relief of pain in patients with confirmed osteoblastic metastatic bone lesions that enhance on a radionuclide bone scan.

Further Clinical Development Related to QUADRAMET

We believe the unique combination of nuclear, chemical, and biologic properties that QUADRAMET possesses makes it an attractive candidate for the addition of a skeletal targeted therapeutic component to a number of systemic therapies currently utilized in the treatment of patients with cancers originating in, or metastasizing to, bone. We believe that future QUADRAMET growth is, in part, dependent upon:

- distinguishing the physical properties of QUADRAMET from earlier generation agents within its class;
- empowering and marketing to key prescribing audiences;
- broadening palliative use within label beyond prostate cancer to include breast, lung and multiple myeloma;
- evaluating the role of QUADRAMET in contemporary oncology settings with other commonly used therapeutics, including chemotherapeutics, bisphosphonates, and others; and

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expanding clinical development to demonstrate the potential tumoricidal versus palliative attributes of QUADRAMET.

Our products, including QUADRAMET, are subject to significant regulation by governmental agencies, including the FDA, as is more fully described under the section entitled Government Regulation herein. We cannot assure you that we will be able to complete any of our market expansion strategies set forth above.

The following studies are designed to evaluate QUADRAMET s potential role as a cancer therapeutic through various synergistic combinations:

Multiple Myeloma:

A Phase I/II study at the Mayo Clinic in Rochester, Minnesota is evaluating the potential benefits of QUADRAMET in combination with bortezomib (VELCADE®, Millenium Pharmaceuticals, Inc.) for the treatment of multiple myeloma. The first patient was dosed in November 2005.

A Phase I study at various sites is evaluating the potential benefits of QUADRAMET in combination with bortezomib for the treatment of multiple myeloma. The first patient was dosed in December 2005.

A Phase I study at the Mayo Clinic in Rochester, Minnesota is evaluating the use of QUADRAMET in combination with bisphosphonates for the treatment of pain associated with metastatic bone disease in patients with recurrent or refractory multiple myeloma. The escalating dose clinical study will evaluate both the safety profile and effects on painful symptoms and analgesic use. In addition, preliminary information regarding the effect of QUADRAMET on the underlying disease will be determined by monitoring levels of M-protein, a marker for multiple myeloma activity. The first patient was dosed in June 2005.

Osteosarcoma:

Two Phase I/II studies at Johns Hopkins Kimmel Cancer Center in Baltimore are evaluating the use of QUADRAMET in the adjuvant treatment of moderate and high-risk osteogenic sarcoma. The moderate risk study is investigating the maximum dose of QUADRAMET in this clinical setting that will result in marrow recovery in a time frame that does not significantly delay further treatment. The high risk study is investigating the use of both an adjuvant dose as well as a subsequent high dose in which patients may receive a stem cell transplant to help overcome the toxicities related to irradiation of the bone marrow.

Additional studies are currently under development to evaluate the use of QUADRAMET in combination with cytotoxic therapy for the treatment of osteogenic sarcoma.

Breast Cancer:

Multi-site Phased I/II studies are currently under development to evaluate the use of QUADRAMET in combination with both cytotoxic and hormonal therapies for the treatment of breast cancer.

Prostate Cancer:

A Phase II study by independent investigators at Umea University in Sweden was recently completed to evaluate the potential benefits of treatments of QUADRAMET in combination with monthly dosing of docetaxel for the treatment of metastatic bone disease arising from prostate cancer. The clinical study evaluated the safety profile and preliminary incidence and duration of the clinical benefits. Results of the study were reported at the 2006 Prostate Cancer Symposium.

A Phase II study by independent investigators at Institut Gustave Roussy and Institut Curie in France is ongoing to evaluate the potential benefits of a maintenance regimen consisting of QUADRAMET in combination with weekly dosing of docetaxel following induction therapy with monthly dosing of docetaxel for the treatment of metastatic bone disease arising from prostate cancer. The primary endpoint of this study is progression-free survival. Preliminary results of the study were reported at the 2006 Prostate Cancer Symposium.

A Phase I/II study at the Memorial Sloan-Kettering Cancer Center in New York is evaluating the potential benefits of treatments of QUADRAMET in combination with monthly dosing of docetaxel

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for the treatment of metastatic bone disease arising from prostate cancer. The clinical study will evaluate the safety profile and preliminary incidence and duration of the clinical benefits. The first patient was dosed in July 2005.

A Phase I/II study at The University of Texas M. D. Anderson Cancer Center in Houston is evaluating the potential benefits of treatments including multiple doses of QUADRAMET in combination with weekly dosing of docetaxel in patients whose cancer has progressed after receiving hormonal therapy. The clinical study will evaluate the safety profile and preliminary incidence and duration of the clinical benefits. The first patient was dosed in November 2004.

A Phase I study at Johns Hopkins Kimmel Cancer Center in Baltimore is investigating the use of QUADRAMET in combination with monthly dosing of docetaxel for the treatment of metastatic bone disease arising from prostate cancer. The clinical study will evaluate the safety profile and preliminary incidence and duration of the clinical benefits of novel escalating dose and administration schedules of docetaxel in combination with multiple doses of QUADRAMET in hormone refractory prostate cancer patients. The first patient was dosed in May 2005.

A Phase I study at Northwestern University in Illinois is investigating the use of QUADRAMET and paclitaxel (Taxol®, Bristol-Myers Squibb Company) in hormone refractory prostate cancer patients was recently completed. The study utilized escalating single doses of QUADRAMET in combination with paclitaxel and estramustine phosphate sodium in order to evaluate the dose level at which dose limiting toxicity is obtained. Preliminary results from the study were presented at the 2004 American Society of Clinical Oncology (ASCO) Annual Meeting.

A Phase I study at Thomas Jefferson University in Philadelphia is investigating escalating single doses of QUADRAMET combined with ongoing hormonal therapy prior to external beam radiation therapy in men with high risk clinically localized prostate cancer. The objectives of this study are to assess the safety of QUADRAMET and determine the maximum tolerated dose of QUADRAMET in this clinical setting. The goal of this type of therapy is to prevent or delay the progression of metastatic disease in bone.

Two Phase I/II studies at the University of Maryland in Baltimore are evaluating the potential benefits of combination treatments including QUADRAMET and zoledronic acid (Zometa®, Novartis AG) in patients with advanced prostate cancer. One study involves patients who are chemotherapy naïve while the other involves patients who have previously received chemotherapy.

In addition to these clinical studies, in November 2004 we also announced the initiation of our National Bone Pain Registry for QUADRAMET. Data regarding both the use of QUADRAMET and best practices in bone pain management will be collected from approximately 185 patients. Results of this initiative are expected to be presented following analysis of the data in 2006.

During 2005, we reported that clinical investigators from cancer research centers around the world presented new clinical data regarding QUADRAMET as follows:

Researchers from the Mayo Clinic reported data from studies involving the use of QUADRAMET both as a monotherapy and in combination with bortezomib (VELCADE®, Millennium Pharmaceuticals, Inc.), a proteasome inhibitor for the treatment of multiple myeloma. In this preclinical study, QUADRAMET demonstrated broad and synergistic activity when administered in combination with bortezomib in a murine myeloma model. This anticancer activity was characterized by significantly prolonged median survival, rapidly reduced clonogenicity of bone-marrow resident 5TGM1 cells, slowed elevation of serum myeloma-associated paraprotein levels, and longer term preservation of bone mineral density. Results from the preclinical study were reported at the 2005 American Society of Hematology (ASH) Annual Meeting and subsequently published as a First Edition Paper in the peer-reviewed journal *Blood* (2005-09-3870).

Clinical investigators reported data from studies involving the use of QUADRAMET in combination with gemcitabine (Gemzar®, Eli Lilly), a nucleoside analog which is known to be a radiation sensitizer. The majority of patients with advanced stage disease who were treated with this combination regimen demonstrated an improvement on imaging studies. The study was conducted by

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independent investigators who evaluated the use of high dose QUADRAMET in conjunction with gemcitabine for the treatment of osteosarcoma. The lead investigator was Peter Anderson, M.D., Ph.D., a Pediatric Oncologist who performed the work at the Mayo Clinic and is now at The University of Texas MD Anderson Cancer Center. Results from the study were reported at the 2005 ASCO Annual Meeting and subsequently published in the peer-reviewed journal *Clinical Cancer Research* (Volume 11(19): pages 6895-6900).

Independent clinical investigators reported data from a phase II study of QUADRAMET in combination with docetaxel (Taxotere®, Aventis Pharmaceuticals, a member of the sanofi-aventis Group) for the treatment of patients with hormone refractory prostate cancer. The phase II study was designed to evaluate the toxicity and efficacy of QUADRAMET in combination with docetaxel in 29 patients with progressive hormone refractory prostate cancer. Mean PSA level at baseline was 838 ng/mL (range 15 to 2330 ng/mL). Docetaxel was administered as a 30-minute infusion at a dose of 30 mg/m2 weekly for 5 weeks. Eighteen to twenty-four hours prior to the fourth administration of docetaxel, the approved palliative dose of QUADRAMET (1 mCi/kg) was injected. Patients received a second cycle of the combination regimen at PSA and/or clinical progression. According to the results of the study, within 12 weeks after start of the first cycle, PSA declines greater than 50% and 75% were seen in 34% and 21% of the patients, respectively. The time from start of the regimen until PSA declines greater than 50% and 75% was 38 and 34 days, respectively. PSA progression was seen in 69% of the patients, with a median time to PSA progression of 126 days. Following the first cycle of therapy, grade 3 or 4 neutropenia was seen in four patients at week three and six, respectively, after QUADRAMET administration. One patient had grade 2 thrombocytopenia five weeks after QUADRAMET and there were no occurrences of grade 3 or 4 toxicity. 17 patients opted to receive the second cycle of treatment, with a median interval between the beginning of the first and second treatment cycles of six months. The mean PSA level for these patients was 880 ng/mL (range 23 to 4773 ng/mL). After the second cycle, PSA declines greater than 50% and 75% were seen in 18% and 6% of patients. The time from start of the second cycle until PSA declines greater than 50% and 75% was 40 and 34 days, respectively. PSA progression was seen in 65% of the patients, with a median time to PSA progression of 151 days. The incidence of grade 3 or 4 hematological toxicity was only slightly increased after the second cycle. The results were presented at the 12th Annual Prostate Cancer Foundation Scientific Retreat held in Phoenix, AZ and the 2006 Prostate Cancer Symposium held in San Francisco, CA. The lead investigator was Anders Widmark, M.D., Ph.D., a Professor in the Department of Oncology at Umea University in Sweden.

Clinical investigators reported data from a study involving the use of a single dose of QUADRAMET as a tumoricidal agent. Of 28 patients with biopsy proven prostate cancer and multiple lesions on bone scan, 20 were evaluable with adequate follow-up data. Patients received the approved palliative dose (1.0 mCi/kg) of QUADRAMET, and blood tests were performed at baseline and post-treatment with a mean follow-up of 5.2 weeks. Of the patients studied, 2 had mild (less than 20 lesions), 7 had moderate (20 to 40 lesions), and 11 had severe (more than 40 lesions) disease on bone scan. Patients were divided into groups according to their response to treatment, which were determined by changes in PSA levels. The authors concluded that QUADRAMET appears to exhibit tumoricidal activity after a single dose as measured by a reduction of stabilization of PSA levels in 11 out of the 20 patients (55%) that may be attributed to a direct effect of the radiopharmaceutical on malignant cells. Mild and transient myelosuppression was seen in all patients. The results were presented at the 2005 Society of Nuclear Medicine Annual Meeting. The lead investigator was Aldo Serafini, M.D., Professor of Radiology at the University of Miami School of Medicine.

Independent clinical investigators reported data from a study involving the use of QUADRAMET alone compared to QUADRAMET plus chemotherapy in the treatment of painful bone metastases from lung cancer. 110 patients with non-surgically treated lung cancer, comprised of non-small cell lung cancer (NSCLC, n=103) or small cell lung cancer (SCLC, n=7), were entered into the study. Patients were randomized into 3 groups: QUADRAMET alone (n=37), QUADRAMET followed by chemotherapy after 3 days (n=42), and chemotherapy followed by QUADRAMET one month later (GROUP C, n=31). The patients with NSCLC received mitomycin C, vincristine, and cisplatin, while patients with SCLC received lomustine, methotrexate, and cyclophosphamide. All patients received the

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standard palliative dose (1 mCi/kg) of QUADRAMET. 89%-93% of patients across treatment groups experienced either complete or partial relief of pain while those receiving combination therapy also experienced significant improvements on bone scan and in the proportion of patients surviving greater than 18 months. The results were presented at the 2005 Society of Nuclear Medicine Annual Meeting.

Independent clinical investigators reported data from a study evaluating the measurement of QUADRAMET skeletal retention with whole-body scintigraphy and to analyze the relationship between skeletal retention and therapeutic effect. 66 patients with painful metastatic bone disease from prostate (n=15), lung (n=20), breast (n=18), colon (n=2), kidney (n=2), and other cancers (n=9) were examined with whole-body scintigraphy at both 10 minutes and 5 hours following administration of QUADRAMET. Patients were categorized into 3 groups: (1) complete response (CR) group indicated by more than 2 sites of bone metastases disappearing, Karnofsky Performance Score (KPS) improving by more than 20 points, and moderate or complete remission of bone pain at day 7 post injection of QUADRAMET, (2) partial response (PR) group indicated by 1-2 sites of bone metastases disappearing, KPS improving by 10-20 points, and moderate remission of bone pain in week 3, or (3) non-response (NR) group indicated by no disappearance or shrinkage of metastases, KPS increasing less than 10 points, and no or slight remission of bone pain. The range of skeletal retention in 66 patients was 31.9% to 86.6% (mean=56.0%). Statistical analysis demonstrated a significant difference between both CR group and PR group (p=0.001) and PR group and NR group (p=0.001). The results indicated that higher skeletal retentions were associated with better therapeutic effect. The results were presented at the 2005 Society of Nuclear Medicine Annual Meeting.

The foregoing discussion describes investigational clinical applications that differ from that reported in the QUADRAMET package insert, and that have not been reviewed or approved by FDA. QUADRAMET is indicated for the relief of pain in patients with confirmed osteoblastic metastatic bone lesions that enhance on a radionuclide bone scan. A copy of the full prescribing information for QUADRAMET may be obtained in the United States from us by calling us toll free at 800-833-3533 or by visiting our web site at www.cytogen.com, which is not part of this Annual Report on Form 10-K. We are sponsoring or supporting the clinical investigations described in the foregoing discussion to explore potential new indications for the use of QUADRAMET.

QUADRAMET causes bone marrow suppression. In clinical trials, white blood cell counts and platelet counts decreased to a nadir of approximately 40% to 50% of baseline in 123 (95%) of patients within 3 to 5 weeks after QUADRAMET, and tended to return to pretreatment levels by 8 weeks. Because of the unknown potential for additive effects on bone marrow, QUADRAMET should not be given concurrently with chemotherapy or external beam radiation therapy unless the clinical benefits outweigh the risks. Blood counts should be monitored weekly for at least 8 weeks, or until recovery of adequate bone marrow function. Non-hematologic adverse events that occurred in 5% or more of patients and greater than placebo were plain flare (7%), diarrhea (6%), infection (7%), spinal cord compression (6.5%), arrhythmias (5%), and hematuria (5%). Patients who receive QUADRAMET should be advised that for several hours following administration, radioactivity will be present in excreted urine. To help protect themselves and others in their environment, precautions need to be taken for 12 hours following administration.

Intellectual Property Position Related to QUADRAMET

In May 1993, we obtained an exclusive license from The Dow Chemical Company to use QUADRAMET, in North America, as a therapeutic radiopharmaceutical for metabolic bone disease or tumor regression for cancer caused by metastatic or primary cancer in bone in humans, and for the treatment of disease characterized by osteoblastic response in humans. Our license was expanded to include Latin America in 1995, and will remain in effect, unless earlier terminated, for a period of 20 years from May 30, 1993 or until the last to expire of the related patents. We currently anticipate such termination date to be May 30, 2013.

Under our agreement with Dow, we are the licensee of five issued United States patents and certain corresponding foreign patents. Dow is responsible, at its own cost and expense, for prosecuting and maintaining any patents or patent applications included in our agreement. One of these, U.S. Pat. No. 4,898,724, includes claims directed to the QUADRAMET product and methods for its use in the treatment of calcific tumors and bone pain. We

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have obtained an extension of the term of this U.S. patent, which will now expire March 28, 2011. Other patents licensed to us under this agreement are: (i) U.S. Pat. No. 4,897,254, which expires on January 30, 2007; (ii) U.S. Pat. No. 4,937,333, which expires August 4, 2009; (iii) U.S. Pat. No. 5,300,279, which expires on November 19, 2008; and (iv) U.S. Pat. No. 5,066,478 which expires on November 19, 2008. Additional patents have been issued, including U.S. Pat. No. 5,714,604, which expires on February 3, 2015, and U.S. Pat. No. 5,762,907, which expires November 21, 2006, which include claims directed to the QUADRAMET product, methods for its manufacture, and methods for its preparation and administration. We are the owner of a registered United States trademark relating to QUADRAMET.

Upon execution of our agreement with Dow, we issued warrants to Dow to purchase shares of our common stock, which have since expired. As of December 31, 2005, we have paid an aggregate of $5.2 million to Dow in milestone payments. We remain obligated to pay Dow additional milestone payments as, and if, our sales of QUADRAMET increase and royalties, which are subject to certain minimum amounts, based on future sales of QUADRAMET.

Manufacturing, Supply and Distribution of QUADRAMET

QUADRAMET is manufactured by Bristol-Myers Squibb Medical Imaging, Inc. (BMS-MI), pursuant to the terms of a manufacturing and supply agreement with us which became effective on January 1, 2004. Under this agreement, BMS-MI has agreed to manufacture, supply and distribute QUADRAMET for us in exchange for a current minimum payment of at least $4.7 million annually, subject to future annual price adjustment, through 2008. The agreement will then renew for five successive one year periods. The agreement is terminable by either us or BMS-MI, at any time, upon two years notice to the other. We also pay BMS-MI a variable amount per month for each order placed to cover the costs of customer service.

The two primary components of QUADRAMET, particularly Samarium-153 and EDTMP, are provided to BMS-MI by outside suppliers. BMS-MI obtains its supply of Samarium-153 from a sole supplier, and EDTMP from another sole supplier. Alternative sources for these components may not be readily available, and any alternate suppliers would have to be identified and qualified, subject to all applicable regulatory guidelines. If BMS-MI cannot obtain sufficient quantities of these components on commercially reasonable terms, or in a timely manner, it would be unable to manufacture QUADRAMET on a timely and cost-effective basis. Additionally, QUADRAMET must be manufactured in compliance with regulatory requirements. Any inability on the part of BMS-MI to manufacture QUADRAMET, or any failure by BMS-MI to comply with all applicable regulatory guidelines, including FDA requirements, and those of the U.S. Nuclear Regulatory Commission, could have a material adverse effect on our business, financial condition and results of operations.

Marketing of QUADRAMET

We market QUADRAMET using our in-house specialty sales force to medical oncologists, radiation oncologists, and nuclear medicine physicist.

In October 1998, we entered into an exclusive agreement with Berlex pursuant to which Berlex would market QUADRAMET for us in the United States. Berlex re-launched QUADRAMET in March 1999, and maintained a sales force that targeted its sales efforts on the oncological community. Pursuant to our agreement with Berlex, we received an upfront payment of $8.0 million and royalty payments based on net sales of QUADRAMET and potential milestone payments based upon sales levels that were achieved. Berlex also received warrants to purchase shares of our common stock.

In June 2003, we entered into an agreement with Berlex to reacquire marketing rights to QUADRAMET in North America and Latin America in exchange for an upfront payment of $8.0 million and royalties based on future sales of QUADRAMET, subject to our receipt of necessary financing for the reacquisition. On August 1, 2003, we reacquired these marketing rights and began recording product revenue from our sales of QUADRAMET. We no longer receive royalty revenue from Berlex.

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Dow is the owner of the technology upon which we developed QUADRAMET. As such, under our license agreement with Dow, we are required to pay Dow royalties or guaranteed contractual minimum payments, whichever is greater, and certain future payments upon the achievement of certain milestones.

Competition Related to QUADRAMET

Current competitive treatments for bone cancer pain include narcotic analgesics, external beam radiation therapy, bisphosphonates, and other skeletal targeting therapeutic radiopharmaceuticals such as Strontium-89 chloride.

QUADRAMET primarily competes with Strontium-89 chloride in the radiopharmaceutical pain palliation market. Strontium-89 chloride is manufactured and marketed either as Metastron®, by GE Healthcare, or in a generic form by Bio-Nucleonics Pharma, Inc. GE Healthcare manufactures Metastron and sells the product through its wholly owned network of radiopharmacies, direct to end-users and through other radiopharmacy distributors. The generic version is distributed directly by the manufacturer, or is sold through radiopharmacy distributors such as Cardinal Health and AnazaoHealth (formerly Custom Care Pharmacy).

