MEDAREX INC
Form 10-K
March 16, 2005

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2004

Commission File No. 0-19312

MEDAREX, INC.

(Exact name of registrant as specified in its charter)

New Jersey	**22-2822175**
(State of Incorporation)	(I.R.S. Employer Identification No.)
707 State Road, Princeton, New Jersey	**08540**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: (609) 430-2880

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

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

Title of Class	**Name of Each Exchange on Which Registered**
Common Stock ($0.01 par value)	The Nasdaq Stock Market, Inc. under symbol MEDX

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

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

The aggregate market value of the voting stock held by non-affiliates of the Registrant was approximately $540.8 million as of June 30, 2004, based upon the closing sale price on the NASDAQ National Market reported for such date. The determination of affiliate status for the purposes of this calculation is not necessarily a conclusive determination for other purposes. The calculation excludes approximately 5,089,221 shares

held by directors, officers and shareholders whose ownership exceeded 5% of the Registrant s outstanding Common Stock as of June 30, 2004. Exclusion of these shares should not be construed to indicate that such person controls, is controlled by or is under common control with the Registrant.

As of February 28, 2005, the registrant had outstanding 110,529,979 shares of Common Stock, $0.01 par value (Common Stock), which is registrant s only class of Common Stock.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement for the Annual Meeting of Shareholders to be held on May 19, 2005 (the Proxy Statement) are incorporated by reference in Parts II and III of this Report. Other documents incorporated by reference in this report are listed in the Exhibit Index.

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PART I

In this Annual Report, Medarex or the company, we, us and our refer to Medarex, Inc., and our wholly owned subsidiaries. This Annual Rep contains forward-looking statements that involve risk and uncertainties. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business as well as those discussed elsewhere in this Annual Report. Actual events or results may differ materially from those discussed in this Annual Report.

Item 1. Business

Overview

We are a biopharmaceutical company focused on the discovery, development and potential commercialization of fully human antibody-based therapeutic products. We believe that our UltiMAb Human Antibody Development System® enables us to rapidly create and develop such products for a wide range of diseases, including cancer, inflammation, autoimmune disorders and other life-threatening and debilitating diseases.

Currently, 22 antibody products generated from our UltiMAb Human Antibody Development System are in human clinical trials(1). Eight of these products are in Phase II or Phase III clinical trials. The 22 antibodies are designed to treat a wide range of diseases, such as cancer, rheumatoid arthritis and other inflammatory, autoimmune and infectious diseases. The most advanced of these products is MDX-010 (Phase III, Phase II and Phase I clinical trials), which we are developing jointly with Bristol-Myers Squibb Company, or BMS, for the treatment of metastatic melanoma and other cancers. Four of these antibody products are fully owned by Medarex and its affiliates: MDX-060 for lymphomas (Phase II clinical trial), MDX-070 for prostate cancer (Phase II clinical trial), MDX-214 for cancer (Phase I/II clinical trial) and MDX-1307 for genitourinary and breast cancers (Phase I clinical trial). We are developing MDX-066 (Phase I clinical trial) jointly with The Massachusetts Biologic Laboratories of the University of Massachusetts Medical School, or MBL, for the treatment of *Clostridium difficile* associated diarrhea. Another antibody, MDX-018 (Phase I/II clinical trial), is being jointly developed with Genmab A/S for autoimmune disease, and three additional antibodies are being developed separately by Genmab: HuMax -CD4 (Phase II clinical trials) for T-cell lymphomas, HuMax-EGFr (Phase I/II clinical trial) for head and neck cancer and HuMax-CD20 (Phase I/II clinical trial) for lymphomas. Genmab and Amgen, Inc. are developing AMG 714 (Phase II clinical trial) for rheumatoid arthritis. Additionally, other licensing partners, including Novartis Pharma AG, Eli Lilly and Company, and Centocor, Inc. (a subsidiary of Johnson & Johnson), are developing a total of ten antibody products, for inflammatory and/or autoimmune diseases and cancer, that are currently in clinical trials. Human Genome Sciences, Inc. has also announced the initiation of a Phase I trial of one anticancer antibody product developed pursuant to a licensing agreement with our partner Kirin Brewery Co., Ltd. We and our partners also have a number of UltiMAb® product candidates in preclinical development.

(1) Information regarding the clinical status of third-party antibody products is based on publicly available information.