To meet future competitive challenges to QUADRAMET, we continue to, among other things, focus our efforts on managing radiopharmacy distributor relationships. We also plan to continue to focus on research supporting additional applications and by documenting the safe and effective use of QUADRAMET when used in conjunction with metastatic disease therapies such as bisphosphonates, chemotherapeutics and hormonal therapy.

SOLTAMOX

Overview

SOLTAMOX (tamoxifen citrate), which was developed by Savient Pharmaceuticals, Inc., received U.S. regulatory approval in October 2005.

On February 8, 2006, Savient and Cytogen announced the execution of a binding letter of intent to negotiate a definitive agreement granting Cytogen exclusive marketing rights for SOLTAMOX in the United States. We cannot market and sell SOLTAMOX until we reach agreement with Savient on definitive licensing and supply agreements. We cannot assure you that we will reach agreement on such agreements on a timely basis, or at all.

Under the terms of the letter of intent, we have agreed to pay Savient, upon closing of the transaction, an upfront licensing fee of $2 million and additional contingent sales-based milestone payments of up to a total of $4 million. Savient will also receive royalties on net sales of SOLTAMOX. Consummation of the transaction, which has been approved by the boards of directors of both companies, is subject to a number of conditions, including satisfactory completion of due diligence by Cytogen and negotiation and execution of definitive licensing and supply agreements by Cytogen, Savient and Rosemont, Savient s wholly owned subsidiary. The parties expect the transaction to close by March 30, 2006.

SOLTAMOX, a cytostatic estrogen receptor antagonist, is the first oral liquid hormonal therapy approved in the U.S. It is indicated for the treatment of breast cancer in adjuvant and metastatic settings and to reduce the risk of breast cancer in women with ductal carcinoma *in situ* (DCIS) or with high risk of breast cancer. Dysphagia (difficulty in swallowing) in women suffering from breast cancer can arise from several causes, including patients receiving combination chemotherapy and/or radiation therapy for metastatic breast cancer. It may also arise from either esophageal or stomach metastasis. Irrespective of the cause, many women with dysphagia are unable to tolerate the solid oral dosage forms of hormonal therapy and might benefit from a liquid dosage form, such as SOLTAMOX. The availability of an oral liquid dosing option could allow more women to benefit from hormonal treatment for estrogen receptor positive breast cancer.

Use of SOLTAMOX in a risk reduction setting (women at high risk for cancer and women with DCIS) has shown to cause cancer of the uterus, stroke, and blood clots. The benefits of SOLTAMOX outweigh its risks in women already diagnosed with breast cancer. SOLTAMOX should not be used in women who require concomitant use of coumarin-type anticoagulant, or in women with history of deep vein thrombosis or pulmonary embolus.

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Women who are pregnant or plan to become pregnant should not take SOLTAMOX. Cataracts and cataract surgery can also occur more frequently with SOLTAMOX. The most frequently reported adverse reactions with SOLTAMOX were hot flashes and vaginal discharge.

Intellectual Property Position Related to SOLTAMOX

If we consummate the exclusive license from Savient, we will be the licensee of an issued United States patent covering SOLTAMOX. This patent, U.S. Pat. No. 6,127,425 which includes claims directed to the SOLTAMOX product and manufacturing process, expires in June 2018.

Manufacturing, Supply and Distribution of SOLTAMOX

If we consummate the exclusive license from Savient, we will enter into a supply agreement with Rosemont Pharmaceuticals Ltd., a wholly owned subsidiary of Savient, for the manufacture and supply of SOLTAMOX.

Competition Related to SOLTAMOX

The current competitive treatments for SOLTAMOX include the tablet form of tamoxifen citrate, a generic drug, and a class of drugs known as aromatase inhibitors.

Marketing of SOLTAMOX

We intend to market SOLTAMOX primarily using our in-house specialty sales force.

MOLECULAR IMAGING PRODUCTS

PROSTASCINT

Overview

Our PROSTASCINT molecular imaging agent is the first, and currently the only, commercial product targeting PSMA, a transmembrane protein that is expressed on prostate cancer cells at all stages of disease, including advanced or metastatic disease. PROSTASCINT consists of a murine monoclonal antibody (7E11-C5) directed against PSMA that is linked to the radioisotope Indium-111. A radioisotope is an element which, because of nuclear instability, undergoes radioactive decay and emits radiation. Due to the selective expression of PSMA by prostate cancer cells, PROSTASCINT can image the extent and spread of prostate cancer using a common gamma camera.

PROSTASCINT is approved for marketing in the United States in two clinical settings: (i) as a diagnostic imaging agent in newly diagnosed patients with biopsy-proven prostate cancer thought to be clinically localized after standard diagnostic evaluation and who are at high risk for spread of their disease to pelvic lymph nodes; and (ii) for use in post-prostatectomy patients with a rising PSA and a negative or equivocal standard metastatic evaluation in whom there is a high clinical suspicion of occult metastatic disease.

During the molecular imaging procedure, PROSTASCINT is administered intravenously into the patient. The 7E11 antibody in PROSTASCINT travels through the bloodstream and binds to PSMA. The radioactivity from the isotope that has been attached to the antibody can be detected from outside the body by a gamma camera. Gamma cameras are found in the nuclear medicine departments of most hospitals. The image captured by the camera assists in the identification of the location of the radiolabeled pharmaceutical thus identifying the sites of tumors.

When deciding on a course of therapy for newly diagnosed prostate cancer, physicians must determine the extent of disease in the patient. Patients are most likely to benefit from local treatment options, such as surgical removal of the prostate gland, when disease has not spread beyond the prostate gland. Patients diagnosed with

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distant disease (not confined to the prostate gland) have a poorer chance of five-year survival than those with disease confined to the gland and require systemic therapy.

Prior to the availability of PROSTASCINT, determining whether newly diagnosed disease was limited to the prostate or had spread beyond the gland, for instance to lymph nodes, was based upon statistical inference from the biopsy appearance of the tumor, the patient s level of serum PSA, and the stage of other primary tumors. Conventional imaging methods such as computed tomography (CT) or magnetic resonance (MR) are all relatively insensitive because they rely on identifying significant changes to normal anatomic structure to indicate the presence of disease. PROSTASCINT images are based upon expression of the PSMA molecule and, therefore, may identify disease not readily detectable with conventional procedures, such as CT or MR imaging alone. Clinical studies conducted to date by physicians on our behalf indicate that PROSTASCINT may provide new and useful information not available from other conventional diagnostic modalities regarding the existence, location and extent of a specific disease throughout the body.

In addition, in the United States, following initial therapy, prostate cancer patients are monitored to ascertain changes in the level of serum PSA. In this setting, a consistent rise in PSA is evidence of recurrence of the patient s prostate cancer. Knowledge of the extent and location of disease recurrence is important in choosing the most appropriate form of treatment.

Partners In Excellence Sites

PROSTASCINT is a technique-dependent product that requires a high degree of proficiency in nuclear imaging technology in order to correctly obtain and interpret the scan. We have established a network of accredited nuclear medicine imaging centers through our Partners In Excellence, or PIE, program. Since PROSTASCINT images are traditionally difficult to interpret, due to inherent limitations of nuclear medicine imaging as opposed to product performance, each PIE site receives initial training and proficiency evaluations. We only sell PROSTASCINT to qualified PIE sites. As of December 31, 2005, there were approximately 400 PIE sites qualified to perform PROSTASCINT imaging. In 2006, we plan to add PIE sites on a selective basis and, under current arrangements, we bear part of the expense of qualifying new sites. We also expect to review and requalify existing PIE sites on a selective basis.

Market Expansion Strategies for PROSTASCINT

We believe that future growth and market penetration of PROSTASCINT is largely dependent upon the implementation and continued research of:

- improving image quality through fusion technology;
- validating the antigen targeted by PROSTASCINT as an independent prognostic factor;
- publishing and presenting outcomes data;
- developing of image-guided applications including brachytherapy, intensity modulated radiation therapy, surgery, and cryotherapy; and
- expanding clinical development to demonstrate the potential for PROSTASCINT to monitor response to cytotoxic therapies and to image PSMA expression in other cancers, initially renal cell carcinoma.

Fusion Imaging. Fusion (or hybrid) imaging is an *in vivo* diagnostic technique that combines anatomic and functional information directly from patient studies to provide information that cannot be obtained with separate imaging modalities. Anatomical information derived from either computed tomography (CT) or magnetic resonance (MR) imaging can be fused with functional information obtained using single-photon emission computed tomography (SPECT) and novel molecular imaging agents, such as PROSTASCINT. SPECT imaging focuses on metabolic abnormalities that may be present earlier than the anatomical changes otherwise seen with CT or MR imaging alone. Registering both anatomic and functional images provides a complete pathology picture in a single exam, helping physicians eliminate guesswork and enabling them to plan better patient treatment. Approximately

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150 of our current PIE sites are proficient in performing fusion imaging with PROSTASCINT, which can be accomplished through either software or hardware solutions. Through alliances discussed in the Strategic Relationships and Collaborations Related to PROSTASCINT section that follows, we believe that we may increase the use of fusion imaging with PROSTASCINT.

Image Enhancement Technologies. Gamma cameras used in nuclear medicine have advanced in recent years. Some manufacturers now sell cameras with wider segmented crystals, providing advantages in medium and high energy imaging of isotopes (e.g., Indium-labeled agents, such as PROSTASCINT) thus enhancing system sensitivity. System enhancements allow improved image quality or reduced scan time, thereby reducing potential risk of patient motion. Equipment vendors have also recently introduced advanced SPECT reconstruction algorithms, as well as three dimensional iterative reconstruction techniques which potentially increase image contrast with inherent system gains in image quality. These prominent new nuclear medicine imaging algorithms enable advances in image quality as compared to conventional Filtered Back Projection techniques. In addition, nuclear medicine SPECT images of agents such as PROSTASCINT may now be co-registered with an anatomic image obtained with either CT or MR imaging. Device manufacturers generally offer two methods to achieve co-registration between metabolic and anatomical images. Some manufacturers merge information in a single SPECT/CT system, while others utilize fusion software, which has become more widely available in the past few years, as computer workstations have become powerful enough to achieve co-registration.

Imaging Other Cancers Expressing PSMA. PSMA was originally thought to be strictly expressed in prostate tissue, but studies have demonstrated PSMA protein expression in the newly forming blood vessels associated with a variety of nonprostatic tumors. The formation of new blood vessels (angiogenesis) is essential for the growth and development of both primary and metastatic tumors and may represent a unique target for the treatment and diagnosis of a variety of diverse tumors. PSMA may be a unique antiangiogenesis target because it is selectively and consistently expressed in nonprostatic tumor-associated neovasculature but not in normal vessels in benign tissue. A renal cell carcinoma discovered through PROSTASCINT imaging forms the basis upon which we believe PSMA s role as a molecular imaging target may be expanded. The PROSTASCINT scan revealed suspicious uptake in a kidney, which subsequent conventional imaging revealed to be a solid renal mass with necrosis. This example might have demonstrated recognition of tumor-associated neovasculature by the PROSTASCINT monoclonal antibody. Detection of other malignancies such as non-Hodgkin s lymphoma, neurofibromatosis, and meningioma have also been reported with PROSTASCINT imaging. Accordingly, we are planning additional research to determine the role of PROSTASCINT imaging in nonprostatic primary and metastatic malignancies.

Image Guided Therapy. Recent advances in nuclear medicine imaging SPECT equipment, computer workstation power, as well as software enhancements allow researchers to utilize cutting-edge imaging technology to explore novel applications of the enhanced PROSTASCINT image. With fusion of an enhanced SPECT, the PROSTASCINT image is registered with CT and/or MR anatomic images; the resulting images have been applied to clinical research in areas of guided brachytherapy (or radioactive seeds), guided external beam radiation therapy (EBRT), intensity modulated radiation therapy (IMRT), and image guided biopsy. An example of this type of application was described in a 2003 publication reporting four-year biochemical outcome after radioimmunoguided (via PROSTASCINT) brachytherapy published in the *International Journal of Radiation Oncology Biology Physics*, (Vol. 57, No. 2, pp. 362-370, 2003).

Monitoring Response to Cytotoxic Therapy. The molecular basis of cancer is widely believed to involve mutations that lead to deregulated cellular proliferation and suppression of mechanisms controlling programmed cell death (apoptosis). Tumor sensitivity to any given therapeutic regimen is commonly mediated by the initiation of apoptosis. Many therapeutically effective anticancer drugs act to interfere with DNA synthesis and cell division, thereby inducing apoptosis in susceptible target tumors. The specific segment of PSMA recognized by the PROSTASCINT monoclonal antibody is located in the internal cellular domain, which may only be accessible in dead or dying cells within tumor sites, although this has not been confirmed. Accordingly, we are planning additional research to determine the effectiveness of various anticancer regimens on a patient-by-patient basis by assessing the degree of apoptosis in target tumors soon after the initial treatment using PROSTASCINT imaging. Assessment of response to cytotoxic therapy would support the decision to continue treatment in responding patients because this group benefits from an improved prognosis. By identifying nonresponding patients, PROSTASCINT could potentially help to avoid ineffective therapy and, therefore, reduce toxic side effects in these patients.

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Our products, including PROSTASCINT, are subject to significant regulation by governmental agencies, including the FDA, as is more fully described under the section entitled Government Regulation herein. We cannot assure you that we will be able to complete any of our market expansion strategies set forth above.

Further Clinical Development Related to PROSTASCINT

To support our market expansion strategies for PROSTASCINT, we are sponsoring or supporting several active clinical studies including:

Researchers at St. Cloud Hospital in St. Cloud, Minnesota are fusing PROSTASCINT scan images with CT scans in order to evaluate men with a higher risk of prostate cancer and a previous negative biopsy.

Researchers at Thomas Jefferson University in Philadelphia are correlating contrast-enhanced sonography to PROSTASCINT scan images of the prostate in order to target areas for prostate biopsy.

Researchers at Case Western University and University Hospital in Cleveland are comparing uptake of PROSTASCINT within the prostate gland of prostate cancer patients with histopathologic findings of the distribution of cancer in the gland based on whole mount pathology specimens prepared following radical prostatectomy. Some of the patients have also been imaged via positron emission tomography (in addition to PROSTASCINT) to provide for additional comparisons between these two imaging methodologies.

Researchers at The Mayo Clinic in Scottsdale, Arizona are using images of PROSTASCINT distribution within the prostate gland to guide the use of intensity modulated radiation therapy (IMRT) for the treatment of prostate cancer. The purpose of this study is to evaluate whether the use of PROSTASCINT in guiding IMRT allows for delivery of increased doses of radiation specifically to the areas of cancer within the prostate without increasing the level of side effects experienced by the patient.

Researchers at Aultman Hospital, Case Western University and University Hospital in Cleveland are using images of PROSTASCINT distribution within the prostate gland to guide the placement of both iodine-125 and palladium-103 brachytherapy sources (or radioactive seeds) for the treatment of prostate cancer. The purpose of this work is to evaluate whether the use of PROSTASCINT in guiding brachytherapy implantation allows for delivery of increased doses of radiation specifically to the areas of cancer within the prostate without increasing the level of side effects experienced by the patient.

During 2005, we reported that clinical investigators presented new clinical data regarding PROSTASCINT as follows:

Clinical investigators at Case Western University and University Hospital in Cleveland presented seven-year outcomes data relating to PROSTASCINT at the 26th American Brachytherapy Society Annual Meeting. The study evaluated the use of PROSTASCINT fusion imaging to assess disease in both the prostate gland and lymph nodes in newly diagnosed prostate cancer patients undergoing brachytherapy. In the study, PROSTASCINT fusion imaging was performed prior to brachytherapy treatment in 239 prostate cancer patients. Brachytherapy consisted of either iodine-125 or palladium-103 radioactive seed implants. Areas of enhanced PSMA expression within the prostate, as indicated by PROSTASCINT fusion imaging, were used to define biologic tumor volume (BTV). Higher doses of radiation were planned for these BTVs provided doses to critical normal tissues could be maintained within pre-defined acceptable limits. PROSTASCINT fusion imaging was also evaluated for uptake in lymph nodes outside of the prostate. Seven-year outcomes for patients treated in this manner were evaluated based on American Society for Therapeutic Radiology and Oncology (ASTRO) consensus criteria as well as more stringent criteria involving prostate-specific antigen (PSA) cut-offs of 1.0 ng/mL and 0.5 ng/mL. For the entire group, biochemical disease free survival (bDFS) at seven-years was 88.0% by the ASTRO criteria, 82.1% by the PSA < 1.0 ng/mL criteria and 80.4% by the PSA <

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0.5 ng/mL criteria. These rates of bDFS exceed those previously published by centers using standard treatment planning methods without dose escalation to BTVs, particularly for patients with intermediate and high risk features associated with their cancer. For patients in whom PROSTASCINT fusion imaging demonstrated uptake confined to the prostate gland and/or seminal vesicles, the overall seven-year bDFS was 85.8% to 90.6% based on the criteria discussed above; whereas for the 22 patients where the images showed uptake in lymph nodes the corresponding rates of bDFS were only 43.8% to 66.1%. A multivariate analysis of these data indicated that PROSTASCINT uptake in lymph nodes independently predicted a three-fold increase in biochemical recurrence of disease in a statistically significant manner (p=0.018).

The foregoing discussion describes clinical applications that differ from that reported in the PROSTASCINT package insert, and that have not been reviewed or approved by FDA. A copy of the full prescribing information for PROSTASCINT may be obtained in the United States from us by calling us toll free at 800-833-3533 or by visiting our web site at www.cytogen.com, which is not part of this Annual Report on Form 10-K. We are sponsoring or supporting the clinical investigations described in the foregoing discussion to explore potential new indications for the use of PROSTASCINT.

Intellectual Property Position Related to PROSTASCINT

In 1987, Dr. Julius S. Horosziewicz first identified PSMA in a prostate cancer cell line, known as LNCaP, by generating a monoclonal antibody against the protein. That monoclonal antibody, known as 7E11-C5, is conjugated via a proprietary linker technology to the radioisotope indium-111 to produce the PROSTASCINT product. Dr. Horosziewicz s original patent claiming the 7E11-C5 antibody, as well as additional patents relating to the PROSTASCINT product and commercialization rights thereto, were assigned to us in 1989. Under our agreement, we have made, and may continue to make, certain payments to Dr. Horosziewicz, which obligation will remain in effect until the expiration of the last related patent in 2015.

As of December 31, 2005, we were the owner of several issued United States patents and certain corresponding foreign patents relating to PROSTASCINT. One of these, U.S. Pat. No. 5,162,504, is the original Horosziewicz patent and includes claims directed to the monoclonal antibody and the cell line that produces it. We have obtained an extension of the term for this U.S. patent, which will now expire October 28, 2010. U.S. Pat. No. 4,671,958 and U.S. Pat. No. 4,741,900, both of which expired on June 9, 2004, included claims directed to antibody conjugates such as PROSTASCINT, methods for preparing such conjugates, methods for using such conjugates for *in vivo* imaging, testing and therapeutic treatment, and methods for delivering radioisotopes by linking them to such antibodies. U.S. Pat. No. 4,867,973, which also expired on June 9, 2004, included claims directed to antibody conjugates such as PROSTASCINT, and methods for preparing such conjugates. The foregoing patents, which will expire in 2010 (or expired in 2004, as noted), provided or provide the primary patent protection for PROSTASCINT. We also currently own the trademark PROSTASCINT. We are responsible for the costs of prosecuting and maintaining this intellectual property.

In September 2004, we announced the settlement of a patent infringement suit against us and C.R. Bard Inc. for an agreed-upon payment, without any admission of fault or liability. Immunomedics, Inc. filed suit on February 17, 2000 against us and Bard, alleging that use of our PROSTASCINT product infringed U.S. Pat. No. 4,460,559, which claims a method for detecting and localizing tumors. Under our agreement with Dr. Horosziewicz, we may offset our litigation expenses against payments we make to Dr. Horosziewicz.

Manufacturing, Supply and Distribution of PROSTASCINT

In September 2004, we entered into a non-exclusive manufacturing agreement with Laureate Pharma, L.P. for the manufacture and supply of our PROSTASCINT product. Laureate is the sole manufacturer of PROSTASCINT and its primary raw materials, which are antibodies. Our agreement with Laureate will terminate, unless terminated earlier pursuant to its terms, upon Laureate s completion of the specified production campaign for PROSTASCINT and shipment of the resulting products from Laureate s facility in Princeton, New Jersey. We believe that the agreement will provide us with a sufficient supply of PROSTASCINT to satisfy our commercial requirements for approximately the next three to four years, based upon recent sales levels. In addition, we believe the agreement will provide sufficient supply of 7E11-C5 antibody required for the initial clinical development of our therapeutic program.

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In October 2004, Laureate was acquired by Safeguard Scientifics, Inc. Laureate has continued to operate as a full service contract manufacturing organization and we have not experienced any disruption in Laureate s performance of its obligations under our agreement. We currently have no alternative manufacturer or supplier for PROSTASCINT or any of its components.

Any failure on Laureate s part to perform its obligations under the agreement with respect to the supply of PROSTASCINT will have a material adverse effect on our business, financial condition and results of operations. Additionally, PROSTASCINT must be manufactured in compliance with regulatory requirements and at commercially acceptable costs.

PROSTASCINT is distributed for us by Cardinal Health 105, Inc., formerly CORD Logistics, Inc., under the terms of a distribution services agreement dated March 1, 1999. Pursuant to the agreement, Cardinal Health is the exclusive distributor of PROSTASCINT in the United States. Although the agreement has expired, we and Cardinal Health are still operating under the terms of such agreement while a new agreement is being negotiated.

Any arrangement that we enter into with respect to the manufacture, supply or distribution of PROSTASCINT will also be subject to FDA oversight. Any failure on our part, or the part of our business partners, to comply with all applicable regulations and FDA requirements will have a material adverse effect on our business, financial condition and results of operations.

Marketing of PROSTASCINT

We currently market PROSTASCINT using our in-house specialty sales force to hospitals, diagnostic imaging centers, radiopharmacies, urologists, radiation oncologists and nuclear medicine physicians. We also employ technical specialists who are a part of this sales force and who assist in the training of nuclear medicine technologists and nuclear medicine physicians. These technical specialists also administer the PIE site qualification process for nuclear imaging centers to perform PROSTASCINT imaging.

Competition Related to PROSTASCINT

The spread of prostate cancer may be evaluated using a number of imaging modalities, including computed tomography, magnetic resonance imaging, or positron emission tomography.

Strategic Relationships and Collaborations Related to PROSTASCINT

In June 2003, we entered into a relationship with Siemens Medical Solutions and the University Hospitals of Cleveland to promote advances in prostate cancer imaging. Through this arrangement, physicians at the University Hospitals of Cleveland are using the Siemens e.cam gamma camera with Flash 3D iterative reconstruction and CT attenuation correction technology in combination with PROSTASCINT. We hope to explore advances in the use and application of imaging software through our relationship with Siemens.

Also, in June 2003, we entered into an alliance with GE Medical Systems, a unit of the General Electric Company, to market a total molecular imaging system to help evaluate the extent and spread of prostate cancer by integrating GE Medical s Infinia Hawkeye® imaging system with our PROSTASCINT imaging agent. GE s Infinia Hawkeye imaging system combines the anatomic detail of computed tomography (CT) with the molecular imaging data provided by nuclear medicine cameras using products such as PROSTASCINT. The Infinia Hawkeye provides CT-based attenuation correction and localization for single-photon emission computed tomography (SPECT) studies that can help address the inherent limitations of SPECT imaging. Our agreement with GE provides that Cytogen and GE will work together to advance patient and physician awareness of fusion imaging. GE Medical Systems will maintain installation and customer service activities, while Cytogen will provide technical support for PROSTASCINT fusion imaging.

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COMBIDEX

Overview

COMBIDEX (ferumoxtran-10), which was developed by Advanced Magnetics, Inc., is currently under review by the FDA. We cannot market or sell COMBIDEX until Advanced Magnetics receives the appropriate regulatory approvals, and we cannot assure you that Advanced Magnetics will receive such approvals on a timely basis, or at all.

On October 19, 2004, Advanced Magnetics and Cytogen announced that Advanced Magnetics had submitted a complete response to an approvable letter received in June 2000 from the FDA for COMBIDEX. On March 3, 2005, the FDA s Oncologic Drugs Advisory Committee (ODAC) voted to not recommend approval of the proposed broad indication for COMBIDEX being sought by Advanced Magnetics. On March 24, 2005, Advanced Magnetics, Inc. informed us that Advanced Magnetics received an approvable letter from the FDA for COMBIDEX, subject to certain conditions. There can be no assurance that Advanced Magnetics will receive FDA approval for COMBIDEX.

COMBIDEX is an investigational functional molecular imaging agent consisting of iron oxide nanoparticles for use in conjunction with magnetic resonance imaging to aid in the differentiation of cancerous from normal lymph nodes. COMBIDEX is administered via a 30 minute infusion and accumulates preferentially in normal lymph node tissue, thus facilitating the differentiation between malignant and non-malignant lymph nodes.

Lymph nodes are frequently the site for metastases of different types of cancer, particularly breast cancer and prostate cancer. Lymph node imaging plays a role in staging patients and determining appropriate patient management. The cross-sectional imaging modalities currently used for imaging lymph nodes are computed tomography (CT) and magnetic resonance imaging (MRI) without contrast. CT and MRI without contrast cannot distinguish between nodes enlarged due to inflammation and enlarged cancerous nodes, nor can they identify cancerous nodes that are not enlarged. Therefore, the current practice is to assume that enlarged nodes (typically greater than ten millimeters in size) are cancerous and to perform biopsy or surgery to establish their true status. Clinical studies have demonstrated that COMBIDEX only accumulates in macrophage cells associated with normal lymph node tissue and can therefore facilitate differentiation between cancerous nodes and other nodes. We believe that COMBIDEX could enable doctors using MRI to have improved diagnostic confidence in differentiating between normal and cancerous lymph nodes, irrespective of node size.

Clinical Data Related to COMBIDEX

In January 2005, Advanced Magnetics and Cytogen announced the publication of certain clinical data relating to COMBIDEX. The data showed the feasibility of computer-assisted lymph node staging using COMBIDEX. The article contains the results of clinical research conducted by researchers at Massachusetts General Hospital and Harvard Medical School. In the 70-patient study, the magnetic tissue parameters of cancer metastases and normal unmatched lymph nodes were measured in pre- and post-COMBIDEX enhanced images using a learning dataset consisting of 97 histologically proven nodes from 36 patients. The accuracy of a variety of these parameters obtained in a semi-automated manner was then prospectively tested against 216 histologically validated lymph nodes from the remaining 34 patients. Unique magnetic characteristics were found that accurately distinguished metastatic from normal nodes with an overall sensitivity of 98% and specificity of 92%. The parameters were applied to datasets in a semi-automated fashion and used to map the nodes to a three-dimensional reconstruction of the vascular anatomy to provide complete nodal anatomy for different primary cancers. Additional details regarding the conduct and results of this study are available in the journal *Public Library of Science Medicine* (1(3): e66 2004).

Agreements with Advanced Magnetics, Inc.

In August 2000, we entered into a license and marketing agreement with Advanced Magnetics, Inc. for COMBIDEX, for all applications, and ferumoxytol (formerly referred to as Code 7228), for oncology applications only. Pursuant to the terms of the license agreement, we have the exclusive right to market, distribute and sell COMBIDEX in the United States. The license agreement will continue until August 25, 2010, and will thereafter automatically renew for successive five year periods, unless notice of non-renewal or termination is given by us or Advanced Magnetics 90 days prior to the commencement of any renewal period.

Upon execution of our agreements with Advanced Magnetics in 2000, we issued 200,000 shares of common stock to Advanced Magnetics. Of those 200,000 shares, 25,000 shares are being held in escrow pending the achievement of certain milestones relating to COMBIDEX and 25,000 shares are being held in escrow pending the achievement of certain milestones relating to ferumoxytol. The remaining 150,000 shares were transferred to

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Advanced Magnetics, subject to certain restrictions. These restrictions have since expired. We remain obligated to make royalty payments, which are subject to certain minimum amounts, to Advanced Magnetics on any sales of COMBIDEX we may make.

In 2000, we also entered into a supply agreement with Advanced Magnetics for COMBIDEX. Under the terms of the supply agreement, Advanced Magnetics has agreed to manufacture and supply us with COMBIDEX at fixed prices, subject to certain adjustments. The supply agreement is coterminous with the license agreement.

In January 2006, we filed a complaint against Advanced Magnetics in the Massachusetts Superior Court for breach of contract, fraud, unjust enrichment, and breach of the implied covenant of good faith and fair dealing in connection with our 2000 license agreement. The complaint seeks damages along with a request for specific performance requiring Advanced Magnetics to take all reasonable steps to secure FDA approval of COMBIDEX in compliance with the terms of the licensing agreement. In February 2006, Advanced Magnetics filed an answer to our complaint and asserted various counterclaims, including tortuous interference, defamation, consumer fraud and abuse of process. We believe these counterclaims have no merit and we plan to conduct a vigorous defense of such counterclaims.

DISCONTINUED PRODUCTS

NMP22® BLADDERCHEK®

In October 2002, we entered into an agreement with Matritech, Inc. to be the sole distributor for NMP22 BLADDERCHEK to urologists and oncologists in the United States. NMP22 BLADDERCHEK is a point-of-care *in vitro* diagnostic test for bladder cancer developed by Matritech. Matritech retained rights to market NMP22 BLADDERCHEK directly to physicians other than oncologists, such as primary care physicians. In October 2003, we executed an amendment to our agreement which provided that, as of November 8, 2003, we had the non-exclusive right to market and sell NMP22 BLADDERCHEK to urologists until December 31, 2003 and the exclusive right to continue to sell NMP22 BLADDERCHEK to oncologists until December 31, 2004. The amended agreement terminated as of December 31, 2004 and we have no further obligations to Matritech with respect to NMP22 BLADDERCHEK.

BRACHYSEED®

In December 2000, we entered into a 10-year agreement with Draximage Inc., the radiopharmaceutical subsidiary of Draxis Health, Inc. to market and distribute Draximage s BRACHYSEED implants in the United States. On January 24, 2003, we provided Draximage with notice of termination for each of our license and distribution agreement and product manufacturing and supply agreement with respect to both of Draximage s BRACHYSEED iodine-125 and BRACHYSEED palladium-103 products and, as of January 2003, we no longer accepted or filled new orders for the BRACHYSEED products. On April 8, 2003, we formally terminated these agreements and announced the amicable resolution of all open matters with Draximage. We also agreed with Draximage to maintain the confidentiality of each other s proprietary information, released each other from all other liability with respect to any claims under such agreements, and agreed to certain indemnification obligations with respect to third party claims.

ONCOSCINT® CR/OV

In December 2002, we discontinued marketing, selling and producing ONCOSCINT CR/OV, a monoclonal antibody diagnostic imaging agent for the detection of the spread of colorectal and ovarian cancer. The market for ONCOSCINT CR/OV for colorectal cancer diagnosis was negatively affected by positron emission tomography (PET), which had been shown to have similar or higher sensitivity than the ONCOSCINT CR/OV scan.

RESEARCH AND DEVELOPMENT

AGGREGATE EXPENDITURES

Our research and development expenses, including our equity in the loss of the PSMA Development Company, LLC, over the past three years were:

2005 $ 9.2 million

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2004 $ 6.1 million

2003 $ 5.8 million

We intend to pursue research and development activities having commercial potential and to review all of our programs to determine whether possible market opportunities provide an adequate return to justify the commitment of human and economic resources to their initiation or continuation. The major components of our research and development programs and expenditures are set forth below.

TECHNOLOGY

Prostate-Specific Membrane Antigen (PSMA)

PSMA is a transmembrane protein that is an important marker associated with prostate cancer. Dr. Julius S. Horosziewicz identified the PSMA protein using a monoclonal antibody in 1987. The antibody technology developed by Dr. Horosziewicz was assigned to us. Later, researchers at the Sloan-Kettering Institute for Cancer Research (SKICR) identified and sequenced the gene encoding PSMA, and we acquired an exclusive worldwide license to that and related technologies. From these technologies, we have put one product on the market, PROSTASCINT, and we are building a pipeline of potential new products which are currently in research and development. These pipeline products are focused primarily on novel vaccine and antibody therapies for prostate and other cancers.

PSMA has also been found to be present at high levels in the new blood vessels or neovasculature formed in association with a variety of major solid tumors other than prostate cancers. Such neovasculature is necessary for the growth and survival of many types of solid tumors. We believe that, due to the unique characteristics of this antigen, technologies utilizing PSMA can yield novel products for the treatment and diagnosis of cancer. If PSMA-targeted therapies can destroy or prevent formation of these new blood vessels, we believe that such therapies may prove valuable in treating a broad range of cancers.

In 1993, we entered into an option and license agreement with the SKICR, and began a development program involving PSMA and our proprietary monoclonal antibody. In November 1996, we exercised our option and obtained an exclusive worldwide license to this technology. Under our agreement with SKICR, we received, or subsequently obtained, rights to patents and patent applications including: U.S. Pat. Nos. 5,538,866 (expiring July 23, 2013), 5,935,818 (expiring August 10, 2016), and 6,569,432 (expiring February 24, 2015), and U.S. Pat. Appln. Nos. 08/403,803 (filed March 17, 1995), 08/466,381 (filed June 6, 1995), 08/470,735 (filed June 6, 1995), 08/481,916 (filed June 7, 1995), 08/894,583 (filed February 23, 1998), 09/724,026 (filed November 28, 2000), 09/990,595 (November 21, 2001), 10/012,169 (filed October 24, 2001), 10/443,694 (filed May 21, 2003), and 10/614,625 (filed July 2, 2003). The filing, prosecution and maintenance of licensed patents, as defined in the agreement, is the responsibility of SKICR, but is at our discretion and expense. In the event that we decide not to file, prosecute or maintain any part of the licensed patents, SKICR may do so at its own expense.

The license shall terminate on the date of expiration of the last to expire of the licensed patents unless it is terminated earlier in accordance with the terms of the agreement. The license agreement is also terminable by us upon 60 days notice to SKICR. Upon execution of our agreement with SKICR, we paid to SKICR an option fee, a license fee and a reimbursement for patent expenses paid by SKICR. We are obligated to make certain royalty payments, which are subject to certain minimum amounts and other annual payments to SKICR for the term of the agreement.

In August 2000, we executed a sublicense agreement with Northwest Biotherapeutics Inc. (NWBT) pursuant to which we granted NWBT the right to develop and commercialize *ex vivo* immunotherapy products for prostate cancer that are produced by pulsing isolated populations of a patient s antigen presenting cells, such as dendritic cells, with PSMA. Following encouraging results from a Phase I/II trial to evaluate the safety and efficacy of using PSMA with NWBT s proprietary dendritic cell immunotherapy, DCVax®, NWBT advanced DCVax-

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Prostate to the initiation of Phase III clinical trials. In November 2002, NWBT suspended all clinical trial activity for its DCVax product candidates and withdrew its Investigative New Drug Application for DCVax- Prostate, which resulted in a termination of the license agreement with us. As a result, we regained the rights to *ex vivo* prostate cancer immunotherapy using PSMA in December 2002. In January 2005, NWBT announced that it received clearance from the FDA to begin assessment of DCVax-Prostate in a Phase III clinical trial. We have requested clarification from NWBT on the status of this PSMA-based program following termination of the license agreement with us.

THERAPEUTIC 7E11-C5 MONOCLONAL ANTIBODY (CYT-500)

Overview

Cytogen s therapeutic 7E11-C5 monoclonal antibody is under development by us using certain linker/chelator technology licensed from The Dow Chemical Company. We plan to file an investigational new drug application for this product candidate near the end of first quarter 2006. We have exclusive rights to this product candidate.

In April 2005, Cytogen and Dowpharma[SM] contract manufacturing services, a business unit of The Dow Chemical Company, announced a collaboration to create a targeted oncology product designed to treat prostate and other cancers. The therapeutic 7E11-C5 monoclonal antibody is a targeted oncology product in which Dow s proprietary MeO-DOTA bifunctional chelant technology will be used to radiolabel Cytogen s PSMA 7E11-C5 antibody with a therapeutic radionuclide. This new product candidate uses the targeting capability of the monoclonal antibody to direct and deliver radiation to tumor cells expressing PSMA.

Under the agreement, proprietary chelation technology and other capabilities, provided through ChelaMed[SM] radiopharmaceutical services from Dowpharma, will be used to attach a therapeutic radioisotope to the same murine monoclonal antibody utilized in Cytogen s PROSTASCINT molecular imaging agent. This 7E11-C5 antibody is directed against an intracellular epitope of PSMA. We intend to develop the resulting innovative molecule for the treatment of various cancers, initially in prostate, that express the PSMA marker. The 7E11-C5 antibody was excluded from the PSMA technology licensed to the PSMA Development Company LLC, the Company s joint venture for certain PSMA product development. Consequently, the joint venture is not involved in this development initiative.

We believe that there is a strong rationale for development of Cytogen s therapeutic 7E11-C5 monoclonal antibody as evidenced by the following:

- Radiolabeled molecules have proven successful for the diagnosis and treatment of both hematologic and solid tumors;
- Murine monoclonal antibodies may be preferable for nuclear medicine-based applications, such as radiotherapy, due to their tendency to clear faster from serum;
- Prior studies of the 7E11-C5 monoclonal antibody at protein doses similar to those needed for delivery of therapeutic radionuclides have shown a low incidence of development of human anti-murine antibodies (HAMA) which was transient and low titer; and
- Tumors are known to have abnormally permeable cell membranes that enable monoclonal antibody targeting of an intracellular epitope, which has been validated by PROSTASCINT imaging and other preclinical data.

Preclinical Data Related To Therapeutic 7E11-C5 Monoclonal Antibody

In November 2005, preclinical data for the therapeutic 7E11-C5 monoclonal antibody product was presented at the American Association for Cancer Research-National Cancer Institute-European Organization for Research and Treatment of Cancer International Conference on Molecular Targets and Cancer Therapeutics. Findings from pharmacokinetic and biodistribution studies of radiolabeled 7E11-C5 in mice demonstrated that the antibody-radionuclide linkage of Lu-177 to 7E11-C5 is stable in serum and successfully accumulates at the tumor site. Acute and expanded acute toxicology studies in rats and dogs, respectively, and safety pharmacology studies in

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dogs did not reveal any significant adverse reactions with unlabeled doses up to 20 times the anticipated human dose.

Manufacturing and Supply for Phase I Trials

In September 2005, we entered into a non-exclusive manufacturing agreement with Laureate Pharma, L.P. for the scale-up for the cGMP manufacturing of a MeO-DOTA chelator conjugate of the 7E11-C5 monoclonal antibody. Laureate is the sole manufacturer of such antibody. Our agreement with Laureate will terminate, unless terminated earlier pursuant to its terms, on December 31, 2006. We believe that the agreement will provide us with a sufficient supply of the MeO-DOTA chelator conjugate of the 7E11-C5 monoclonal antibody to satisfy our requirements for Phase I clinical trials of such product. We believe that we have a sufficient supply of 7E11-C5 monoclonal antibody from our September 2004 manufacturing agreement with Laureate.

PSMA Development Company LLC

In 1999, we entered into a joint venture with Progenics Pharmaceuticals, Inc. to develop *in vivo* immunotherapeutic products utilizing PSMA. These product candidates currently include antibody-based immunotherapies for prostate cancer, a therapeutic prostate cancer vaccine utilizing the PSMA gene and a vector delivery system, and a recombinant form of the PSMA protein as a basis for immune stimulation. We believe that these product candidates, if successfully developed, could play an important role in the treatment of prostate cancer. We believe there are significant unmet needs for treatment and monitoring of this disease.

We are currently pursuing three research and development programs through the joint venture:

Monoclonal Antibody Program. The PSMA monoclonal antibody program is currently in the preclinical development stage. The joint venture is utilizing fully human monoclonal antibodies, derived from Abgenix s Xenomouse technology, initially in conjunction with toxin-labeled approaches to treat prostate cancer.

Viral Vector Vaccine Program. The joint venture is developing a novel, *in vivo* alphavirus vaccine for prostate cancer that is designed to induce both antibodies and cytotoxic T cells against PSMA. The joint venture is currently working with AlphaVax and Greer Laboratories to use the Alphavax Replicon Vector(ArV) system to develop a prostate cancer vaccine using the PSMA antigen. To date, preclinical and clinical batches have been manufactured and stability and preclinical toxicology studies have been initiated and are ongoing.

Recombinant Soluble PSMA Vaccine Program. The joint venture is developing an *in vivo* therapeutic recombinant protein vaccine, which is designed to stimulate a patient s immune response system to recognize and destroy prostate cancer cells. The vaccine combines the PSMA cancer antigen with an immune stimulant to induce an immune response against prostate cancer cells. The genetically engineered PSMA vaccine generated potent immune responses in preclinical animal testing. A Phase I clinical trial was designed to evaluate the safety and immune-stimulating properties of the vaccine in patients with either newly diagnosed or recurrent prostate cancer. Enrollment in this clinical trial is now complete.