In November 2004, we announced a worldwide collaboration with BMS to develop and commercialize MDX-010, an antibody product targeting the CTLA-4 receptor, that was developed by us using our UltiMAb Human Antibody Development System. The BMS collaboration also includes MDX-1379, an investigational gp100 melanoma peptide vaccine, which will be developed for potential use in combination with MDX-010 in melanoma. MDX-010 in combination with the MDX-1379 tumor vaccine is currently in Phase III clinical development for the treatment of metastatic melanoma under a Special Protocol Assessment, or SPA, agreement with the U.S. Food and Drug Administration, or FDA, and has been granted Fast Track status by the FDA for the treatment of high risk Stage II, Stage III and Stage IV melanoma. We received an initial cash payment from BMS of $50.0 million, of which $25.0 million was for the purchase of our common stock at a small premium to the market price at the time we entered into the collaboration. We and BMS have agreed to jointly continue the investigation and the development of MDX-010 in additional tumor types and have jointly committed to an initial multi-year budget of approximately $192.0 million to fund such development. BMS will be responsible for 65% of all development costs related to clinical trials intended to support regulatory approval in both the U.S. and Europe, with the remaining 35% of the development costs to be paid by us. The parties will share equally the costs of any clinical trials of products intended solely for regulatory approval in the U.S., and BMS will be fully responsible for all development costs that relate solely to regulatory approval in Europe and other parts of the world. Under the terms of the collaboration, we could receive up to an additional $205.0 million pursuant to the collaboration if all regulatory milestones are met, and up to $275.0 million in sales-related milestones. We will have an option to co-promote and share profits with BMS in the U.S. based on a 45:55 percentage split. BMS will receive an exclusive license to MDX-010 outside of the U.S. and pay us royalties on commercial sales.

In September 2004, we entered into a series of agreements with Pfizer, Inc. The first agreement amended our existing collaborative research and license and royalty agreements with Pfizer to provide for the discovery and development of up to 50 antibody products over ten years. Under this amendment, we have the potential to receive research funding, license fees and milestone payments (if certain development milestones are met), as well as royalties on any commercial sales of the products. The second and third agreements were a sublicense from us to Pfizer and a cross-license of certain patents and patent applications, in each case, solely relating to our respective anti-CTLA-4 antibody programs. Under these licenses, we have the potential to receive milestones and royalty payments based upon commercial sales of any Pfizer anti-CTLA-4 antibody product. In contrast, we have no future payment obligations to Pfizer in connection with any anti-CTLA-4 product we may develop. The fourth agreement was a stock purchase agreement also related to the anti-CTLA-4 programs. Pursuant to certain of these agreements, Pfizer made a total initial cash payment to us of $110.0 million, of which $30.0 million was for the purchase of our common stock at a small premium to market price at the time we entered into the collaboration.

As of March 1, 2005, we have more than 50 partnerships with pharmaceutical and biotechnology companies to jointly develop and commercialize products or to enable other companies to use our proprietary technology in their development of new therapeutic products. These companies include industry leaders such as Abbott Laboratories, Amgen, Centocor, Eli Lilly, Human Genome Sciences, MedImmune, Inc., Novartis, Novo Nordisk A/S and Schering AG.

In addition to our UltiMAb Human Antibody Development System, we have considerable experience in preclinical and clinical development as well as in manufacturing antibodies for clinical trials. Our existing manufacturing facility in Annandale, New Jersey currently has the capacity to undertake multiple antibody projects concurrently for clinical development purposes, meeting our near-term production demands. We have assembled a team of experienced scientific, production, clinical and regulatory personnel to facilitate the discovery and development of antibody-based products for us and for our partners. We intend to add sales and marketing and additional manufacturing capabilities as needed.

Products in Development

The following table summarizes potential therapeutic indications and development stages for our product candidates and those of our partners (based on publicly available information), and is followed by brief descriptions of each specific program:

Phase III and Phase II Product Candidates in Clinical Development

PRODUCT	INDICATION	CLINICAL STATUS	PARTNER
MDX-010 + MDX-1379	Melanoma	Phase III	Co-developing with BMS*
MDX-010	Melanoma, Prostate, Breast, Renal Cell Cancer and Others	Phase II	Co-developing with BMS*
MDX-060	Lymphoma	Phase II	Wholly-owned
MDX-070	Prostate cancer	Phase II	Wholly-owned
CNTO 148	Inflammatory diseases	Phase II	Centocor♦
CNTO 1275	Inflammatory diseases	Phase II	Centocor♦
HuMax-CD4	T-cell lymphomas	Phase II	Genmab
AMG 714	Rheumatoid arthritis	Phase II	Genmab (under agreement with Amgen)
Amgen Antibody-1	Undisclosed disease	Phase II	Amgen♦
Pfizer CP-675,206	Melanoma and Others	Phase II	Pfizer♣

Phase I/II Product Candidates in Clinical Development

PRODUCT	INDICATION	CLINICAL STATUS	PARTNER
MDX-214	Cancer	Phase I/II	Wholly-owned
MDX-018	Inflammatory disease	Phase I/II	Co-developing with Genmab
HuMax-EGFr	Head and neck cancer	Phase I/II	Genmab
HuMax-CD20	Lymphoma	Phase I/II	Genmab

* We have the option to co-promote and share profits in the U.S. We expect to receive milestone payments as these product candidates move toward product approval, and royalties on product sales outside the U.S., should commercialization occur.