The joint venture is owned equally by Progenics and us. We have exclusively licensed to the joint venture certain immunotherapeutic applications of our PSMA patent rights and know-how. Progenics had funded the first $3.0 million of development costs, in addition to $2.0 million in supplemental capital contributions funded at certain dates prior to December 2001. Progenics subsequently received full reimbursement for the initial $3.0 million of government grants related to the PSMA research programs. Beginning in December 2001, we began sharing equally the costs of the programs with Progenics.

In 2005, we incurred expenses of $3.2 million relating to our half of the expenses for the programs at the joint venture, compared to $2.9 million in 2004. The joint venture is funded by equal capital contributions from each of Progenics and Cytogen in accordance with an annual budget approved by the joint venture representatives from each such party. As of March 15, 2006, we and Progenics have not agreed on a 2006 work plan and annual budget for the joint venture. We cannot give any assurances that agreement will be reached on such matters in the near future, if at all. The failure to reach agreement with Progenics on these matters could significantly and adversely affect the development of PSMA technologies and products.

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Contract research and development services were provided by Progenics and Cytogen to the joint venture during 2005. We believe that if mutual agreement is not achieved with respect to the provision of services by Cytogen and Progenics, the parties can successfully negotiate with outside third parties for necessary services.

In 2004, $8.0 million of grants were awarded over four years from the National Institutes of Health, or NIH. The awards were made under the National Cancer Institute s FLAIR program, or Flexible System to Advance Innovative Research for Cancer Drug Discovery by Small Business. The NIH grants are in the form of two Phase II Small Business Innovation Research grants, and will be used to develop novel immunotherapies for prostate cancer based on PSMA. We cannot assure you that the joint venture will continue to receive the benefits of these NIH grants if the operations of the joint venture are terminated.

We have North American marketing rights to products developed by the joint venture and a right of first negotiation with respect to marketing activities in any territory outside North America. We anticipate initiation of marketing efforts for any product developed upon approval by the FDA or requisite foreign regulatory bodies, as applicable. If approved, we anticipate marketing these products with our own sales force and will be reimbursed by the joint venture for these costs. We will split the net profit equally with Progenics for any products developed by the joint venture, assuming there is no change in our existing ownership interests.

Preclinical and Clinical Data Related to PSMA

In September 2005, Progenics and Cytogen announced preclinical findings of its prostate cancer drug, PSMA antibody-drug conjugate (ADC). The findings were reported by Progenics at the 12th Annual Prostate Cancer Foundation Scientific Retreat in Phoenix, Arizona. In a mouse model of human prostate cancer, PSMA ADC significantly prolonged overall survival up to nine-fold as compared to untreated animals (p=0.0018, log-rank test, two-sided). Established tumors in two of the five animals treated at the highest dose were eradicated and remained undetectable over 500 days through the completion of the study. No overt evidence of toxicity was observed in any of these animal model tests.

In December 2002, the joint venture announced the initiation of a Phase I clinical trial for the testing of a novel therapeutic prostate cancer vaccine directed against PSMA. This trial was conducted through a physician s IND by the Memorial Sloan Kettering Cancer Center. Requisite follow-up of the last patient, which concluded the Phase I trial, was conducted in March 2005.

Strategic Relationships, Collaborations and Licensing Arrangements Related to PSMA

AlphaVax Human Vaccines, Inc. During 2001, the joint venture entered into a worldwide exclusive licensing agreement with AlphaVax Human Vaccines, Inc. to use the Alphavax Replicon Vector(ArV) system to create a therapeutic prostate cancer vaccine incorporating the PSMA antigen. In consideration for the license, the joint venture paid a nonrefundable, noncreditable license fee and is obligated to pay additional payments upon the occurrence of certain defined milestones associated with the development and commercialization program for products incorporating the ArV technology. In addition, the joint venture is required to pay an annual maintenance fee until the commencement of commercial sales of products and then royalties based on net sales of products. The joint venture has the right to terminate this agreement upon 30 days prior written notice. We believe that this technology, if successfully deployed, may have important advantages in targeting immune stimulating cells *in vivo* which impact on the progression of cancer.

Abgenix, Inc. During 2001, the joint venture entered into an agreement with Abgenix, Inc. regarding the development of fully human antibodies to PSMA using Abgenix s Xenomouse™ technology. In consideration for the license, the joint venture paid a nonrefundable, noncreditable license fee and is obligated to pay additional license fees on each of the first three anniversary dates and milestone payments upon the occurrence of certain defined milestones associated with the development and commercialization program for products incorporating an antibody generated utilizing the Xenomouse technology. In addition, the joint venture is required to pay royalties based upon net sales of antibody products sold thereunder. If not terminated early, the agreement continues until the expiration of the joint venture s obligation to pay royalties under the agreement to Abgenix. The joint venture has

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the right to terminate this agreement upon 30 days prior written notice. In August 2003, the joint venture entered into a manufacturing agreement with Abgenix for the production of clinical supplies for the PSMA human monoclonal antibody program. Such agreement has been terminated and the joint venture is currently pursuing alternative manufacturing arrangements for the monoclonal antibody program.

Seattle Genetics, Inc. In June 2005, the joint venture entered into a collaboration agreement (the SGI Agreement) with Seattle Genetics, Inc. (SGI). Under the SGI Agreement, SGI provided an exclusive worldwide license to its proprietary antibody-drug conjugate technology (the ADC Technology) to the joint venture. Under the license, the joint venture has the right to use the ADC Technology to link cell-killing drugs to the joint venture s monoclonal antibodies that target prostate-specific membrane antigen. During the initial research term of the SGI Agreement, SGI also is required to provide technical information to the joint venture related to implementation of the licensed technology, which period may be extended for an additional period upon payment of an additional fee. The joint venture may replace prostate-specific membrane antigen with another antigen, subject to certain restrictions, upon payment of an antigen replacement fee. The ADC Technology is based, in part, on technology licensed by SGI from third parties (the Licensors). The joint venture is responsible for research, product development, manufacturing and commercialization of all products under the SGI Agreement. The joint venture may sub-license the ADC Technology to a third-party to manufacture the ADC s for both research and commercial use. The joint venture made a $2.0 million technology access payment to SGI upon execution of the SGI Agreement and will make additional maintenance payments during the term of the SGI Agreement. In addition, the joint venture will make payments, aggregating $15.0 million, upon the achievement of certain defined milestones and will pay royalties to SGI and its Licensors, as applicable, on a percentage of net sales, as defined. In the event that SGI provides materials or services to the joint venture under the SGI Agreement, SGI will receive supply and/or labor cost payments from the joint venture at agreed-upon rates. The joint venture s monoclonal antibody project is currently in the pre-clinical phase of research and development. All costs incurred by the joint venture under the SGI Agreement during the research and development phase of the project will be expensed in the period incurred. The SGI Agreement terminates at the later of (a) the tenth anniversary of the first commercial sale of each licensed product in each country or (b) the latest date of expiration of patents underlying the licensed products. The joint venture may terminate the SGI Agreement upon advance written notice to SGI. SGI may terminate the SGI Agreement if the joint venture breaches an SGI in-license that is not cured within a specified time period after written notice. In addition, either party may terminate the SGI Agreement upon breach by the other party that is not cured within a specified time period after written notice or in the event of bankruptcy of the other party. The ability of the joint venture to comply with the terms of the SGI Agreement will depend on agreement by the Progenics and us regarding work plans and budgets of the joint venture in future years.

Cardinal Health PTS, LLC Gala Unit. In June 2005, the joint venture entered into a development and manufacturing agreement with Cardinal Gala for the cGMP manufacturing of bulk PSMA monoclonal antibody for use in Phase I and Phase II clinical trials. Aggregate costs under this agreement are expected to be approximately $900,000.

In connection with the agreements discussed above, the joint venture has recognized contractual payments, including license fees, which are included in research and development expenses, totaling approximately $2.1 million, $550,000 and $300,000 for the years ended December 31, 2005, 2004 and 2003, respectively. In addition, as of December 31, 2005, remaining potential payments associated with milestones and defined objectives with respect to the existing agreements total approximately $26.5 million. Future annual minimum royalties under the existing agreements described above are not significant. Upon termination of these agreements, only financial obligations maturing and accruing prior to such termination are due and payable.

AxCell Biosciences

In 1993, we licensed from the University of North Carolina at Chapel Hill (UNC) exclusive worldwide rights to novel reagents and technology for identifying targeting peptides that were developed under sponsored research funded by us. This process utilizes random peptide libraries (Genetic Diversity Library, GDL) expressing an extensive collection of long peptides that, unlike conventional drugs or short peptides, can mimic natural proteins in terms of their folding and their corresponding molecular recognition functions. This is similar to the ability of antibody molecules to selectively bind to antigens, or enzymes to bind to their substrates. This proprietary approach facilitated the screening of a more diverse family of compounds than was practical with

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previous methods and yielded several novel reagents (totally synthetic affinity reagents, TSAR s). Originally, we expected to utilize these libraries to discover specific binding molecules that would represent attractive alternatives to monoclonal antibodies for diagnostic and therapeutic products.

In 1996, we entered into a research and licensing agreement with Elan Corporation, plc, which marked our first external collaboration in which GDL -derived products would be utilized for their ability to target drugs to specific sites within the body. The research program with Elan was designed to discover GDL-derived peptides that could be used to target therapeutic agents to receptors expressed within the lining of the intestinal tract known to be involved in certain cellular uptake and transport processes. In contrast to most biotechnology drugs that cannot be administered orally due to the fact that they break down prior to reaching the bloodstream, such peptides could be administered orally. Under the agreement, Elan had the option for worldwide licensing rights to any products developed collaboratively and we would receive royalties based on the sale of any such products. In July 2004, we assumed ownership and responsibility for Elan s pending patent portfolio related to GDL-derived peptides that could be used to target therapeutic agents to receptors expressed within the lining of the intestinal tract known to be involved in certain cellular uptake and transport processes. We are seeking strategic partners for this program.

Our subsidiary, AxCell Biosciences was incorporated in 1996 to further commercialize the GDL technology in the field of accelerated new target discovery and validation. Based on the prevalence of modular protein domains, such as Src homology domain 3 and 2 (SH3 and SH2), among many other important signaling molecules known to mediate protein-protein interactions, UNC researchers advanced the use of ligands generated using GDL as probes to systematically isolate entire repertoires of modular domain-containing proteins from cloned DNA expression libraries. This became AxCell s Cloning of Ligand Targets (CLT) technology.

As an initial proof of concept for the automation and application of GDL and CLT technologies to rapidly and efficiently identify protein signaling pathways, AxCell created a comprehensive database (ProChart) of domain and ligand interactions throughout 2001. Because protein signaling pathways play a role in many diseases, researchers are working to develop drugs that specifically target these pathways. While some interactions are likely to have positive clinical results, others can lead to unwanted drug side effects and toxicity. By referring to a comprehensive map of the body s protein interactions, researchers may be better able to identify drugs that target a specific disease related interaction while avoiding those unspecific interactions associated with unwanted side effects.

Beginning in 2002, AxCell began applying its existing protein interaction data in several major areas of scientific interest by entering into academic, governmental, and corporate research collaborations designed to both provide *in vivo* validation of novel protein-protein interactions discovered using its *in vitro* approach and the discovery of novel drug targets. In most circumstances, AxCell has an exclusive option to negotiate an exclusive, worldwide, royalty-bearing license for inventions that result from the research collaboration.

In March 2004, the first *in vivo* validation of a novel interaction discovered using AxCell s technology was published (Functional association between Wwox tumor suppressor protein and p73, a p53 homolog. *Proceedings of the National Academy of Sciences,* March 30, 2004: vol. 101; no. 13 pp. 4401 4406). In November 2004, a second demonstration of *in vivo* validation for a novel interaction discovered using AxCell s technology was published (Physical and functional interactions between the Wwox tumor suppressor protein and the AP-2gamma transcription factor. Cancer Res. November 2004: vol. 64; no. 22 pp. 8256-61).

In addition to research done under collaboration with AxCell, other groups also validated AxCell s technology via publications confirming interactions contained in the ProChart database. One such example is the publication of The RING-H2 protein RNF11 is differentially expressed in breast tumours and interacts with HECT-type E3 ligases. (Biochim Biophys Acta. 2003 Oct 15;1639(2):104-12.). This paper was published nearly two years after the RNF11/AIP4 interaction data was deposited into ProChart.

In view of recent biological validation and progress through both internal data mining efforts and external research collaborations, we are currently considering strategic transactions for AxCell to create value. AxCell has a proprietary high-throughput platform for the systematic identification and characterization of domain-mediated intracellular pathways, which can be combined with many levels of biological information to understand how they work together in a systems biology approach. AxCell has made technical progress over the past several years by

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applying its proprietary protein pathway content and knowledge to accelerate the development of targeted drugs in certain therapeutic categories through both internal efforts and external research collaborations with corporate, governmental and academic partners.

The application of AxCell s technology may accelerate research and drug development by:

- discovering novel signal transduction pathways and their relevant protein-protein interactions;
- rapidly identifying qualified drug targets;
- identifying structure and activity relationship (SAR) information regarding domain and ligand interactions that can facilitate small molecule drug design; and
- providing high throughput screening reagents (eg, cloned domains and ligands).

The patents and patent applications we have licensed from UNC include: U.S. Pat. Nos. 5,498,538 (expiring March 12, 2013), 5,625,033 (expiring April 29, 2014), 5,747,334 (expiring May 5, 2015), 5,844,076 (expiring December 1, 2015), 5,852,167 (expiring December 22, 2015), 5,935,823 (expiring August 10, 2016), 6,011,137 (expiring April 3, 2016), 6,184,205 (expiring July 22, 2014), 6,303,574 (expiring July 22, 2014), 6,309,820 (expiring April 7, 2015), 6,432,920 (expiring July 22, 2014), 6,703,482 (expiring July 22, 2014), and 6,709,821 (expiring April 7, 2015), and U.S. Pat. Appln. Nos. 10/161,791 (filed May 31, 2002), and 10/185,050 (filed June 28, 2002). We are responsible for the costs of filing, prosecuting and maintaining domestic and foreign patents and patent applications under our agreement with UNC.

The agreement commenced on March 10, 1993 and will expire, unless earlier terminated as provided therein, upon the expiration of the last to expire of the licensed patents that cover a licensed product. Under the agreement, we are required to make certain milestone and royalty payments to UNC, which are subject to certain minimum amounts.

In September 2002, we significantly reduced AxCell s workforce to reduce the cash expenditures relating to AxCell in order to leverage our oncology franchise. Further, in July 2004, as part of our continuing efforts to reduce non-strategic expenses, we initiated the closure of AxCell s facilities.

Research projects through academic, governmental and corporate collaborators and additional applications for the intellectual property and technology at AxCell are being pursued.

OTHER STRATEGIC RELATIONSHIPS

We frequently enter into alliances with other companies to, among other things, increase our financial resources, reduce risk and retain an appropriate level of ownership of products currently in development. In addition, through alliances with other pharmaceutical and biotechnology companies and other collaborators, we may obtain funding, expand existing programs, learn of new technologies and gain additional expertise in developing and marketing products.

Antisoma Research Limited. In September 2003, Antisoma Research Limited acquired certain royalty rights to its lead product, R1549 (formerly Pemtumomab), from us. In connection with Antisoma s acquisition of these rights, Antisoma made a cash payment to us of $500,000 and agreed to make an additional payment of $500,000 to us upon the first commercial sale, if any, of the R1549 product. In return, we relinquished our right to receive royalties of 1.65% on future net sales, if any, of the R1549 product. In April 2004, Antisoma and Roche announced that the R1549 product did not meet the primary endpoints in a Phase III study in ovarian cancer, and that it is unlikely that development of R1549 will continue.

Elan Corporation, plc. In December 1995, we entered into a license agreement granting Elan worldwide rights to a group of peptides and associated technology for orally administered drugs that are transported across the gastrointestinal epithelium, as well as rights to other orally delivered drugs derived from related research programs. Elan is responsible for the further development and commercialization of this technology. We are entitled to

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royalties from sales of any product developed and commercialized based on this technology. In July 2004, we were assigned rights to certain patents and patent applications developed under the agreement, including U.S. Pat. No. 6,703,362 (expiring May 15, 2018), and U.S. Pat. Appln. Nos. 09/079,678 (filed May 15, 1998) and 09/079,819 (filed May 15, 1998).

Northwest Biotherapeutics, Inc. In August 2002, we entered into an agreement with Northwest Biotherapeutics that gave Northwest Biotherapeutics a license to develop and commercialize *ex vivo* immunotherapy products for prostate cancer that are produced by pulsing isolated populations of a patient s antigen presenting cells, such as dendritic cells, with PSMA. Northwest Biotherapeutics advanced their program to the initiation of Phase III clinical trials before terminating the program in November 2002, which resulted in a termination of the license agreement and Cytogen regaining rights to *ex vivo* prostate cancer immunotherapy using PSMA. Based on data demonstrating a favorable safety and clinical response in prostate cancer patients treated to date using PSMA-based *ex vivo* immunotherapy, we are pursuing other collaborations or partnerships to realize the clinical and commercial potential of this approach.

PRODUCT CONTRIBUTION TO REVENUES

PROSTASCINT and QUADRAMET account for, and, prior to their discontinuation in December 2004 and January 2003, NMP22 BLADDERCHEK and BRACHYSEED, respectively, accounted for substantially all of our total revenues. For the years ended December 31, 2005, 2004 and 2003, revenues related to PROSTASCINT accounted for approximately 46%, 49% and 47%, respectively, of our total revenues; and revenues related to QUADRAMET accounted for approximately 52%, 50% and 28%, respectively, of our total revenues. Prior to their discontinuation in December 2004 and January 2003, NMP22 BLADDERCHEK and BRACHYSEED, respectively, each accounted for approximately 2% of our total revenues for the year ended December 31, 2003. In April 2003, we announced the termination of our agreements with Draximage with respect to the BRACHYSEED products.

CONCENTRATION OF SALES

During the year ended December 31, 2005, we received 67% of our total revenues from three customers, as follows: 47% from Cardinal Health (formerly Syncor International Corporation); 11% from Mallinckrodt Inc., and 9% from GE Healthcare (formerly Amersham Health).

COMPETITION

The biotechnology and pharmaceutical industries are subject to intense competition, including competition from large pharmaceutical companies, biotechnology companies and other companies, universities and research institutions. Our existing therapeutic and imaging/diagnostic products compete with the products of a wide variety of other firms, including firms that provide products used in more traditional therapies or procedures, such as external beam radiation, chemotherapy agents, narcotic analgesics and other imaging/diagnostics. In addition, our existing and potential competitors may be able to develop technologies that are as effective as, or more effective than those offered by us, which would render our products noncompetitive or obsolete. Moreover, many of our existing and potential competitors have substantially greater financial, marketing, sales, manufacturing, distribution and technological resources than we do. Our existing and potential competitors may be in the process of seeking FDA or foreign regulatory approval for their respective products or may also enjoy substantial advantages over us in terms of research and development expertise, experience in conducting clinical trials, experience in regulatory matters, manufacturing efficiency, name recognition, sales and marketing expertise and established distribution channels. We believe that competition for our products is based upon several factors, including product efficacy, safety, cost-effectiveness, ease of use, availability, price, patent position and effective product promotion.

We expect competition to intensify in the fields in which we are involved, as technical advances in such fields are made and become more widely known. We cannot assure you, however, that we or our collaborative partners will be able to develop our products successfully or that we will obtain patents to provide protection against competitors. Moreover, we cannot assure you that our competitors will not succeed in developing therapeutic or imaging/diagnostic products that circumvent our products or that these competitors will not succeed in developing technologies or products that are more effective than those developed by us. In addition, many of these companies may have more experience in establishing third-party reimbursement for their products. Accordingly, we cannot

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assure you that we will be able to compete effectively against existing or potential competitors or that competition will not have a material adverse effect on our business, financial condition and results of operations.

INTELLECTUAL PROPERTY

We believe that our success depends, in part, on our ability to protect our products and technology through patents and trade secrets. Accordingly, our policy is to pursue a vigorous program of securing and maintaining patent and trade secret protection to preserve our right to exploit the results of our research and development activities and, to the extent it may be necessary or advisable, to exclude others from appropriating our proprietary technology.

We aggressively protect our proprietary technology by selectively seeking patent protection in a worldwide program. In addition to the United States, we file patent applications in Canada, major European countries, Japan and additional foreign countries on a selective basis to protect inventions important to the development of our business. We believe that the countries in which we have obtained and are seeking patent coverage for our proprietary technology represent the major focus of the pharmaceutical industry in which we will market our respective products.

We also rely upon, and intend to continue to rely upon, trade secrets, unpatented proprietary know-how and continuing technological innovation to develop and maintain our competitive position. It is our policy to require our employees, consultants, licensees, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements also provide that all confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual shall be our exclusive property. We cannot assure you, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

We believe that our valuable proprietary information is protected to the fullest extent commercially reasonable; however, we cannot assure you that:

- additional patents will be issued to us in any or all appropriate jurisdictions;
- litigation will not be commenced seeking to challenge our patent protection or that challenges will not be successful;
- our processes or products do not or will not infringe upon the patents of third parties; or
- the scope of patents issued will successfully prevent third parties from developing similar and competitive products.

The technology applicable to our products is developing rapidly. A substantial number of patents have been issued to other biotechnology companies relating to PSMA. In addition, competitors have filed applications for, have been issued, or may otherwise obtain patents and other proprietary rights relating to products or processes that are competitive with ours. In addition, others may have filed patent applications and may have been issued patents relating to products and technologies potentially useful to us or necessary to commercialize our products or to achieve our business goals. We cannot assure you that we will be able to obtain licenses to such patents on commercially reasonable terms if at all. The failure to obtain licenses to such patents could prevent us from commercializing products or services covered by such patents.

We cannot predict how any patent litigation will affect our efforts to develop, manufacture or market our products.

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GOVERNMENT REGULATION

The development, manufacture and sale of medical products utilizing our technology are governed by a variety of federal, state and local statutes and regulations in the United States and by comparable laws and agency regulations in most foreign countries. Our two actively marketed products consist of a biologic (PROSTASCINT) and a drug (QUADRAMET). Future applications for these may include expanded indications and could result in additional drugs, biologics, devices or combination products. Our product development pipeline contains various other products, the majority of which will likely be classified as new drugs or biologics.

In the United States, medical products that we currently market or intend to develop are regulated by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (FDC Act) and the Public Health Service Act (PHS Act), and the rules and regulations promulgated thereunder. These laws and regulations require, among other things, carefully controlled research and preclinical and clinical testing of products, government notification, review and/or approval or clearance prior to investigating or marketing the product, inspection of manufacturing and production facilities, adherence to current Good Manufacturing Practices (cGMP), and compliance with product and manufacturer specifications or standards, and requirements for reporting, advertising, promotion, export, packaging, and labeling, and other applicable regulations.

The FDC Act requires that our products be manufactured in FDA registered facilities subject to inspection. The manufacturer must be in compliance with cGMP, which imposes certain procedural, substantive, and recordkeeping requirements upon us and our manufacturing partners with respect to manufacturing and quality control activities, and, for devices, product design. To ensure full technical compliance with such regulations, a manufacturer must spend funds, time and effort in the areas of production and quality control. These regulations may also apply to us. Any failure by us or our manufacturing partners to comply with the requirements of cGMP could have a material adverse effect on our business, financial condition and results of operations.

FDA approval of our proposed products, including a review of the manufacturing processes, controls and facilities used to produce such products, will be required before such products may be marketed in the United States. The process required by the FDA before drug, biological or medical device products may be approved for marketing in the United States generally involves:

- preclinical laboratory and animal tests that are conducted consistent with the FDA s good laboratory practice regulations;
- submission to the FDA of an Investigational New Drug Application (IND) (for a drug or biologic) or Investigational Device Exemption (IDE) (for a device), which must become effective before clinical trials may begin; further, approval of the investigation by an Institutional Review Board (IRB) must also be obtained before the investigational product may be given to human subjects;
- human clinical trial(s) to establish the safety and efficacy of the product for its intended indication;
- submission to the FDA of a marketing application-New Drug Application (NDA) for a drug, Biologics License Application (BLA) for a biologic, and a premarket approval application (PMA) or premarket notification (510(k)) for a device; and
- FDA review and approval or clearance of the marketing application. Radiopharmaceutical drugs are subject to additional requirements pertaining to the description and support of their indications for use, and the evaluation of product effectiveness and safety, including, radiation safety. We cannot assure you that the FDA review of marketing applications will result in product approval or clearance on a timely basis, or at all.

Clinical trials for drugs, devices, and biologics typically are performed in three phases to evaluate the safety and efficacy of the product. In Phase I, a product is tested in a small number of healthy subjects or patients primarily for safety at one or more dosages. Phase II evaluates, in addition to safety, the efficacy of the product against particular diseases in a patient population that is generally somewhat larger than Phase I. Clinical trials of certain diagnostic and cancer therapeutic agents may combine Phase I and Phase II into a single Phase I/II study. In Phase III, the product is evaluated in a larger patient population sufficient to generate data to support a claim of

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safety and efficacy within the meaning of the FDC Act or PHS Act. Permission by the FDA must be obtained before clinical testing can be initiated within the United States. This permission is obtained by submission of an IND/IDE application which typically includes, among other things, the results of *in vitro* and non-clinical testing and any previous human testing done elsewhere. The FDA has 30 days to review the information submitted and makes a final decision whether to permit clinical testing with the drug, biologic or device. However, this process can take longer if the FDA raises questions or asks for additional information regarding the IND/IDE application. Unless the FDA notifies the sponsor that the IND/IDE is subject to a clinical hold during the 30 day review period, the IND/IDE is considered effective and the trial may commence.

We cannot assure you that submission of an IND or IDE will result in the ability to commence clinical trials. In addition, after a trial begins, the FDA may place it on hold or terminate it if, among other reasons, it concludes that clinical subjects are being exposed to an unacceptable health risk. In addition, clinical trials require IRB approval before the drug may be given to subjects and are subject to continuing IRB review. An IRB may suspend or terminate approval if the IRB s requirements are not followed or if unexpected serious harm to subjects is associated with the trial. The FDA may decide not to consider, in support of an application for approval or clearance, any data that was collected in a trial without IRB approval and oversight. After completion of *in vitro*, non-clinical and clinical testing, authorization to market a drug, biologic or device must be granted by the FDA. The FDA grants permission to market through the review and approval or clearance of either an NDA, BLA, PMA, or 510(k). Historically, monoclonal antibodies have been regulated through the FDA s Center for Biologics Evaluation and Research (CBER) . As of late 2003, monoclonal antibodies, which include PROSTASCINT, were transferred to the Center for Drug Evaluation and Research (CDER), for regulation, review and approval.

An NDA is an application to the FDA to market a new drug. A BLA is an application to the FDA to market a biological product. An NDA or BLA, depending on the submission, must contain, among other things, information on chemistry, manufacturing controls and potency and purity; nonclinical pharmacology and toxicology; human pharmacokinetics and bioavailability; and clinical data. The new drug or biologic may not be approved for marketing in the United States until the FDA has determined that the NDA product is safe and effective or that the BLA product is safe, pure, and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure its continued safety, purity, and potency. For both NDAs and BLAs, the application will not be approved until the FDA conducts a manufacturing inspection and approves the applicable manufacturing process for the drug or biologic. A PMA is an application to the FDA to market certain medical devices, which must be approved in order for the product to be marketed. It must be supported by valid scientific evidence, which typically includes extensive data, including pre-clinical data and clinical data from well-controlled clinical trials to demonstrate the safety and effectiveness of the device. Product testing, manufacturing, controls, specifications and information must also be provided, and a pre-approval inspection is normally conducted. NDA, BLA, and PMA submissions may be refused review if they do not meet submission requirements.

Conducting the studies, preparing these applications and securing approval from the FDA is expensive and time consuming, and takes several years to complete. Difficulties or unanticipated costs may be encountered by us or our licensees in their respective efforts to secure necessary governmental approval or licenses, which could delay or preclude us or our licensees from marketing their products. We cannot assure you that approvals of our proposed products, processes or facilities will be granted on a timely basis, or at all. Limited indications for use or other conditions could also be placed on any approvals that could restrict the commercial applications of products. With respect to patented products or technologies, delays imposed by the government approval process may materially reduce the period during which we will have the exclusive right to exploit them, because patent protection lasts only for a limited time, beginning on the date the patent is first granted (in the case of United States patent applications filed prior to June 6, 1995) and when the patent application is first filed (in the case of patent applications filed in the United States after June 6, 1995, and applications filed in the European Economic Community). We intend to seek to maximize the useful lives of our patents under the Patent Term Restoration Act of 1984 in the United States and under similar laws if available in other countries.

Our new drug products may be subject to generic competition. Once a NDA is approved, the product covered thereby becomes a listed drug which can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application (ANDA). An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Federal law provides for a period of three

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years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor. Federal law also provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval. Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an ANDA referencing that drug are required to make certifications including that it believes one or more listed patents are invalid or not infringed. If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then the FDA cannot grant effective approval of the ANDA until those patents expire. The first of the abbreviated new drug applicant(s) submitting substantially complete applications certifying that listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days exclusivity running from when the generic product is first marketed, during which subsequently submitted ANDAs cannot be granted effective approval.

Certain of our future products may be regulated by the FDA as combination products. Combination products are products comprised of a combination of two or more different types of components, *(e.g.,* drug/device, device/biologic, drug/device/biologic), or are comprised of two or more separate different types of products packaged together for use, or two or more different types of products packaged separately but labeled for use in combination with one another. The regulation of a combination product is determined by the product s primary mode of action. For example, a combination drug/device that has a primary mode of action as a drug would be regulated by the Center for Drug Evaluation and Research under an NDA. In some cases, however, consultative reviews and/or separate approvals by each agency Center with jurisdiction over a component may be required. The product designation, approval pathway, and submission requirements for a combination product may be difficult to predict, and the approval process may be fraught with unanticipated delays and difficulties. In addition, post-approval requirements may be more extensive than for single entity products. Even if products such as PROSTASCINT or QUADRAMET that we intend to develop for use with other separately regulated products are not regulated as combination products, they may be subject to similar multi-Center consultative reviews and additional post-market requirements.

Once the FDA approves a product, we are required to maintain approval status of the product by providing certain updated safety and efficacy information at specified intervals. Most product or labeling changes to drugs or biologics as well as any change in a manufacturing process or equipment that has a substantial potential to adversely affect the safety or effectiveness of the product for a drug or biologic, or, for a device, changes that affect safety and effectiveness, would necessitate additional FDA review and approval. Post approval changes in packaging or promotional materials may also necessitate further FDA review and approval. Additionally, we are required to meet other requirements specified by the FDC Act, including but not limited to, cGMPs, enforced by periodic inspections, adverse event reporting, requirements governing labeling and promotional materials and, for drugs, biologics and restricted and PMA devices, requirements regarding advertising, and the maintenance of records. Failure to comply with these requirements or the occurrence of unanticipated safety effects from the products during commercial marketing could result in product marketing restrictions, product withdrawal or recall and/or public notifications, or other voluntary or FDA-initiated action, which could delay further marketing until the products are brought into compliance. Similar laws and regulations apply in most foreign countries where these products may be marketed.

Violations of the FDC Act, PHS Act, or regulatory requirements at any time during the product development process, approval process, or after approval may result in agency enforcement actions, including voluntary or mandatory recall, license suspension or revocation, new drug approval suspension or withdrawal, pre-market approval withdrawal, seizure of products, fines, injunction and/or civil or criminal penalties. Any agency enforcement action could have a material adverse effect on our business, financial condition and results of operations.

Orphan Drug Act

The Orphan Drug Act is intended to provide incentives to pharmaceutical companies to develop and market drugs and biologics for rare diseases or conditions affecting fewer than 200,000 persons in the United States at the time of application for orphan drug designation. A drug that receives orphan drug designation and is the first product

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to receive FDA marketing approval for a particular indication is entitled to orphan drug status, which confers a seven-year exclusive marketing period in the United States for that indication. Clinical testing requirements for orphan drugs are the same as those for products that have not received orphan drug designation but pharmaceutical companies may receive grants or tax credits for research, as well as protocol assistance. Under the Orphan Drug Act, the FDA cannot approve any application by another party to market the same drug for treatment of an identical indication unless the holder consents, the party has a license from the holder of orphan drug status, or the holder of orphan drug status is unable to assure an adequate supply of the drug, or it has been shown to be clinically superior to the approved orphan drug. However, a drug that is considered by the FDA to be different from a particular orphan drug is not barred from sale in the United States during the seven-year exclusive marketing period even if it receives marketing approval for the same product claim. In addition, holders of orphan drug status must notify the FDA of any decision to discontinue active pursuit of drug approval or biologics license, or, if such approval or license is in effect, notify the FDA at least one year prior to any discontinuance of product production. If the holder of an orphan designation cannot assure the availability of sufficient quantities of the product to meet the needs of affected patients, the FDA may withdraw orphan drug status.

Fraud and Abuse

We are subject to various federal and state laws pertaining to health care fraud and abuse, including anti-kickback laws, false claims laws and physician self-referral laws. Violations of these laws are punishable by criminal, civil and/or administrative sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state health care programs, including Medicare, Medicaid and veterans health programs. Because of the far-reaching nature of these laws, we cannot assure you that the occurrence of one or more violations of these laws would not result in a material adverse effect on our business, financial condition and results of operations.

Anti-Kickback Laws. Our operations are subject to federal and state anti-kickback laws. Certain provisions of the Social Security Act prohibit entities such as us from knowingly and willingly offering, paying, soliciting or receiving any form of remuneration (including any kickbacks, bribes or rebates) in return for the referral of items or services for which payment may be made under a federal health care program, or in return for the recommendation, arrangement, purchase, lease or order of items or services for which payment may be made under a federal health care program. Violation of the federal anti-kickback law is a felony, punishable by criminal fines and imprisonment for up to five years or both. In addition, the Department of Health and Human Services may impose civil penalties and exclude violators from participation in federal health care programs such as Medicare and Medicaid. Many states have adopted similar prohibitions against payments intended to induce referrals of products or services paid by Medicaid or other third party payors.

Physician Self-Referral Laws. We also may be subject to federal and/or state physician self-referral laws. Federal physician self-referral legislation (known as the Stark law) prohibits, subject to certain exceptions, a physician from referring Medicare or Medicaid patients to an entity to provide designated health services, including, among other things, certain radiology and radiation therapy services and clinical laboratory services in which the physician or a member of his immediate family has an ownership or investment interest or has entered into a compensation arrangement. The Stark law also prohibits the entity receiving the improper referral from billing any good or service furnished pursuant to the referral. The penalties for violations include a prohibition on payment by these government programs and civil penalties of as much as $15,000 for each improper referral and $100,000 for participation in a circumvention scheme. Various state laws also contain similar provisions and penalties.

False Claims. The federal False Claims Act imposes civil and criminal liability on individuals or entities who submit (or cause the submission of) false or fraudulent claims for payment to the government. Violations of the federal False Claims Act may result in penalties equal to three times the damages which the government sustained, an assessment of between $5,000 and $10,000 per claim, civil monetary penalties and exclusion from participation in the Medicare and Medicaid programs.

The federal False Claims Act also allows a private individual to bring a *qui tam* suit on behalf of the government against an individual or entity for violations of the False Claims Act. In a *qui tam* suit, the private plaintiff is responsible for initiating a lawsuit that may eventually lead to the government recovering money of which it was defrauded. In return for bringing the suit on the government s behalf, the statute provides that the

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private plaintiff is entitled to receive up to 30% of the recovered amount from the litigation proceeds if the litigation is successful plus reasonable expenses and attorneys fees. Recently, the number of *qui tam* suits brought against entities in the health care industry has increased dramatically. In addition, a number of states have enacted laws modeled after the False Claims Act that allow those states to recover money which was fraudulently obtained from the state.

Other Fraud and Abuse Laws. The Health Insurance Portability and Accountability Act of 1996 created, in part, two new federal crimes: (i) Health Care Fraud; and (ii) False Statements Relating to Health Care Matters. The Health Care Fraud statute prohibits the knowing and willful execution of a scheme or artifice to defraud any health care benefit program. A violation of the statute is a felony and may result in fines and/or imprisonment. The False Statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact by any trick, scheme or device or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. A violation of this statute is a felony and may result in fines and/or imprisonment.

We currently maintain several programs designed to minimize the likelihood that we would engage in conduct or enter into contracts in violation of the fraud and abuse laws. Contracts of the types subject to these laws are reviewed and approved by legal department personnel. We also maintain various educational programs designed to keep our managers updated and informed on developments with respect to the fraud and abuse laws and to reinforce to all employees the policy of strict compliance in this area. While we believe that all of our applicable agreements, arrangements and contracts comply with the various fraud and abuse laws and regulations, we cannot provide assurance that further administrative or judicial interpretations of existing laws or legislative enactment of new laws will not have a material adverse impact on our business.

Other regulations

In addition to regulations enforced by the FDA, and federal and state laws pertaining to health care fraud and abuse, we are also subject to regulation under the state and local authorities and other federal statutes and agencies including the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and the Nuclear Regulatory Commission.

Foreign regulatory approval

The regulatory approval process in Europe has changed over the past few years. There are two regulatory approval processes in Europe for products developed by us. Beginning in 1995, the centralized procedure became mandatory for all biotechnology products. Under this regulatory scheme, the application is reviewed by two scientific project leaders referred to as the rapporteur and co-rapporteur. Their roles are to prepare assessment reports of safety and efficacy and for recommending the approval for full European Union marketing.

The second regulatory scheme, referred to as the Mutual Recognition Procedure, is a process whereby a product s national registration in one member state within the European Union may be mutually recognized by other member states within the European Union.

Substantial requirements, comparable in many respects to those imposed under the FDC Act, will have to be met before commercial sale is permissible in most countries. We cannot assure you, however, as to whether or when governmental approvals, other than those already obtained, will be obtained or as to the terms or scope of those approvals.

HEALTH CARE REIMBURSEMENT

Sales of our products depend in part on the coverage status of our products and the availability of reimbursement by various payers, including federal health care programs, such as Medicare and Medicaid, as well as private health insurance plans. Whether a product receives favorable coverage depends upon a number of factors, including the payer s determination that the product is medically reasonable and necessary for the diagnosis or treatment of the illness or injury for which it is administered and not otherwise excluded from coverage by law or

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regulation. There may be significant delays in obtaining coverage for newly-approved products, and coverage may be limited or expanded outside the purpose(s) for which the product is approved by the FDA.

Eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us or any health care provider to make a profit or even cover costs, including research, development, production, sales, and distribution costs. Although new laws provide for expedited coverage for new technology, interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the approved and covered use of the product and the place of service in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid claims data. Net prices for products may be reduced by mandatory discounts or rebates required by law under government health care programs or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the U.S.

In December 2003, the Medicare Prescription Drug, Improvement and Modernization Act of 2003 was signed into law. This Act includes provisions that reduced Medicare reimbursement for many drugs and biologicals from a reimbursement rate of 95% of the average wholesale price to 80% of the average wholesale price, effective January 1, 2004. As of January 2005, the general reimbursement methodology for many drugs and biologicals is now based on average sales price , as defined by the Act, plus 6%.

Third party payers often mirror Medicare coverage policy and payment limitations in setting their own reimbursement payment and coverage policy and may have sufficient market penetration to demand significant price reductions. Even if successful, securing reimbursement coverage at adequate payment levels from government and third party payers can be a time consuming and costly process that could require us to provide additional supporting scientific, clinical and cost-effectiveness data to permit payment and coverage of our products to payers. Our inability to promptly obtain product coverage and profitable reimbursement rates from government-funded and private payers could have a material adverse effect on our business, financial condition and our results of operations.

Although health care funding has and will continue to be closely monitored by the government, the ability to diagnose patients quickly and more effectively has been one of the few areas where the government has increased health care spending. Approval of payment for new technology has been another area with required spending outlined in the 2004 legislative requirements.

The Centers for Medicare and Medicaid Services (CMS) continually monitor and update product descriptors, coverage policies, product and service codes, payment methodologies, and reimbursement values. Although it is not possible to predict or identify all of the risks relating to such changes, we believe that such risks include, but are not limited to: (i) increasing price pressures (including those imposed by regulations and practices of managed care groups and institutional and governmental purchasers); and (ii) judicial decisions and government laws related to health care reform including radiopharmaceutical, pharmaceutical and device reimbursement. In addition, an increasing emphasis on managed care has and will continue to increase the pressure on pricing of these products and services.

Our business, financial condition and results of operations will continue to be affected by the efforts of governmental and third-party payers to contain or reduce the costs of health care. There have been, and we expect that there will continue to be, federal and state proposals to constrain expenditures for medical products and services, which may affect payments for therapeutic and diagnostic imaging agents. We rely heavily on the ability to monitor changes in reimbursement and coverage and proactively influence policy and legislative changes in the areas of health care that directly impact our products. We have proven our ability to monitor changes that impact our products and have worked with the government and private payers to take advantage of the opportunities offered by legislative and policy changes for our products. While we cannot predict if legislative or regulatory proposals will be adopted or the effects managed care may have on our business, the changes in reimbursement and the adoption of new health care proposals could have a material adverse effect on our business, financial condition and results of operations. Further, to the extent that changes in health care reimbursement have a material adverse effect on other prospective corporate partners, our ability to establish strategic alliances may be materially and adversely affected.

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In certain foreign markets, the pricing and profitability of our products are generally subject to governmental controls.