♦ We expect to receive milestone payments, as these product candidates move through clinical trials, and royalties on product sales, should commercialization occur.

We received an equity interest in Genmab in exchange for a license of our proprietary antibody technology. We are not entitled to license fees, milestone payments or royalties from the license of this product candidate.

♣ We expect to receive milestone payments and royalty payments on product sales, should commercialization occur.

Phase I and Selected Preclinical Product Candidates

PRODUCT	INDICATION	CLINICAL STATUS	PARTNER
MDX-1307	Cancer	Phase I	Wholly-owned
MDX-066	*C. difficile*	Phase I	Co-developing with MBL
CNTO 95	Cancer	Phase I	Centocor ♦
Novartis Antibody-1	Autoimmune disease	Phase I	Novartis Pharma ♦
Novartis Antibody-2	Autoimmune disease	Phase I	Novartis Pharma ♦
Amgen Antibody-2	Undisclosed disease	Phase I	Amgen ♦
Amgen Antibody-3	Undisclosed disease	Phase I	Amgen ♦
FG-3019	Idiopathic pulmonary fibrosis; Diabetic nephropathy	Phase I	FibroGen ♦
HGS-TR2J	Cancer	Phase I	Kirin Brewery Co., Ltd.§
Lilly Antibody	Undisclosed disease	Phase I	Eli Lilly ♦
MDX-1100	Inflammation	Preclinical	Wholly-owned
MDX-1103	Lupus	Preclinical	MedImmune*
MDX-1333	Lupus	Preclinical	MedImmune*
MDX-1303	Anthrax infection	Preclinical	Co-developing with PharmAthene

Phase III and Phase II Product Candidates in Clinical Development

MDX-010 (Anti-CTLA-4 Antibody)* *Melanoma; Prostate Cancer; Breast Cancer; Renal Cell Cancer and Others.* MDX-010 is a fully human antibody that targets an immune receptor known as CTLA-4. This receptor, which is a protein found on the surface of T-cells, has been shown to diminish or down-regulate the immune response to tumors or infectious agents. By using a fully human antibody to block the activity of CTLA-4, we believe that patients immune systems may be able to mount a stronger immune response against foreign pathogens and cancers. We initially focused on the use of this antibody for the treatment of melanoma and prostate cancer and have expanded clinical studies into other indications such as breast cancer, renal cell cancer and HIV. We have also expanded the MDX-010 clinical program to include combination studies with chemotherapy, immunotherapy and vaccines. Effective January 2005, we are collaborating with BMS to develop and potentially commercialize MDX-010 for melanoma and additional disease indications. BMS is responsible for all development outside the U.S. and Europe. For a more detailed description of our collaboration with BMS, see the section herein entitled Our Human Antibody Partnering Business BMS.

We are in the process of a possible initial public offering of a portion of the common stock of our wholly-owned subsidiary Celldex Therapeutics, Inc., or Celldex. As part of this transaction, in April 2004, we assigned our rights to this product candidate, including the associated IND, to Celldex. In the event this offering is completed, we will not be entitled to license fees or milestone payments with respect to this product. We may be entitled to receive royalty payments on any commercial sales.

♦ We expect to receive milestone payments, as these product candidates move through clinical trials, and royalties on product sales, should commercialization occur.

§ We expect to receive royalties on product sales, should commercialization occur.

* We have the option to co-promote and share profits in the U.S. We expect to receive milestone payments as these product candidates move toward product approval, and royalties on product sales outside the U.S., should commercialization occur.

We or BMS are currently conducting the following human clinical trials for this product under our collaboration:

Melanoma: We are conducting a number of clinical studies investigating MDX-010 for the treatment of melanoma. Under a SPA agreement with the FDA, a Phase III trial of MDX-010 in combination with MDX-1379 (a melanoma peptide vaccine based on gp100) commenced enrollment in September 2004. Approximately 750 patients with previously treated Stage III and Stage IV metastatic melanoma are expected to be enrolled in 75-100 centers worldwide. The patients are randomized to receive one of three regimens on a 3:1:1 basis, with 450 patients receiving a MDX-010/MDX-1379 combination, 150 patients receiving MDX-1379 alone and 150 patients receiving MDX-010 alone. All patients receiving MDX-010 will receive a dose of three mg/kg every three weeks for up to four doses. Best objective response rate (complete and partial responses) will be used as the basis for an expected initial Biologics License Application, or BLA, submission. Secondary endpoints of disease progression and survival data will continue to be collected from patients being followed in the Phase III trial. Treatment assignment will be blinded, with oversight by an independent Data Monitoring Committee, or DMC.