KEY EMPLOYEES

Michael D. Becker currently serves as our President and Chief Executive Officer. Mr. Becker joined Cytogen in April 2001 and has served in positions of increasing responsibility, including Chief Executive Officer of our AxCell Biosciences subsidiary and Vice President, Business Development and Industry Relations. Prior to joining Cytogen, Mr. Becker was with Wayne Hummer Investments LLC, a Chicago-based regional brokerage firm from July 1996 to April 2001, where he held senior positions as a biotechnology analyst, investment executive and portfolio manager in addition to participating in sales management activities. From October 1998 to April 2001, Mr. Becker also served on the board of directors for the Chicago Biotech Network, a nonprofit trade association for the biotechnology industry in Illinois. Mr. Becker attended DePaul University in Chicago, Illinois. In September 2004, Mr. Becker was named Vice Chairman of the Biotechnology Council of New Jersey, Inc. Mr. Becker is a member of the Governing Body of Biotechnology Industry Organization s (BIO) Emerging Companies Section.

William F. Goeckeler, Ph.D. was promoted to Senior Vice President, Operations in December 2003. Previously, he served as Vice President, Operations since January 2003 and Vice President of Research and Development since June 2001. He joined Cytogen in March of 1994 as the Assistant Director, Pharmaceutical Development. In 1995, he was promoted to Associate Director, Technical Support Operations and in June 1997 became our Director, Pharmaceutical Development, a position he held until June 2001. Before joining us, Dr. Goeckeler spent nine years as a scientist in the Bioproducts Laboratory of Central Research and Development at The Dow Chemical Company. Dr. Goeckeler did his undergraduate and graduate work at the University of Missouri where he received his Ph.D. in Radiochemistry for research that involved the discovery of QUADRAMET and other skeletal targeting radiopharmaceuticals.

Christopher P. Schnittker, CPA, joined Cytogen in September 2003 and currently serves as our Senior Vice President and Chief Financial Officer. Prior to joining Cytogen, Mr. Schnittker served as Chief Financial Officer of Genaera Corporation (formerly Magainin Pharmaceuticals, Inc.) from June 2000 to August 2003. Prior to Genaera, Mr. Schnittker served as Director of Finance from August 1999 to May 2000 and Controller from December 1997 to August 1999 at GSI Commerce, Inc., a publicly-traded technology company. From June 1995 to December 1997, Mr. Schnittker held several positions of increasing responsibility at Rhône-Poulenc Rorer, Inc. (now Aventis). Prior to that, Mr. Schnittker held various positions at Price Waterhouse LLP s (now PricewaterhouseCoopers LLP) Life Sciences audit practice from 1990 to 1995. Mr. Schnittker received his Bachelor of Arts Degree from Lafayette College, and is a certified public accountant licensed in the State of New Jersey.

William J. Thomas joined Cytogen in August 2004 as our Senior Vice President and General Counsel. Prior to joining Cytogen, Mr. Thomas was a senior partner at Wilmer Cutler Pickering Hale and Dorr LLP. From 1994 through 2001, Mr. Thomas was a partner at Buchanan Ingersoll P.C. His law practice concentrated on emerging growth and high technology business issues, including securities law compliance, strategic alliances and mergers and acquisitions. Mr. Thomas received a J.D. degree from Fordham University School of Law where he was an associate editor of the Law Review. He holds a B.A. degree in Political Science from Rutgers University where he graduated with highest honors.

Michael J. Manyak, M.D., joined Cytogen in January 2005 as our Vice President of Medical Affairs. Prior to joining Cytogen, Dr. Manyak was Professor of Urology, Microbiology, and Tropical Medicine at The George Washington University Medical Center (GWUMC) where he was also Chairman of the Department of Urology. After completing his urological residency at GWUMC, Dr. Manyak became an American Foundation for Urological Disease (AFUD) Scholar at the National Cancer Institute (NCI), completed a fellowship in Biotechnology in 1988, and joined the urological staff at GWUMC. Dr. Manyak has also served on the Medicare Coverage Advisory Committee for the Center for Medicare and Medicaid Services (CMS) where he was a member of the Imaging Subcommittee. In addition, he received a presidential appointment to the National Kidney and Urological Disease Advisory Board. He was formerly a voting member of the Food and Drug Administration (FDA) Regulatory Panel for Genitourinary and Gastrointestinal Devices. He has been a reviewer for the NIH Special Study Section for Small Business Grants and several professional journals. Dr. Manyak received his Bachelor of Arts Degree from the University of Notre Dame and his medical degree from the University of the East, Manila, Philippines.

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Thu A. Dang has served as our Vice President, Finance since January 2003. Ms. Dang joined Cytogen in September 1988 as our Senior Financial Reporting Accountant, and was promoted to Director of Finance in May 2000. Prior to joining Cytogen, Ms. Dang held numerous positions with Harrisburg Dairies for six years, serving ultimately as their Controller. Ms. Dang received her Bachelor of Science Degree in Accounting from Elizabethtown College.

Rita A. Auld has served as our Vice President, Human Resources and Administration since January 2003 and as Corporate Secretary since March 2003. Ms. Auld joined Cytogen as our Director of Human Resources in October 2000. For a period of six years prior to joining Cytogen, Ms. Auld was the Director of Human Resources of Flexpaq Corporation, where she established the Human Resources Department, developing procedures, handbooks and benefit and safety programs. Ms. Auld has over 20 years of experience with sales, manufacturing, accounting and engineering organizations, directing the activities of human resources and administrative functions, specializing in small-sized companies, both public and private. Ms. Auld holds Associates and Bachelor of Science Degrees in Business Administration from Thomas A. Edison State College and is certified as a Human Resources Professional.

EMPLOYEES

As of March 1, 2006, we employed 79 persons, 77 of whom are employed full-time and two of whom are employed part-time. Of such 79 persons, 50 were employed in sales and marketing, 8 in medical affairs, 3 in regulatory, and 19 in administration and management. We believe that we have been successful in attracting skilled and experienced employees. None of our employees is covered by a collective bargaining agreement. All of our employees have executed confidentiality agreements. We consider relations with our employees to be excellent.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with other information included or incorporated by reference in this Annual Report on Form 10-K in your decision as to whether or not to invest in our common stock. If any of the following risks or uncertainties actually occur, our business, financial condition or results of operations would likely suffer. In that case, the trading price of our common stock could fall, and you may lose all or part of the money you paid to buy our common stock.

We have a history of operating losses and an accumulated deficit and expect to incur losses in the future.

Given the high level of expenditures associated with our business and our inability to generate revenues sufficient to cover such expenditures, we have had a history of operating losses since our inception. We had net losses of $26.3 million, $20.5 million and $9.4 million for the years ended December 31, 2005, 2004 and 2003, respectively. We had an accumulated deficit of $412.6 million as of December 31, 2005.

In order to develop and commercialize our technologies, particularly our prostate-specific membrane antigen technology, and expand our products, we expect to incur significant increases in our expenses over the next several years. As a result, we will need to generate significant additional revenue to become profitable.

To date, we have taken affirmative steps to address our trend of operating losses. Such steps include, among other things:

undergoing steps to realign and implement our focus as a product-driven biopharmaceutical company;

establishing and maintaining our in-house specialty sales force;

reacquiring North American and Latin American marketing rights to QUADRAMET from Berlex Laboratories in August 2003; and

enhancing our marketed product portfolio through marketing alliances and strategic arrangements.

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Although we have taken these affirmative steps, we may never be able to successfully implement them, and our ability to generate and sustain significant additional revenues or achieve profitability will depend upon the factors discussed elsewhere in this section entitled, Risk Factors. As a result, we may never be able to generate or sustain significant additional revenue or achieve profitability.

We depend on sales of QUADRAMET and PROSTASCINT for substantially all of our near-term revenues.

We expect QUADRAMET and PROSTASCINT to account for substantially all of our product related revenues in the near future. For the year ended December 31, 2005, revenues from QUADRAMET and PROSTASCINT accounted for approximately 53% and 47%, respectively, of our product related revenues. For the year ended December 31, 2004, revenues from QUADRAMET and PROSTASCINT each accounted for approximately 50% of our product related revenues. For the year ended December 31, 2003, royalty and product revenues from QUADRAMET and sales revenues from PROSTASCINT accounted for approximately 35% and 60%, respectively, of our product related revenues. If QUADRAMET or PROSTASCINT does not achieve broader market acceptance, either because we fail to effectively market such products or our competitors introduce competing products, we may not be able to generate sufficient revenue to become profitable.

A Small Number of Customers Account for the Majority of Our Sales, and the Loss of One of Them, or Changes in Their Purchasing Patterns, Could Result in Reduced Sales, Thereby Adversely Affecting Our Operating Results.

We sell our products to a small number of radiopharmacy networks. During the year ended December 31, 2005, we received 67% of our total revenues from three customers, as follows: 47% from Cardinal Health (formerly Syncor International Corporation); 11% from Mallinckrodt Inc.; and 9% from GE Healthcare (formerly Amersham Health). During the year ended December 31, 2004, we received 68% of our total revenues from three customers, as follows: 46% from Cardinal Health (formerly Syncor International Corporation); 12% from Mallinckrodt Inc.; and 10% from GE Healthcare (formerly Amersham Health). During the year ended December 31, 2003, we received 69% of our total revenues from four customers, as follows: 24% from Cardinal Health (formerly Syncor International Corporation); 23% from Berlex Laboratories Inc.; 14% from Mallinckrodt Inc., and 8% from GE Healthcare (formerly Amersham Health).

The small number of radiopharmacies, consolidation in this industry or financial difficulties of these radiopharmacies could result in the combination or elimination of customers for our products. We anticipate that our results of operations in any given period will continue to depend to a significant extent upon sales to a small number of customers. As a result of this customer concentration, our revenues from quarter to quarter and business, financial condition and results of operations may be subject to substantial period-to-period fluctuations. In addition, our business, financial condition and results of operations could be materially adversely affected by the failure of customer orders to materialize as and when anticipated. None of our customers have entered into an agreement requiring on-going minimum purchases from us. We cannot assure you that our principal customers will continue to purchase products from us at current levels, if at all. The loss of one or more major customers could have a material adverse effect on our business, financial condition and results of operations.

We depend on acceptance of our products by the medical community for the continuation of our revenues.

Our business, financial condition and results of operations depend on the acceptance of our marketed products as safe, effective and cost-efficient alternatives to other available treatment and diagnostic protocols by the medical community, including:

- health care providers, such as hospitals and physicians; and
- third-party payors, including Medicare, Medicaid, private insurance carriers and health maintenance organizations.

With respect to PROSTASCINT, our customers, including technologists and physicians, must successfully complete our Partners in Excellence, or PIE, Program, a proprietary training program designed to promote the correct acquisition and interpretation of PROSTASCINT images. This product is technique-dependent and requires a learning commitment by technologists and physicians and their acceptance of this product as part of their treatment

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practices. With respect to QUADRAMET, we believe that challenges we may encounter in generating market acceptance for this product include the need to further educate patients and physicians about QUADRAMET s properties, approved uses and how QUADRAMET may be differentiated from other radiopharmaceuticals and used in combination with other treatments for the palliation of pain due to metastatic bone disease, such as analgesics, opioids, bisphosphonates, and chemotherapeutics. If we are unable to educate our existing and future customers about PROSTASCINT and QUADRAMET, our revenues may decrease. If PROSTASCINT or QUADRAMET does not achieve broader market acceptance, we may not be able to generate sufficient revenue to become profitable.

Generating market acceptance and sales of our products has proven difficult. We launched ONCOSCINT CR/OV in December 1992, PROSTASCINT in October 1996, QUADRAMET in March 1997, a brachytherapy product in February 2001 and NMP22 BLADDERCHEK in November 2002. Revenues for PROSTASCINT grew from $55,000 in 1996 to $7.4 million in 2005. Royalties and sales of QUADRAMET grew from $3.3 million in 1997 to $8.4 million in 2005. Royalties from sales of QUADRAMET in the initial years of sales were supported by a guaranteed minimum revenue arrangement with the third party licensor of QUADRAMET. We discontinued selling ONCOSCINT CR/OV in December 2002, brachytherapy products in January 2003 and NMP22 BLADDERCHEK in December 2004. Currently, substantially all of our revenues are derived from sales of PROSTASCINT and QUADRAMET.

We rely heavily on our collaborative partners.

Our success depends largely upon the success and financial stability of our collaborative partners. We have entered into the following agreements for the development, sale, marketing, distribution and manufacture of our products, product candidates and technologies:

- a license agreement with The Dow Chemical Company relating to the QUADRAMET technology;
- a manufacturing and supply agreement for the manufacture of QUADRAMET with Bristol-Myers Squibb Medical Imaging, Inc.;
- a manufacturing agreement for the manufacture of PROSTASCINT with Laureate Pharma, L.P.;
- marketing, license and supply agreements with Advanced Magnetics, Inc. related to COMBIDEX and ferumoxytol (formerly Code 7228);
- a distribution services agreement with Cardinal Health 105, Inc. (formerly Cord Logistics, Inc.) for PROSTASCINT;
- various agreements which form and control our joint venture with Progenics Pharmaceuticals, Inc. for the development of PSMA for *in vivo* immunotherapy for prostate and other cancers;
- a license agreement with The Dow Chemical Company relating to Dow s proprietary MeO-DOTA bifunctional chelant technology for use with our Therapeutic 7E11-C5 Monoclonal Antibody program;
- a development and manufacturing agreement with Laureate Pharma, L.P. for the scale-up for the cGMP manufacturing of a MeO-DOTA chelator conjugate of the 7E11-C5 monoclonal antibody;
- a collaboration agreement between our joint venture and Seattle Genetics, Inc. for an exclusive worldwide license to SGI s proprietary ADC Technology; and

a license agreement between our joint venture and AlphaVax Human Vaccines, Inc.

Because our collaborative partners are responsible for certain manufacturing and distribution activities, among others, these activities are outside our direct control and we rely on our partners to perform their obligations. In the event that our collaborative partners are entitled to enter into third party arrangements that may economically

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disadvantage us, or do not perform their obligations as expected under our agreements, our products may not be commercially successful. As a result, any success may be delayed and new product development could be inhibited with the result that our business, financial condition and results of operation could be significantly and adversely affected.

In January 2006, we filed a complaint against Advanced Magnetics in the Massachusetts Superior Court for breach of contract, fraud, unjust enrichment, and breach of the implied covenant of good faith and fair dealing in connection with the parties 2000 license agreement. The complaint seeks damages along with a request for specific performance requiring Advanced Magnetics to take all reasonable steps to secure FDA approval of COMBIDEX in compliance with the terms of the licensing agreement. In February 2006, Advanced Magnetics filed an answer to our complaint and asserted various counterclaims, including tortuous interference, defamation, consumer fraud and abuse of process. We believe these counterclaims have no merit and we plan to conduct a vigorous defense of these claims.

Our business could be harmed if certain agreements expire or are terminated.

If our collaborative agreements expire or are terminated and we cannot renew or replace them on commercially reasonable terms, our business and financial results may suffer. If the licenses and/or agreements described below expire or are terminated, we may not be able to find suitable alternatives to them on a timely basis or on reasonable terms, if at all. The loss of the right to use these technologies that we have licensed or the loss of any services provided to us under these agreements would significantly and adversely affect our business, financial condition and results of operations. For example, in January 2003, we provided Draximage Inc. with notice of our intent to terminate our product manufacturing and supply agreement and license agreement with Draximage relating to the brachytherapy products which represented 20% of our product-related revenues for the year ended December 31, 2002. In April 2003, we entered into an agreement with Draximage formally terminating each of these agreements. We no longer market and sell the brachytherapy products.

We currently depend on the following agreements for our present and future operating results:

Dow Chemical. In May 1993, we obtained an exclusive license from The Dow Chemical Company to use QUADRAMET, in North America, as a therapeutic radiopharmaceutical for metabolic bone disease or tumor regression for cancer caused by metastatic or primary cancer in bone in humans, and for the treatment of disease characterized by osteoblastic response in humans. Our license was expanded to include Latin America in 1995. Our license agreement with Dow with respect to QUADRAMET will remain in effect, unless earlier terminated, for a period of twenty (20) years from May 30, 1993 or until the last to expire of the related patents. We anticipate such termination date to be May 30, 2013.

Bristol-Myers Squibb Medical Imaging, Inc. QUADRAMET is manufactured by BMS-MI under the terms of a manufacturing and supply agreement with us which became effective on January 1, 2004. Under this agreement, BMS-MI has agreed to manufacture, supply and distribute QUADRAMET for us in exchange for a minimum payment of at least $4.2 million annually, subject to future annual price adjustment, through 2008. After 2008, the agreement will then renew for five successive one-year periods. The agreement is terminable by either party, at any time, upon two years notice to the other. We also pay BMS-MI a variable amount per month for each order placed to cover the cost of customer service.

Agreement with Dr. Horosziewicz regarding PROSTASCINT. In 1989, we entered into an agreement with Dr. Julius S. Horosziewicz. Under this agreement, we were assigned certain rights to the patent claiming the 7E11-C5 antibody, as well as additional patents relating to the PROSTASCINT product and commercialization rights thereto. Under this agreement, we have made, and may continue to make, certain payments to Dr. Horosziewicz, which obligation will remain in effect until the expiration of the last related patent in 2015.

Laureate Pharma, L.P. In September 2004, we entered into a non-exclusive manufacturing agreement with Laureate Pharma, L.P. Under this agreement, Laureate is manufacturing PROSTASCINT for us in exchange for expected payments of at least an aggregate of $5.1 million through the end of the contract. This agreement will terminate, unless terminated earlier pursuant to its terms, upon Laureate s completion of the production campaign of PROSTASCINT and shipment of the resulting products from Laureate s facility in Princeton, NJ. We believe that

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this agreement will provide us with a sufficient supply of PROSTASCINT to satisfy our commercial requirements for approximately the next three to four years, based upon recent sales levels. In addition, we believe the agreement will provide sufficient supply of 7E11-C5 required for the initial clinical development of our therapeutic program. In October 2004, Laureate was acquired by Safeguard Scientifics, Inc. Laureate has continued to operate as a full service contract manufacturing organization and we have not experienced any disruption in Laureate s performance of its obligations to produce PROSTASCINT.

Advanced Magnetics, Inc. In August 2000, we entered into a license and marketing agreement with Advanced Magnetics, Inc. for COMBIDEX, for all applications, and ferumoxytol (formerly Code 7228) for oncology applications only. In 2000, we also entered into a supply agreement with Advanced Magnetics for COMBIDEX. We have exclusive United States marketing rights to COMBIDEX for all applications. COMBIDEX (ferumoxtran-10) is an investigational functional molecular imaging agent consisting of iron oxide nanoparticles for use in conjunction with magnetic resonance imaging to aid in the differentiation of cancerous from normal lymph nodes, and is currently under review by the FDA. In September 2004, Advanced Magnetics submitted a complete response to an approvable letter received in June 2000 from the FDA for COMBIDEX. On March 3, 2005, the FDA s Oncologic Drugs Advisory Committee (ODAC) voted 15 to 4 to not recommend approval of the proposed broad indication for COMBIDEX being sought by Advanced Magnetics. On March 24, 2005, Advanced Magnetics informed us that Advanced Magnetics received an approvable letter from the FDA for COMBIDEX, subject to certain conditions. We cannot assure you that Advanced Magnetics will receive FDA approval for COMBIDEX or ferumoxytol (for oncology applications). Our license and marketing agreement with Advanced Magnetics will continue until August 25, 2010, and will thereafter automatically renew for successive five year periods, unless notice of non-renewal or termination is given by us or Advanced Magnetics, 90 days prior to the commencement of any renewal period. In January 2006, we filed a complaint against Advanced Magnetics in the Massachusetts Superior Court for breach of contract, fraud, unjust enrichment, and breach of the implied covenant of good faith and fair dealing in connection with the parties 2000 license agreement. The complaint seeks damages along with a request for specific performance requiring Advanced Magnetics to take all reasonable steps to secure FDA approval of COMBIDEX in compliance with the terms of the licensing agreement. In February 2006, Advanced Magnetics filed an answer to our complaint and asserted various counterclaims, including tortuous interference, defamation, consumer fraud and abuse of process. We believe these counterclaims have no merit and we plan to conduct a vigorous defense of these counterclaims.

Sloan Kettering Institute for Cancer Research. In 1993, we began a development program with SKICR involving PSMA and our proprietary monoclonal antibody. In November 1996, we exercised an option for, and obtained, an exclusive worldwide license from the SKICR to its PSMA-related technology. The license will terminate on the date of expiration of the last to expire of the licensed patents unless it is terminated earlier.

Our intellectual property is difficult to protect.