We initiated the Phase III clinical trial based on data from a Phase II clinical trial in which 41 patients with metastatic melanoma were treated with one of two dose regimens of MDX-010 in combination with MDX-1379. As of January 5, 2005, of the 14 patients treated in the high-dose treatment cohort, two patients experienced complete responses ongoing for over 28 months, and one patient experienced a partial response ongoing for over 32 months. Of the 27 patients treated in the low-dose treatment cohort, three patients experienced partial responses, two of which have had ongoing responses of approximately two years. Median survival after diagnosis of metastatic melanoma is six to nine months.

In June 2004, the FDA granted orphan drug designation to MDX-010 for the treatment of high risk Stage II, Stage III and Stage IV melanoma, and in October 2004, granted Fast Track status to the development program for MDX-010 in combination with MDX-1379 for this indication. Orphan drug designation is granted to products that treat rare diseases or conditions that affect fewer than 200,000 people in the U.S. and provides eligibility for a special seven-year period of market exclusivity after marketing approval, potential tax credits for research, grant funding for research and development, possibly reduced filing fees for marketing applications, and assistance with the review of clinical trial protocols. Under the FDA Modernization Act of 1997, designation as a Fast Track product means that the FDA has determined that a new drug or biologic is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet medical needs for such condition, and that the FDA will facilitate and expedite the development and review of the application for the approval of such product.

Multi-dose Studies: As part of our joint MDX-010 clinical development program with BMS, multiple Phase II studies of MDX-010 in melanoma are underway. These studies are designed to evaluate tumor and immune responses in patients treated with MDX-010 at higher doses.

Prostate Cancer: An ongoing Phase II prostate cancer trial is designed to study MDX-010 as a single agent and in combination with Taxotere® (docetaxel) and is expected to enroll up to 40 chemotherapy naïve patients with hormone refractory prostate cancer, or HRPC.

Breast Cancer: An ongoing multi-center, open-label Phase II breast cancer trial is expected to enroll up to 33 patients with metastatic breast cancer. The study is intended to evaluate tumor and immune responses.

Renal Cell Cancer: A Phase II renal cell cancer clinical trial is underway. The trial is designed to study MDX-010 as a single agent and is expected to enroll up to 103 patients with renal cell cancer.

Other Cancers: MDX-010 is under investigation for a variety of cancer indications and exploratory clinical studies are also underway for MDX-010 in colorectal cancer, non-Hodgkin s lymphoma and ovarian cancer.

HIV Viremia: A multi-center, open-label Phase I clinical trial is underway to enroll up to 18 patients with HIV who have an extensive treatment history but whose virus is no longer suppressed by highly active antiretroviral therapy, or HAART. In the trial, MDX-010 has been found to have a favorable safety profile and to be well-tolerated in patients infected with HIV. This trial was expanded in 2004 to evaluate safety, tolerability and clinical efficacy.

Additional Combination Studies: As part of our joint MDX-010 clinical development program with BMS, separate clinical trials of MDX-010 in combination with various agents are currently underway. In addition to the Phase III trial of MDX-010 in combination with the MDX-1379 melanoma vaccine, there are Phase II clinical trials of MDX-010 in combination with IL-2 and in combination with DTIC dacarbazine chemotherapy for melanoma. There is also a Phase I clinical trial of MDX-010 in previously vaccinated metastatic melanoma and ovarian cancer patients and a separate Phase I clinical trial of MDX-010 in combination with Cell Genesys GVAX® prostate cancer vaccine.

Adverse Events: Generally, our clinical trials, including our MDX-010 trials, are conducted in patients with serious life-threatening diseases for whom conventional treatments have been unsuccessful or for whom no conventional treatment exists, and in some cases, our product is used in combination with approved therapies that themselves have significant adverse event profiles. The most common events experienced in trials of MDX-010, which were anticipated and consistent with an immune-based mechanism of action due to MDX-010 mediated CTLA-4 blockade, now termed Autoimmune Breakthrough Events (ABEs), were diarrhea, rash, reduced pituitary function, colitis and increased liver enzymes. Other than a very small number of fatalities, which may or may not be attributable to our product candidates, almost all ABEs resolved with treatment.