In addition to our key agreements referenced above, our business and competitive positions are also dependent upon our ability to protect our proprietary technology. Because of the substantial length of time and expense associated with the development of new products, we, like the rest of the biopharmaceutical industry, place considerable importance on obtaining and maintaining patent and trade secret protection for new technologies, products and processes. We have filed patent applications for certain aspects of our technology for diagnostic and therapeutic products and/or the methods for their production and use.

In addition, the protection afforded by a duly issued patent is limited in duration. With respect to our PROSTASCINT product, we rely or have relied primarily on United States patent numbers 5,162,504 (expiring October 28, 2010), 4,741,900 (expired June 9, 2004), 4,671,958 (expired June 9, 2004), and 4,867,973 (expired June 9, 2004). With respect to QUADRAMET, we rely primarily on United States patent numbers 4,898,724 (expiring March 28, 2011), 4,937,333 (expiring August 4, 2009), 4,897,254 (expiring January 30, 2007), 5,066,478 (expiring November 19, 2008), and 5,300,279 (expiring November 19, 2008), which were licensed to us by The Dow Chemical Company. In addition, we rely on United States patent number 5,495,042 (expiring November 4, 2013), which is assigned to us, and United States patent numbers 5,714,604 (expiring February 3, 2015) and 5,762,907 (expiring November 21, 2006).

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The patent positions of pharmaceutical, biopharmaceutical and biotechnology companies, including us, are generally uncertain and involve complex legal and factual questions. Our patents and patent applications may not protect our technologies and products because, among other things:

- there is no guarantee that any of our pending patent applications will result in issued patents;
- we may develop additional proprietary technologies that are not patentable;
- there is no guarantee that any patents issued to us, our collaborators or our licensors will provide a basis for a commercially viable product;
- there is no guarantee that any patents issued to us or our collaborators will provide us with any competitive advantage;
- there is no guarantee that any patents issued to us or our collaborators will not be challenged, circumvented or invalidated by third parties; and
- there is no guarantee that any patents previously issued to others or issued in the future will not have an adverse effect on our ability to do business.

In addition, patent law in the technology fields in which we operate is uncertain and still evolving. The degree of protection that may be afforded by any patents we are issued or license from others may not be sufficient to protect our commercial interests. Furthermore, others may independently develop similar or alternative technologies, duplicate our technologies, or, if patents are issued to us, design around the patented technologies developed by us. We could incur substantial costs in litigation if we are required to defend ourselves in patent suits by third parties or if we initiate such suits. In addition, if challenged by others in litigation, the patents we have been issued, which we have been assigned or we have licensed from others may be found invalid. It is also possible that our activities may infringe patents owned by others. Defense and prosecution of patent matters can be expensive and time-consuming and, regardless of whether the outcome is favorable to us, can result in the diversion of substantial financial, managerial and other resources. An adverse outcome could:

- subject us to significant liability to third parties;
- require us to cease any related research and development activities and product sales; or
- require us to obtain licenses from third parties.

Any licenses required under any of these third-party patents or proprietary rights may not be available on commercially reasonable terms, if at all. Moreover, the laws of certain countries may not protect our proprietary rights to the same extent as the laws of the United States. We cannot predict whether our or our competitors pending patent applications will result in the issuance of valid patents which may significantly and adversely affect our business, financial condition and results of operations.

There are risks associated with the manufacture and supply of our products.

If we are to be successful, our products will have to be manufactured by contract manufacturers in compliance with regulatory requirements and at costs acceptable to us. If we are unable to successfully arrange for the manufacture of our products and product candidates, either because potential manufacturers are not cGMP compliant, are not available or charge excessive amounts, we will not be able to successfully commercialize our products and our business, financial condition and results of operations will be significantly and adversely affected.

PROSTASCINT is currently manufactured at a current Good Manufacturing Practices, or cGMP, compliant manufacturing facility operated by Laureate Pharma, L.P. We entered into a development and manufacturing agreement with DSM Biologics Company B.V. in July 2000, which we intended would replace an earlier arrangement we had with Laureate with respect to PROSTASCINT. Our relationship with DSM was

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subsequently terminated. Although we entered into another agreement with Laureate in September 2004 which provides for Laureate s manufacture of PROSTASCINT for us, our failure to maintain a long term supply agreement on commercially reasonable terms will have a material adverse effect on our business, financial condition and results of operations. In October 2004, Laureate was acquired by Safeguard Scientifics, Inc. Laureate has continued to operate as a full service contract manufacturing organization and we have not experienced any disruption in Laureate s performance of its obligations to produce PROSTASCINT.

We have an agreement with BMS-MI to manufacture QUADRAMET for us. Both primary components of QUADRAMET, particularly Samarium-153 and EDTMP, are provided to BMS-MI by outside suppliers. Due to radioactive decay, Samarium-153 must be produced on a weekly basis. BMS-MI obtains its requirements for Samarium-153 from a sole supplier and EDTMP from another sole supplier. Alternative sources for these components may not be readily available, and any alternative supplier would have to be identified and qualified, subject to all applicable regulatory guidelines. If BMS-MI cannot obtain sufficient quantities of the components on commercially reasonable terms, or in a timely manner, it would be unable to manufacture QUADRAMET on a timely and cost-effective basis, which would have a material adverse effect on our business, financial condition and results of operations.

The Company, our contract manufacturers and testing laboratories are required to adhere to FDA regulations setting forth requirements for cGMP, and similar regulations in other countries, which include extensive testing, control and documentation requirements. Ongoing compliance with cGMP, labeling and other applicable regulatory requirements is monitored through periodic inspections and market surveillance by state and federal agencies, including the FDA, and by comparable agencies in other countries. Failure of our contract vendors or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market clearance or pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of products, operating restrictions and criminal prosecutions any of which could significantly and adversely affect our business, financial condition and results of operations.

Our products, generally, are in the early stages of development and commercialization and we may never achieve the revenue goals set forth in our business plan.

We began operations in 1980 and have since been engaged primarily in research directed toward the development, commercialization and marketing of products to improve the diagnosis and treatment of cancer and other diseases. In October 1996, we introduced for commercial use our PROSTASCINT imaging agent. In March 1997, we introduced for commercial use our QUADRAMET therapeutic product.

In February 2006, we executed a binding letter of intent with Savient Pharmaceuticals, Inc. to negotiate a definitive agreement granting us exclusive marketing rights for SOLTAMOX (tamoxifen citrate) in the United States. SOLTAMOX, an oral liquid hormonal therapy, is approved for marketing in the United States. Consummation of the transaction is subject to a number of conditions, including satisfactory completion of due diligence by us and negotiation and execution of definitive licensing and supply agreements.

In August, 2000, we entered into a license and marketing agreement with Advanced Magnetics for COMBIDEX, for all applications, and ferumoxytol (formerly Code 7228) for oncology applications only. We have exclusive United States marketing rights to COMBIDEX. On March 3, 2005, the FDA s Oncologic Drugs Advisory Committee (ODAC) voted 15 to 4 to not recommend approval of the proposed broad indication for COMBIDEX being sought by Advanced Magnetics. On March 24, 2005, Advanced Magnetics, Inc. informed us that Advanced Magnetics received an approvable letter from the FDA for COMBIDEX, subject to certain conditions.

We cannot assure you, however, that Advanced Magnetics will obtain approval from the FDA for COMBIDEX on a timely basis, if at all. If Advanced Magnetics does not secure regulatory approval for COMBIDEX, we will not be permitted to sell and market COMBIDEX as we have anticipated and we will not realize any return on the significant amount of time and resources we have allocated to COMBIDEX. Ferumoxytol is being developed by Advanced Magnetics for use as an iron replacement therapeutic in chronic kidney disease patients and Advanced Magnetics has stated that no clinical applications are currently planned or contemplated for oncology applications. We cannot assure you that ferumoxytol will be developed for oncology applications.

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In July 2004, as part of our continuing efforts to reduce non-strategic expenses, we initiated the closure of facilities at our AxCell Biosciences subsidiary. Research projects through academic, governmental and corporate collaborators will continue to be supported and additional applications for the intellectual property and technology at AxCell are being pursued. We may be unable to further develop or commercialize any of these products and technologies in the future.

Further, our PSMA technologies are still in the early stages of development. All of our PSMA programs are either in preclinical or Phase I stages.

Our business is therefore subject to the risks inherent in an early-stage biopharmaceutical business enterprise, such as the need:

- to obtain sufficient capital to support the expenses of developing our technology and commercializing our products;
- to ensure that our products are safe and effective;
- to obtain regulatory approval for the use and sale of our products;
- to manufacture our products in sufficient quantities and at a reasonable cost;
- to develop a sufficient market for our products; and
- to attract and retain qualified management, sales, technical and scientific staff.

The problems frequently encountered using new technologies and operating in a competitive environment also may affect our business, financial condition and results of operations. If we fail to properly address these risks and attain our business objectives, our business could be significantly and adversely affected.

All of our potential oncology products will be subject to the risks of failure inherent in the development of diagnostic or therapeutic products based on new technologies.

Product development for cancer treatment involves a high degree of risk. The product candidates we develop, pursue or offer may not prove to be safe and effective, may not receive the necessary regulatory approvals, may be precluded by proprietary rights of third parties or may not ultimately achieve market acceptance. These product candidates will require substantial additional investment, laboratory development, clinical testing and regulatory approvals prior to their commercialization. We may experience difficulties, such as the inability to agree with our collaborative partners on development, initiate clinical trials or receive timely regulatory approvals, that could delay or prevent the successful development, introduction and marketing of new products.

Before we obtain regulatory approvals for the commercial sale of any of our products under development, we must demonstrate through preclinical studies and clinical trials that the product is safe and effective for use in each target indication. The results from preclinical studies and early-stage clinical trials may not be predictive of results that will be obtained in large-scale, later-stage testing. Our clinical trials may not demonstrate safety and efficacy of a proposed product, and therefore, may not result in marketable products. A number of companies in our industry have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. Clinical trials or marketing of any potential diagnostic or therapeutic products may expose us to liability claims for the use of these diagnostic or therapeutic products. We may not be able to maintain product liability insurance or sufficient coverage may not be available at a reasonable cost. In addition, internal development of diagnostic or therapeutic products will require significant investments in product development, marketing, sales and regulatory compliance resources. We will also have to establish or contract for the manufacture of products, including supplies of drugs used in clinical trials, under the cGMP of the FDA. We cannot assure you that product issues will not arise following successful clinical trials and FDA approval.

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The rate of completion of clinical trials also depends on the rate of patient enrollment. Patient enrollment depends on many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites and the eligibility criteria for the study. Delays in planned patient enrollment may result in increased costs and delays, which could have a harmful effect on our ability to develop the products in our pipeline. If we are unable to develop and commercialize products on a timely basis or at all, our business, financial condition and results of operations could be significantly and adversely affected.

Competition in our field is intense and likely to increase.

All of our products and product candidates are subject to significant competition from organizations that are pursuing technologies and products that are the same as or similar to our technology and products. Many of the organizations competing with us have greater capital resources, research and development staffs and facilities and marketing capabilities.

We face, and will continue to face, intense competition from one or more of the following entities:

- pharmaceutical companies;
- biotechnology companies;
- diagnostic companies;
- medical device companies;
- radiopharmaceutical distributors;
- academic and research institutions; and
- government agencies.

QUADRAMET primarily competes with Strontium-89 chloride in the radiopharmaceutical pain palliation market. Strontium-89 chloride is manufactured and marketed either as Metastron, by GE HealthCare, or in a generic form by Bio-Nucleonics Pharma, Inc. GE HealthCare manufactures Metastron and sells the product through its wholly-owned network of radiopharmacies, direct to end-users and through other radiopharmacy distributors. The generic version is distributed directly by the manufacturer or is sold through radiopharmacy distributors such as Cardinal Health and AnazaoHealth (formerly Custom Care Pharmacy).

Competitive imaging modalities to PROSTASCINT include computed tomography (CT), magnetic resonance (MR) imaging, and position emission tomography (PET).

Additionally, we face competition in the development of PSMA-related technology and products primarily from Millennium Pharmaceuticals, Inc. and Medarex, Inc.

Before we recover development expenses for our products and technologies, the products or technologies may become obsolete as a result of technological developments by others or us. Our products could also be made obsolete by new technologies, which are less expensive or more effective. We may not be able to make the enhancements to our technology necessary to compete successfully with newly emerging technologies and failure to do so could significantly and adversely affect our business, financial condition and results of operations.

We have limited sales, marketing and distribution capabilities for our products.

We have established an internal sales force that is responsible for marketing and selling PROSTASCINT and QUADRAMET. Although we are continuing to expand our internal sales force, it still has limited sales, marketing and distribution capabilities compared to those of many of our competitors. Effective August 1, 2003, we reacquired marketing rights to QUADRAMET from Berlex Laboratories, Inc. in North and Latin America, for an

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upfront payment of $8.0 million and the obligation to pay royalties to Berlex on future sales of QUADRAMET. If our internal sales force is unable to successfully market QUADRAMET and PROSTASCINT, our business and financial condition may be adversely affected. If we are unable to establish and maintain significant sales, marketing and distribution efforts within the United States, either internally or through arrangements with third parties, our business may be significantly and adversely affected. In locations outside of the United States, we have not established a selling presence. To the extent that our sales force, from time to time, markets and sells additional products, we cannot be certain that adequate resources or sales capacity will be available to effectively accomplish these tasks.

Failure of third party payors to provide adequate coverage and reimbursement for our products could limit market acceptance and affect pricing of our products and affect our revenues.

Sales of our products depend in part on the availability of favorable coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid as well as private health insurance plans. Each payor has its own process and standards for determining whether and, if so, to what extent it will cover and reimburse a particular product or service. Whether and to what extent a product may be deemed covered by a particular payor depends upon a number of factors, including the payor s determination that the product is reasonable and necessary for the diagnosis or treatment of the illness or injury for which it is administered according to accepted standards of medical practice, cost effective, not experimental or investigational, not found by the FDA to be less than effective, and not otherwise excluded from coverage by law, regulation, or contract. There may be significant delays in obtaining coverage for newly-approved products, and coverage may not be available or could be more limited than the purposes for which the product is approved by the FDA.

Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs, which include, for example, research, development, production, sales, and distribution costs. Interim payments for new products, if applicable, also may not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower-cost products that are already reimbursed, may be incorporated into existing payments for other products or services, and may reflect budgetary constraints and/or imperfections in Medicare or Medicaid data. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs, or other payors, or by any future relaxation of laws that restrict imports of certain medical products from countries where they may be sold at lower prices than in the United States.

Third party payors often follow Medicare coverage policy and payment limitations in setting their own coverage policies and reimbursement rates, and may have sufficient market power to demand significant price reductions. Even if successful, securing coverage at adequate reimbursement rates from government and third party payors can be a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products among other data and materials to each payor. Our inability to promptly obtain favorable coverage and profitable reimbursement rates from government-funded and private payors for our products could have a material adverse effect on our business, financial condition and results of operations, and our ability to raise capital needed to commercialize products.

Our business, financial condition and results of operations will continue to be affected by the efforts of governmental and third-party payors to contain or reduce the costs of healthcare. There have been, and we expect that there will continue to be, a number of federal and state proposals to regulate expenditures for medical products and services, which may affect payments for therapeutic and diagnostic imaging agents such as our products. In addition, an emphasis on managed care increases possible pressure on the pricing of these products. While we cannot predict whether these legislative or regulatory proposals will be adopted, or the effects these proposals or managed care efforts may have on our business, the announcement of these proposals and the adoption of these proposals or efforts could affect our stock price or our business. Further, to the extent these proposals or efforts have an adverse effect on other companies that are our prospective corporate partners, our ability to establish necessary strategic alliances may be harmed.

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If we are unable to comply with applicable governmental regulation we may not be able to continue our operations.

Any products tested, manufactured or distributed by us or on our behalf pursuant to FDA approvals are subject to pervasive and continuing regulation by numerous regulatory authorities, including primarily the FDA. We may be slow to adapt, or we may never adapt, to changes in existing requirements or adoption of new requirements or policies. Our failure to comply with regulatory requirements could subject us to enforcement action, including product seizures, recalls, withdrawal, suspension, or revocation of approvals, restrictions on or injunctions against marketing our products based on our technology, and civil and criminal penalties. We may incur significant costs to comply with laws and regulations in the future or compliance with laws or regulations may create an unsustainable burden on our business.

Numerous federal, state and local governmental authorities, principally the FDA, and similar regulatory agencies in other countries, regulate the preclinical testing, clinical trials, manufacture and promotion of any compounds or agents we or our collaborative partners develop, and the manufacturing and marketing of any resulting drugs. The product development and regulatory approval process is lengthy, expensive, uncertain and subject to delays.

The regulatory risks we face also include the following:

- any compound or agent, including generics, we or our collaborative partners develop must receive regulatory agency approval before it may be marketed as a drug in a particular country;

- the regulatory process, which includes preclinical testing and clinical trials of each compound or agent in order to establish its safety and efficacy, varies from country to country, can take many years and requires the expenditure of substantial resources;

- in all circumstances, approval of the use of previously unapproved radioisotopes in certain of our products requires approval of the Nuclear Regulatory Commission and/or equivalent state regulatory agencies, which may be a lengthy process. A radioisotope is an unstable form of an element which undergoes radioactive decay, thereby emitting radiation which may be used, for example, to image or destroy harmful growths or tissue;

- data obtained from preclinical and clinical activities are susceptible to varying interpretations which could delay, limit or prevent regulatory agency approval; and

- delays or rejections may be encountered based upon changes in regulatory agency policy during the period of product development and/or the period of review of any application for regulatory agency approval. These delays could adversely affect the marketing of any products we or our collaborative partners develop, impose costly procedures upon our activities, diminish any competitive advantages we or our collaborative partners may attain and adversely affect our ability to receive royalties.

Regulatory agency approval for a product or agent may not be received and may entail limitations on the indicated uses that could limit the potential market for that product. For example, as disclosed in our press releases and periodic filings, we have exclusive United States marketing rights to COMBIDEX, an investigational functional molecular imaging agent consisting of iron oxide nanoparticles, which is currently being developed for use in conjunction with magnetic resonance imaging to aid in the differentiation of cancerous from normal lymph nodes, and is under review by the FDA. In June 2000, Advanced Magnetics received an approvable letter from the FDA with respect to COMBIDEX. An approvable letter is a written communication to an applicant from the FDA stating that the agency will approve the application or abbreviated application if specific and satisfactory additional information or material is submitted or specific conditions are met. An approvable letter does not constitute approval of any part of an application or abbreviated application and does not permit marketing of the drug that is the subject of the application or abbreviated application. In September 2004, Cytogen and Advanced Magnetics announced that Advanced Magnetics submitted a complete response to the approvable letter for COMBIDEX. On March 3, 2005, the FDA s Oncologic Drugs Advisory Committee, or ODAC, voted 15 to 4 to not recommend approval of the proposed broad indication for COMBIDEX being sought by Advanced Magnetics. On March 24, 2005, Advanced

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Magnetics informed us that Advanced Magnetics received an approvable letter from the FDA for COMBIDEX, subject to certain conditions.

If and when we obtain approval or clearance for our products, the marketing, manufacture, labeling, packaging, adverse event and other reporting, storage, advertising and promotion and record keeping related to our products would remain subject to extensive regulatory requirements. Discovery of previously unknown problems with a drug, its manufacture or its manufacturer may result in restrictions on that drug, manufacture or manufacturer, including withdrawal of the drug from the market.

The Food, Drug and Cosmetics Act and the Public Health Service Act require: (i) that our products be manufactured in FDA registered facilities subject to inspection; and (ii) that we comply with cGMP, which imposes certain procedural and documentation requirements upon us and our manufacturing partners with respect to manufacturing and quality assurance activities. If we or our contract partners do not comply with cGMP or we do not comply with any of the FDA s other postmarket requirements we may be subject to sanctions, including fines, injunctions, civil penalties, recalls or seizures of products, total or partial suspension of production, product recalls, failure of the government to grant clearance or premarket approval for devices or premarket approval for drugs or biologics, suspension, revocation or withdrawal of marketing approvals and criminal prosecution.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of these changes, if any, may be.

We depend on attracting and retaining key personnel.

We are highly dependent on the principal members of our management and scientific staff. The loss of their services might significantly delay or prevent the achievement of development or strategic objectives. Our success depends on our ability to retain key employees and to attract additional qualified employees. Competition for personnel is intense, and therefore we may not be able to retain existing personnel or attract and retain additional highly qualified employees in the future.