MDX-060 (Anti-CD30 Antibody) *Lymphoma.* MDX-060 is a fully human antibody that targets CD30, which is a marker for activated lymphocytes and is present on the malignant cells of Hodgkin s disease, or HD, and anaplastic large cell lymphoma, or ALCL, as well as other CD30-positive cancers. Through its ability to target CD30 expressing tumor cells, we believe that MDX-060 may facilitate the elimination of such cells by the human immune system.

In December 2004, we announced findings from an ongoing Phase I and II clinical trial of MDX-060 in 56 patients with relapsed or refractory HD, ALCL or other CD30-positive lymphomas which indicated that MDX-060 demonstrated clinical activity, including two complete responses and four partial responses. In addition, stable disease was observed in 18 patients. All patients had failed multiple prior treatments and most had failed bone marrow transplantation. One episode of a possible serious drug-related adverse event (elevated liver transaminase levels, grade III) was reported in a patient with a history of Graft versus Host Disease, which resolved with steroid treatment. No maximum tolerated dose has been identified. The Phase II trial has been expanded to further explore the activity profile of MDX-060. In October 2004, the FDA granted orphan drug designation to MDX-060 for the treatment of Hodgkin s disease.

MDX-070 (Anti-PSMA Antibody) *Prostate Cancer.* MDX-070 is a fully human antibody that targets Prostate Specific Membrane Antigen, or PSMA. PSMA is a cell surface marker that is preferentially expressed on malignant prostate tissues and also on blood vessels in other tumors. In June 2004, we initiated a multi-dose, dose-escalation Phase II clinical study of MDX-070 in patients with hormone refractory prostate cancer, following Phase I clinical trial findings that MDX-070 was well-tolerated.

CNTO 148 (Anti-TNF α Antibody)♦ *Inflammatory Diseases.* In September 2002, Centocor reported that it was developing CTNO 148, a high affinity, fully human antibody for inflammatory diseases, including Crohn s disease, rheumatoid arthritis and uveitis. According to publicly available information, CTNO-148, also known as golimumab, is in full development (Phase II).

♦ We expect to receive milestone payments, as these product candidates move through clinical trials, and royalties on product sales, should commercialization occur.

CNTO 1275 (Anti-IL-12 Antibody)♦ *Inflammatory Diseases.* In September 2002, Centocor reported that it was developing CNTO 1275, a high affinity, fully human antibody for the treatment of inflammatory diseases such as moderate to severe psoriasis and multiple sclerosis. According to publicly

HuMax-CD4 (Anti-CD4 Antibody) *T-cell Lymphomas.* Genmab is developing HuMax-CD4 (also known as zanolimumab), a fully human antibody that targets the CD4 receptor on cells known as T-cells, which are believed to be involved in promoting autoimmune disease. Genmab has reported that preclinical and clinical studies suggest that an antibody that targets CD4 may be useful for the treatment of cutaneous T-cell lymphomas, or CTCL. In February 2005, Genmab announced updated Phase II duration of response data in CTCL.

In March 2004, Genmab announced that HuMax-CD4 had received Fast Track status by the FDA for patients with CTCL. In April, 2004, HuMax-CD4 was designated an orphan drug for the treatment of CTCL by the European Agency for the Evaluation of Medicinal Products and, in August 2004, by the FDA. Also, in August 2004, Genmab announced the initiation of a Phase II study of HuMax-CD4 in refractory or relapsed non-cutaneous T-cell lymphoma.

AMG 714 (Anti-IL-15 Antibody) *Rheumatoid Arthritis.* AMG 714, formerly known as HuMax-IL15, is a fully human antibody being developed under an agreement between Genmab and Amgen against Interleukin-15 (IL-15), an immune system signaling molecule that appears early in the cascade of events that ultimately lead to inflammatory disease. According to Amgen, interim data from Phase II clinical trials for rheumatoid arthritis are suggestive of a clinical effect in this condition. The Phase II trials are expected to be completed in 2005.

Amgen Antibody-1♦ *Undisclosed disease*. We are aware of one antibody product candidate derived from our technology being developed by Amgen that is in Phase II clinical trials for an undisclosed indication.

Pfizer CP-675,206 (Anti-CTLA-4 Antibody)♣ *Melanoma*. Pfizer is developing CP-675,206, a fully human antibody for the treatment of melanoma. Enrollment is currently underway for a Phase II clinical trial. This product candidate was not generated using our UltiMAb technology.

Phase I/II Product Candidates in Clinical Development

MDX-214 (Anti-EGFr/CD89 Antibody) *Cancer.* MDX-214 is a fusion protein consisting of human epidermal growth factor, or EGF, genetically linked to a fully human antibody fragment that targets CD89, a trigger molecule expressed on immune effector cells. Through the use of EGF, the natural ligand to the epidermal growth factor receptor, or EGFr, MDX-214 is believed to have the ability to direct CD89 positive effector cells to EGFr-overexpressing tumor cells, potentially facilitating the interaction of the immune system with the cancer. A Phase I/II clinical trial is underway for the treatment of cancers that overexpress EGFr. The study is expected to enroll up to 48 patients with refractory or relapsed EGFr-expressing cancers, including cancers of the head and neck, breast, colon, prostate, lung and ovary.