On December 17, 2002, we entered into a letter agreement with Michael D. Becker in connection with Mr. Becker s promotion to President and Chief Executive Officer of the Company. Mr. Becker s annual base salary for 2006 is $312,000. Mr. Becker is also eligible to participate in our Cytogen Corporation Performance Bonus Plan, as and if approved by our Board of Directors, with a target bonus rate of 35% of base salary based upon performance objectives. Mr. Becker is also entitled to all existing Company benefits. In addition, Mr. Becker was granted options to purchase 200,000 shares of our common stock under our 1995 Stock Option Plan, of which options to purchase 150,000 shares are performance-based and will vest, if at all, upon the achievement of milestones as determined by our Board of Directors. Mr. Becker has subsequently received additional options to purchase shares of our common stock. Under the terms of the letter agreement, in the event we terminate Mr. Becker s employment for reasons other than for cause, as defined therein, Mr. Becker shall be entitled to receive twelve months base pay and continuation of benefits under COBRA, and a pro rata portion of any incentive benefits earned through the date of termination.

We do not carry key person life insurance policies and we do not typically enter into long-term arrangements with our key personnel. If we are unable to hire and retain personnel in key positions, our business, financial condition and results of operations could be significantly and adversely affected unless qualified replacements can be found.

Our business exposes us to product liability claims that may exceed our financial resources, including our insurance coverage, and may lead to the curtailment or termination of our operations.

Our business is subject to product liability risks inherent in the testing, manufacturing and marketing of our products and product liability claims may be asserted against us, our collaborators or our licensees. While we

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currently maintain product liability insurance in the amount of $10.0 million, such coverage may not be adequate to protect us against future product liability claims. In addition, product liability insurance may not be available to us in the future on commercially reasonable terms, if at all. Although we have not had a history of claims payments that have exceeded our insurance coverage or available financial resources, if liability claims against us exceed our financial resources or coverage amounts, we may have to curtail or terminate our operations. In addition, while we currently maintain directors and officers liability insurance in the amount of $25.0 million and an additional $5.0 million of personal liability coverage for directors and officers, such coverage may not be available on commercially reasonable terms or be adequate to cover any claims that we may be required to satisfy in the future. Our insurance coverage is subject to industry standard and certain other limitations.

Our security measures may not protect our unpatented proprietary technology.

We also rely upon trade secret protection for some of our confidential and proprietary information that is not subject matter for which patent protection is available. To help protect our rights, we require all employees, consultants, advisors and collaborators to enter into confidentiality agreements that require disclosure, and in most cases, assignment to us, of their ideas, developments, discoveries and inventions, and that prohibit the disclosure of confidential information to anyone outside Cytogen or our subsidiaries. Although we are unaware of any unauthorized use or disclosure of our unpatented proprietary technology to date, these agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information or prevent such unauthorized use or disclosure.

We may not be able to implement AxCell s business plan.

In September 2002, we began the restructuring of our subsidiary, AxCell Biosciences Corporation, in an effort to reduce expenses and position Cytogen for stronger long-term growth in oncology. In July 2004, as part of our continuing efforts to reduce non-strategic expenses, we initiated the closure of facilities at our AxCell Biosciences subsidiary. Research projects through academic, governmental and corporate collaborators will continue to be supported and additional applications for the intellectual property and technology at AxCell are being pursued. We may be unable to further develop or commercialize any of AxCell s technologies in the future.

We may need to raise additional capital, which may not be available.

Our cash, cash equivalents and short-term investments were $30.3 million at December 31, 2005. We expect that our existing capital resources should be adequate to fund our operations and commitments into 2007.

We have incurred negative cash flows from operations since our inception and have expended, and expect to continue to expend in the future, substantial funds based upon the:

- success of our product commercialization efforts;
- success of any future acquisitions of complementary products and technologies we may make;
- magnitude, scope and results of our product development and research and development efforts;
- progress of preclinical studies and clinical trials;
- progress toward regulatory approval for our products;
- costs of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;

competing technological and market developments; and

expansion of strategic alliances for the sale, marketing and distribution of our products.

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Our business or operations may change in a manner that would consume available resources more rapidly than anticipated. We expect that we will have additional requirements for debt or equity capital, irrespective of whether and when we reach profitability, for further product development costs, product and technology acquisition costs and working capital. To the extent that our currently available funds and revenues are insufficient to meet current or planned operating requirements, we will be required to obtain additional funds through equity or debt financing, strategic alliances with corporate partners and others, or through other sources. These financial sources may not be available when we need them or they may be available, but on terms that are not commercially acceptable to us. If adequate funds are not available, we may be required to delay, further scale back or eliminate certain aspects of our operations or attempt to obtain funds through arrangements with collaborative partners or others that may require us to relinquish rights to certain of our technologies, product candidates, products or potential markets. If adequate funds are not available, our business, financial condition and results of operations will be materially and adversely affected.

Our capital raising efforts may dilute stockholder interests.

If we raise additional capital by issuing equity securities or convertible debentures, such issuance will result in ownership dilution to our existing stockholders, and new investors could have rights superior to those of our existing stockholders. The extent of such dilution will vary based upon the amount of capital raised.

We may need to raise funds other than through the issuance of equity securities.

If we raise additional funds through collaborations and licensing arrangements, we may be required to relinquish rights to certain of our technologies or product candidates or to grant licenses on unfavorable terms. If we relinquish rights or grant licenses on unfavorable terms, we may not be able to develop or market products in a manner that is profitable to us.

Our PSMA product development program is novel and, consequently, inherently risky.

We are subject to the risks of failure inherent in the development of product candidates based on new technologies, including our PSMA technology. These risks include the possibility that:

- the technologies we use will not be effective;
- our product candidates will be unsafe;
- our product candidates will fail to receive the necessary regulatory approvals;
- the product candidates will be hard to manufacture on a large scale or will be uneconomical to market; and
- we will not successfully overcome technological challenges presented by our potential new products.

Our other research and development programs involve similarly novel approaches to human therapeutics. Consequently, there is no precedent for the successful commercialization of therapeutic products based on our PSMA technologies. If we fail to develop such products, our business financial condition and results of operations could be significantly and adversely affected.

We could be negatively impacted by future interpretation or implementation of federal and state fraud and abuse laws, including anti-kickback laws, false claims laws and federal and state anti-referral laws.

We are subject to various federal and state laws pertaining to health care fraud and abuse, including anti-kickback laws, false claims laws and physician self-referral laws. Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, imprisonment and exclusion from participation in federal and state health care programs, including Medicare, Medicaid, and veterans health programs. We have not been challenged by a governmental authority under any of these laws and believe that our operations are in compliance with such laws.

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However, because of the far-reaching nature of these laws, we may be required to alter one or more of our practices to be in compliance with these laws. Health care fraud and abuse regulations are complex, and even minor, inadvertent irregularities can potentially give rise to claims that the law has been violated. Any violations of these laws could result in a material adverse effect on our business, financial condition and results of operations. If there is a change in law, regulation or administrative or judicial interpretations, we may have to change our business practices or our existing business practices could be challenged as unlawful, which could have a material adverse effect on our business, financial condition and results of operations.

We could become subject to false claims litigation under federal or state statutes, which can lead to civil money penalties, criminal fines and imprisonment, and/or exclusion from participation in federal health care programs. These false claims statutes include the federal False Claims Act, which allows any person to bring suit alleging the false or fraudulent submission of claims for payment under federal programs or other violations of the statute and to share in any amounts paid by the entity to the government in fines or settlement. Such suits, known as qui tam actions, have increased significantly in recent years and have increased the risk that companies like us may have to defend a false claim action. We could also become subject to similar false claims litigation under state statutes. If we are unsuccessful in defending any such action, such action may have a material adverse effect on our business, financial condition and results of operations.

The healthcare fraud and abuse laws to which we are subject include the following, among others:

Federal and State Anti-Kickback Laws and Safe Harbor Provisions. The federal anti-kickback law makes it a felony to knowingly and willfully offer, or pay remuneration to induce a person to refer an individual or to recommend or arrange for the purchase, lease or ordering of any item or service for which payment may be made under the Medicare or state healthcare programs. The anti-kickback prohibitions apply regardless of whether the remuneration is provided directly or indirectly, in cash or in kind. Interpretations of the law have been very broad. Under current law, courts and federal regulatory authorities have stated that this law is violated if even one purpose, as opposed to the sole or primary purpose, of the arrangement is to induce referrals. Violations of the anti-kickback law carry potentially severe penalties including imprisonment of up to five years, criminal fines, civil money penalties and exclusion from the Medicare and Medicaid programs.

The U.S. Department of Health and Human Services Office of Inspector General, or OIG, has published safe harbors that exempt some arrangements from enforcement action under the anti-kickback statute. These statutory and regulatory safe harbors protect various bona fide employment relationships, personal service arrangements, certain discount arrangements, among other things, provided that certain conditions set forth in the statute and regulations are satisfied. The safe harbor regulations, however, do not comprehensively describe all lawful arrangements, and the failure of an arrangement to satisfy all of the requirements of a particular safe harbor does not mean that the arrangement is unlawful. Failure to comply with the safe harbor provisions, however, may mean that the arrangement will be subject to scrutiny by the OIG.

Many states have adopted similar prohibitions. Some of these state laws lack specific safe harbors that may be available under federal law. Sanctions under these state anti-kickback laws may include civil money penalties, license suspension or revocation, exclusion from Medicare or Medicaid, and criminal fines or imprisonment.

We believe that our contracts and arrangements are not in violation of applicable anti-kickback or related laws. We cannot assure you, however, that these laws will ultimately be interpreted in a manner consistent with our practices.

False Claims Acts. We are subject to state and federal laws that govern the submission of claims for reimbursement. The Federal Civil False Claims Act imposes civil liability on individuals or entities that submit, or cause to be submitted, false or fraudulent claims for payment to the government. Violations of the Civil False Claims Act may result in treble damages, civil monetary penalties for each false claim submitted and exclusion from the Medicare and Medicaid programs. In addition, we could be subject to criminal penalties under a variety of federal statutes to the extent that we knowingly violate legal requirements under federal health programs or otherwise present or cause the presentation of false or fraudulent claims or documentation to the government. In addition, the OIG may impose extensive and costly corporate integrity requirements upon entities and individuals

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subject to a false claims judgment or settlement. These requirements may include the creation of a formal compliance program, the appointment of an independent review organization, and the imposition of annual reporting requirements and audits conducted by an independent review organization to monitor compliance with the terms of the agreement and relevant laws and regulations.

The Federal Civil False Claims Act also allows a private individual to bring a qui tam suit on behalf of the government for violations of the Civil False Claims Act, and if successful, the qui tam relator shares in the government s recovery. A qui tam suit may be brought by, with only a few exceptions, any private citizen who has material information of a false claim that has not yet been previously disclosed. Recently, the number of qui tam suits brought in the healthcare industry has increased dramatically. In addition, several states have enacted laws modeled after the Federal Civil False Claims Act.

Civil Monetary Penalties. The Civil Monetary Penalties Statute states that civil penalties ranging between $10,000 and $50,000 per claim or act may be imposed on any person or entity that knowingly submits, or causes the submission of, improperly filed claims for federal health benefits, or makes payments to induce a beneficiary or provider to reduce or limit the use of healthcare services or to use a particular provider or supplier. Civil monetary penalties may be imposed for violations of the anti-kickback statute and for the failure to return known overpayments, among other things.

Prohibition on Employing or Contracting with Excluded Providers. The Social Security Act and federal regulations state that individuals or entities that have been convicted of a criminal offense related to the delivery of an item or service under the Medicare or Medicaid programs or that have been convicted, under state or federal law, of a criminal offense relating to neglect or abuse of residents in connection with the delivery of a healthcare item or service cannot participate in any federal healthcare programs, including Medicare and Medicaid.

Health Insurance Portability and Accountability Act of 1996. HIPAA created new healthcare related crimes, and granted authority to the Secretary of the Department of Health and Human Services, or HHS, to impose certain civil penalties. Particularly, the Secretary may now exclude from Medicare any individual with a direct or indirect ownership interest in an entity convicted of healthcare fraud or excluded from the program. Under HIPAA and other healthcare laws, it is a crime to knowingly and willfully commit a healthcare fraud, and knowingly and willfully falsify, or conceal material information or make any materially false or fraudulent statements in connection with claims and payment for healthcare services by a healthcare benefit plan. HIPAA also created new programs to control fraud and abuse, and requires new investigations, audits and inspections.

We believe that our operations materially comply with applicable regulatory requirements. We cannot assure you of the outcome of any inquiry audit or investigation undertaken by HHS, OIG or DOJ. If we are ever found to have engaged in improper practices, we could be subjected to civil, administrative or criminal fines, penalties or restitutionary relief, and suspension or exclusion of the entity or individuals from participation in federal and state healthcare programs.

Patient Information and Privacy. HIPAA also mandates, among other things, the establishment of regulatory standards addressing the electronic exchange of health information, standards for the privacy and security of health information maintained or exchanged electronically, and standards for assigning unique health identifiers to healthcare providers. Sanctions for failure to comply with HIPAA standards include civil and criminal penalties. The Security Standards require us to implement certain security measures to protect certain individually identifiable health information, called protected health information, or PHI, in electronic format. The Standards for Privacy of Individually Identifiable Information restrict use and disclosure of PHI unless patient authorization for such disclosures are obtained. These Privacy Standards not only require our compliance with standards restricting the use and disclosure of PHI, but also require us to obtain satisfactory assurances that any business associate of ours who has access to our PHI similarly will safeguard such PHI.

We have evaluated these rules to determine the effects of the rules on our business, and we believe that we have taken the appropriate steps to ensure that we will comply with these standards in all material respects by their respective compliance deadlines.

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Our business involves environmental risks that may result in liability.

We are subject to a variety of local, state, federal and foreign government regulations relating to storage, discharge, handling, emission, generation, manufacture and disposal of toxic, infectious or other hazardous substances used to manufacture our products. If we fail to comply with these regulations, we could be liable for damages, penalties, or other forms of censure and our business could be significantly and adversely affected. We currently do not carry insurance for contamination or injury resulting from the use of such materials.

PROSTASCINT and QUADRAMET utilize radioactive materials. PROSTASCINT is not manufactured or shipped as a radioactive material because the radioactive component is not added until the product has arrived at its final destination (a radiopharmacy). Laureate Pharma, our contract manufacturer of PROSTASCINT, holds a radioactive materials license because such license is required for certain release and stability tests of the product.

QUADRAMET, however, is manufactured and shipped as radioactive, and therefore, the manufacturing and distribution of this product must comply with regulations promulgated by the U.S. Nuclear Regulatory Commission. BMS-MI manufacturers and distributes QUADRAMET, and is, therefore, subject to these regulations.

We have been and, in the future, may be subject to patent litigation.

On March 17, 2000, we were served with a complaint filed against us in the United States District Court for the District of New Jersey by M. David Goldenberg and Immunomedics, Inc. The litigation claimed that our PROSTASCINT product infringes a patent purportedly owned by Goldenberg and licensed to Immunomedics. We believe that PROSTASCINT did not infringe this patent, and that the patent was invalid and unenforceable. In June 2004, the U.S. Court of Appeals for the Federal Circuit affirmed the district court s grant of summary judgment of no literal infringement. Regarding infringement under the doctrine of equivalents, however, the U.S. Court of Appeals for the Federal Circuit disagreed with the district court s conclusion that there was no issue of material fact and reversed the district court s grant of summary judgment on this point and remanded for further proceedings on the issue. In September 2004, we settled the patent infringement suit for an undisclosed payment, without any admission of fault or liability.

We cannot give any assurance that we will not become subject to additional patent litigation in the future, which could result in material expenditures to us.

Our stock price has been and may continue to be volatile, and your investment in our stock could decline in value or fluctuate significantly.

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. The market price of our common stock has fluctuated over a wide range and may continue to fluctuate for various reasons, including, but not limited to, announcements concerning our competitors or us regarding:

- results of clinical trials;
- technological innovations or new commercial products;
- changes in governmental regulation or the status of our regulatory approvals or applications;
- changes in earnings;
- changes in health care policies and practices;

developments or disputes concerning proprietary rights;

litigation or public concern as to safety of the our potential products; and

changes in general market conditions.

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These fluctuations may be exaggerated if the trading volume of our common stock is low. These fluctuations may or may not be based upon any of our business or operating results. Our common stock may experience similar or even more dramatic price and volume fluctuations which may continue indefinitely.

We have adopted various anti-takeover provisions which may affect the market price of our common stock and prevent or frustrate attempts by our stockholders to replace or remove our management team.

Our Board of Directors has the authority, without further action by the holders of common stock, to issue from time to time, up to 5,400,000 shares of preferred stock in one or more classes or series, and to fix the rights and preferences of the preferred stock. We have implemented a stockholder rights plan by which one preferred stock purchase right is attached to each share of common stock, as a means to deter coercive takeover tactics and to prevent an acquirer from gaining control of us without some mechanism to secure a fair price for all of our stockholders if an acquisition was completed. These rights will be exercisable if a person or group acquires beneficial ownership of 20% or more of our common stock and can be made exercisable by action of our Board of Directors if a person or group commences a tender offer which would result in such person or group beneficially owning 20% or more of our common stock. Each right will entitle the holder to buy one one-thousandth of a share of a new series of our junior participating preferred stock for $20. If any person or group becomes the beneficial owner of 20% or more of our common stock (with certain limited exceptions), then each right not owned by the 20% stockholder will entitle its holder to purchase, at the right s then current exercise price, common shares having a market value of twice the exercise price. In addition, if after any person has become a 20% stockholder, we are involved in a merger or other business combination transaction with another person, each right will entitle its holder (other than the 20% stockholder) to purchase, at the right s then current exercise price, common shares of the acquiring company having a value of twice the right s then current exercise price.

We are subject to provisions of Delaware corporate law which, subject to certain exceptions, will prohibit us from engaging in any business combination with a person who, together with affiliates and associates, owns 15% or more of our common stock for a period of three years following the date that the person came to own 15% or more of our common stock unless the business combination is approved in a prescribed manner.

These provisions of the stockholder rights plan, our certificate of incorporation, and of Delaware law may have the effect of delaying, deterring or preventing a change in control of Cytogen, may discourage bids for our common stock at a premium over market price and may adversely affect the market price, and the voting and other rights of the holders, of our common stock. In addition, these provisions make it more difficult to replace or remove our current management team in the event our stockholders believe this would be in the best interest of the Company and our stockholders.

The liquidity of our common stock could be adversely affected if we are delisted from The Nasdaq National Market.

In the event that we are unable to maintain compliance with all relevant Nasdaq Listing Standards, our securities may be subject to delisting from the Nasdaq National Market. If such delisting occurs, the market price and market liquidity of our common stock may be adversely affected. Such listing standards include, among other things, requirements related to the market value of our listed securities and publicly-held shares, and the minimum bid price for such shares. The minimum bid requirement is $1.00 per share. On March 1, 2006, the closing sale price of our common stock as reported by Nasdaq was $3.37.

If faced with delisting, we may submit an application to transfer the listing of our common stock to the Nasdaq SmallCap Market. Alternatively, if our common stock is delisted by Nasdaq, our common stock would be eligible to trade on the OTC Bulletin Board maintained by Nasdaq, another over-the-counter quotation system, or on the pink sheets where an investor may find it more difficult to dispose of or obtain accurate quotations as to the market value of our common stock. In addition, we would be subject to a rule promulgated by the Securities and Exchange Commission that, if we fail to meet criteria set forth in such rule, imposes various practice requirements on broker-dealers who sell securities governed by the rule to persons other than established customers and accredited investors. Consequently, such rule may deter broker-dealers from recommending or selling our common stock, which may further affect the liquidity of our common stock.

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Delisting from Nasdaq would make trading our common stock more difficult for investors, potentially leading to further declines in our share price. It would also make it more difficult for us to raise additional capital. Further, if we are delisted, we would also incur additional costs under state blue sky laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our shareholders to sell our common stock in the secondary market.

A large number of our shares are eligible for future sale which may adversely impact the market price of our common stock.

A large number of shares of our common stock are already outstanding, issuable upon exercise of options and warrants, or the achievement of certain milestones under previously completed acquisitions and may be eligible for resale. This availability of a significant number of additional shares of our common stock for future sale and issuance could depress the price of our common stock.

At December 31, 2005, stock options to purchase 1,134,296 shares of our common stock were outstanding and the weighted-average exercise price per share of these options was $9.18. At December 31, 2005, warrants to purchase 3,803,086 shares of our common stock were outstanding and the weighted-average exercise price per share of these warrants was $8.16.

The following table summarizes information about outstanding warrants to purchase our common stock at December 31, 2005:

Exercise Price	Outstanding Warrants	Aggregate Exercise Price
$4.25	1,118,868	$ 4,755,189
$5.65	70,000	$ 395,500
$6.00	776,096	$ 4,656,576
$6.91	315,790	$ 2,182,108
$10.97	250,000	$ 2,742,500
$12.80	1,272,332	$ 16,285,850

The warrants exercisable at $10.97 per share and $12.80 per share become automatically exercised, in full, if our common stock trades for 30 consecutive trading days at 130% of the respective exercise prices.

Because we do not intend to pay, and have not paid, any cash dividends on our shares of common stock, our stockho