♦ We expect to receive milestone payments, as these product candidates move through clinical trials, and royalties on product sales, should commercialization occur.

We received an equity interest in Genmab in exchange for a license of our proprietary antibody technology. We are not entitled to license fees, milestone payments or royalties from the license of this product candidate.

♣ We expect to receive milestone payments and royalty payments on product sales, should commercialization occur.

MDX-018 (Anti-inflammatory Antibody) *Inflammatory Disease.* MDX-018, also known as HuMax-Inflam, is a fully human antibody that we are co-developing with Genmab. In December 2004, we and Genmab announced safety and efficacy results from an ongoing Phase I/II European clinical trial of MDX-018 in patients suffering from an undisclosed autoimmune disease. In a pooled analysis of all dose groups after eight weeks, a statistically significant mean reduction in disease activity of 56% was seen. Neither of the serious adverse events reported (one event of syncope and one event of acute myocardial infarction) was determined by the investigator to be related to the antibody.

HuMax-EGFr (Anti-EGFr Antibody) *Head, Neck and Other Cancers.* According to Genmab, HuMax-EGFr, a fully human antibody targeting EGFr, a receptor molecule that has been found in excess on many tumor cells, is under development for the treatment of carcinoma of the head and neck. In December 2004, Genmab reported partial and stable disease data for a Phase I/II clinical trial for the treatment of head and neck cancer with HuMax-EGFr.

HuMax-CD20 (Anti-CD20 Antibody) *Lymphoma*. Genmab is developing HuMax-CD20, a fully human antibody targeting CD20, a molecule found on B cells. Two Phase I/II clinical trials using HuMax-CD20 in patients with non-Hodgkin s lymphoma, or NHL, and chronic lymphocytic leukemia, or CLL, are ongoing. In December 2004, Genmab reported interim complete and partial response data in patients with NHL. Also in December 2004, Genmab announced that this product candidate has been granted Fast Track designation by the FDA for the treatment of CLL and that the FDA had accepted an Investigational New Drug Application, or IND, for a Phase I/II dose escalation trial for HuMax-CD20 in patients with active rheumatoid arthritis who have failed one treatment with one or more disease modifying anti-rheumatic drugs.

Phase I and Selected Preclinical Product Candidates

We and our partners have active early clinical and preclinical development programs that we anticipate may lead to the identification of new antibody product candidates and novel combinations with antibodies currently in development. We expect these development efforts to lead to additional clinical candidates in both the near and long term. Our programs and those of our partners include, among others, the following:

MDX-1307 (Anti-Mannose Receptor/hCG-ß Antibody) *Colorectal, Pancreatic and/or Bladder Cancers.* MDX-1307 (also known as ßHCG-VAC) is a fusion protein composed of a mannose receptor-specific human antibody conjugated to the beta chain of human chorionic gonadotropin, or ßhCG. This therapeutic cancer vaccine is designed to induce antibody and cytotoxic T-cell responses directed at cancer cells in patients with ßhCG-expressing tumors. In February 2004, the FDA accepted our IND application to initiate a dose-escalation, multi-dose Phase I study. This ongoing study is expected to enroll up to 18 patients with metastatic or locally advanced colorectal, pancreatic or bladder cancers. In September 2004, investigators at the Duke Comprehensive Cancer Center working with us were awarded a two-year $500,000 grant from the Avon Foundation and the National Cancer Institute to initiate a Phase I clinical trial with MDX-1307/ßHCG-VAC for the treatment of breast cancer. We have submitted the protocol for this study to the FDA and expect to begin enrolling patients in 2005.

We received an equity interest in Genmab in exchange for a license of our proprietary antibody technology. We are not entitled to license fees, milestone payments or royalties from the license of this product candidate.

We are in the process of a possible initial public offering of a portion of the common stock of Celldex. As part of this transaction, in April 2004, we assigned our rights to this product candidate, including the associated IND, to Celldex. In the event this offering is completed, we will not be entitled to license fees or milestone payments with respect to this product. We may be entitled to receive royalty payments on any product sales, should commercialization occur.

MDX-066 (Anti-Toxin A Antibody) *Clostridium difficile Associated Diarrhea.* MDX-066 (also known as CDA-1) is a fully human antibody that we are co-developing with the Massachusetts Biologic Laboratories of the University of Massachusetts Medical School, or MBL. MDX-066 is designed to target Toxin A, a toxin produced by the bacterium *Clostridium difficile*, which is associated with a serious and sometimes deadly form of diarrhea called *Clostridium difficile* associated diarrhea, or CDAD. Preclinical studies suggest that MDX-066 may neutralize the effects of Toxin A, the toxin associated with CDAD. We and MBL have initiated a dose-escalation Phase I trial which is expected to enroll up to 30 healthy volunteers. The participants will be monitored for any adverse side effects, and their blood will be tested to measure the concentration of the antibody in their systems.

CNTO 95 (Anti-integrin receptors Antibody)♦ *Cancer.* In December 2003, we announced that Centocor had commenced a dose escalation Phase I trial of CTNO 95, a high affinity, fully human antibody targeting the integrin receptors (αvß3 and αvß5) that are implicated in tumor-induced angiogenesis. Angiogenesis is the formation of new blood vessels and is believed to play an important role in tumor growth and metastasis.

FG-3019 (Anti-CTGF)♦ *Idiopathic Pulmonary Fibrosis and Diabetic Nephropathy.* FibroGen has reported that it has completed a Phase I clinical trial of a fully human antibody therapeutic in patients with idiopathic pulmonary fibrosis and expects to initiate a Phase II clinical trial in 2005. The product candidate is FibroGen s lead anti-CTGF (connective tissue growth factor) therapeutic antibody, also known as FG-3019. According to publicly available sources, FG-3019 is also in a Phase Ib clinical trial in type 1 and type 2 diabetic patients with early-stage kidney disease.

MDX-1100 (Anti-IP-10 Antibody) *Inflammatory Diseases.* We are developing MDX-1100, a fully human antibody product candidate that targets IP-10 (also known as CXCL10), a chemokine expressed in association with multiple inflammatory disease indications such as rheumatoid arthritis, inflammatory bowel disease and multiple sclerosis. We expect to file an IND application with the FDA in the first half of 2005 for a Phase I trial of MDX-1100 in patients with inflammatory bowel disease. We acquired full rights to MDX-1100 as part of our acquisition of Ability Biomedical Corporation in August 2004.

MDX-1333 and MDX-1103 (Anti-Type 1 IFN Antibodies)* *Systemic Lupus Erythematosus.* MDX-1333 and MDX-1103 are fully human antibodies that target two different components of the Type 1 IFN pathway, which is believed to be involved with systemic lupus erythematosus, or SLE, disease activity. MDX-1333 is an antibody that we believe blocks the receptor of Type 1 IFN, and MDX-1103 is an antibody that we believe blocks multiple Type 1 IFN subtypes. In November 2004, we announced a collaboration with MedImmune, whereby MedImmune will be responsible for continued development of these antibodies. Prior to the initiation of a pivotal trial, we may elect to co-develop and co-promote in return for a profit-share in the U.S. We understand that MedImmune expects to file an IND with respect to these antibodies before the end of 2006.

MDX-1303 (Anti-Anthrax Antibody) *Bacillus anthracis Infection.* MDX-1303, also known as Valortim , is a fully human antibody in preclinical development that we are co-developing with PharmAthene. MDX-1303 is designed to protect against inhalation anthrax by targeting a protein component of lethal toxins produced by the *Bacillus anthracis* bacterium known as the anthrax

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♦ We expect to receive milestone payments, as these product candidates move through clinical trials, and royalties on product sales, should commercialization occur.

* We expect to receive milestone payments as these products move toward product approval, and royalties on product sales outside the U.S., should commercialization occur.

protective antigen. In preclinical studies, MDX-1303 both protected against infection, and, when administered some time after exposure, it induced recovery and survival in animals exposed to lethal doses of inhalation anthrax spores. An IND application could be submitted as early as 2005 to commence a Phase I dose escalation clinical trial evaluating the safety, tolerability and pharmacokinetics of MDX-1303 in healthy adults. In 2004, we received two grants from a division of the National Institutes of Health, or NIH, for up to $7.2 million over three years to support our research and development of MDX-1303.

Other Product Candidates. We are aware of a number of other antibody product candidates derived from our UltiMab technology for which our partners have commenced Phase I clinical trials, including two Novartis antibodies for the treatment of autoimmune disease, two Amgen antibodies for undisclosed indications, an anti-TRAIL-R2 antibody (HGS-TR2J) being developed by Human Genome Sciences pursuant to a license with Kirin, and Eli Lilly s antibody for an undisclosed indication. No additional information has been made public regarding any of these Phase I clinical trials.

In April 2003, we and Diatos SA entered into an agreement in which Diatos licensed from us the exclusive European rights to develop and commercialize a potential new cancer treatment, Super-Leu-Dox. This product consists of doxorubicin conjugated to a proprietary prodrug peptide. Preclinical studies have suggested that when prodrug molecules reach the vicinity of a tumor, the peptide is cleaved off by enzymes that are released by the cancer cells, freeing the cytotoxic compounds. The unconjugated compound is believed to then act as an anti-cancer agent, exerting its cytotoxic effects locally on the cancer cells.

Our Human Antibody Partnering Business

As of March 1, 2005, we have more than 50 partnerships with pharmaceutical and biotechnology companies to jointly develop and commercialize products or to enable other companies to use our UltiMab Human Antibody Development System in their development and commercialization of new therapeutic and, in some cases, diagnostic products. We expect that a significant portion of our operating revenues over the next few years will come from licensing fees and milestone payments from our existing and future partners.

BMS

In November 2004, we announced a collaboration and co-promotion agreement and a related securities purchase agreement with BMS. This collaboration became effective in January 2005. Under the terms of the collaboration, we and BMS have each granted the other certain intellectual property licenses and product rights on a worldwide basis in order to enable us to collaborate in research and development of certain therapeutic antibody-based products for the treatment of cancer and other diseases, and, in the event that further development work is successful, to commercialize any resulting products. In particular, the collaboration includes a grant by us to BMS of a license to commercialize MDX-010, a fully human antibody product candidate developed using our UltiMAb Human Antibody Development System, that is antagonistic to cytotoxic T-lymphocyte antigen 4 (CTLA-4). MDX-010 is currently under investigation for the treatment of a broad range of cancers and other diseases. The collaboration also includes the grant by us to BMS of a sub-license to MDX-1379, a gp100 melanoma peptide vaccine licensed by us from the U.S. Public Health Service, for use with MDX-010 for the treatment of metastatic melanoma. The FDA has granted orphan drug designation for MDX-010 for the treatment of Stage IIc, Stage III and Stage IV melanoma, and we and BMS are currently conducting a Phase III clinical trial with MDX-010 and MDX-1379 combination therapy in Stage III and Stage IV metastatic melanoma patients, under a SPA agreement with the FDA, at multiple sites within the U.S. This program has been granted Fast Track status by the FDA.

As part of the collaboration, we and BMS have committed to an initial multi-year budget of approximately $192.0 million to fund the development of MDX-010 as a potential treatment for a broad range of cancers. BMS will be responsible for 65% of all development costs related to clinical trials intended to support regulatory approval in both the U.S. and Europe, with the remaining 35% to be paid by us. The parties will share equally the costs of any clinical trials of products intended solely for regulatory approval in the U.S., and BMS will be fully responsible for all development costs that relate solely to regulatory approval in Europe and other parts of the world.

Under the terms of the collaboration, we could receive up to $205.0 million from BMS if all regulatory milestones are met, plus up to an additional $275.0 million in sales-related milestones. We will also have the option to co-promote any products in the U.S., and, if we elect to exercise this option and have participated in the funding of the applicable Phase III clinical trial(s), we will receive 45% of any profits from commercial sales. In the event we choose not to exercise our co-promotion rights, BMS will have exclusive commercial rights in the U.S. and will pay us royalties on commercial sales. Outside the U.S., BMS will have exclusive commercial rights and will pay us royalties on commercial sales.

Pursuant to these agreements, BMS made an initial cash payment to us on January 21, 2005 of $25.0 million. In addition, BMS purchased a total of 2,879,223 unregistered shares of our common stock at a purchase price equal to $8.6829 per share for an aggregate purchase price of $25.0 million. These shares were issued in a private placement pursuant to the exemption from registration provided by Section 4(2) of the Securities Act of 1933, as amended. The purchase price represented a small premium to the market price on the date we entered into the collaboration. BMS has agreed to a two-year lock-up period with respect to any sales of such stock. We have no future obligation to register such stock.

Unless terminated earlier, the BMS collaboration will continue for as long as development and/or commercialization of any collaborative products continue. BMS, however, may terminate the collaboration on a country-by-country basis at any time and, under certain conditions, on a product-by-product basis, resulting in the return of all rights to us with respect to such country and/or product. In addition, BMS may terminate our co-promotion rights in the U.S. in the event that we fail to satisfy certain performance criteria. We may terminate the BMS collaboration in the event of certain specified material breaches by BMS (in which case product rights would revert to us), and we may terminate BMS s co-promotion rights in the event that BMS fails to satisfy certain performance criteria.

MedImmune

In November 2004, we entered into a collaboration with MedImmune to develop antibodies targeting interferon-alpha and the Type I interferon receptor 1. The collaboration will initially focus on two fully human antibodies, MDX-1103 and MDX-1333, that are currently in preclinical development by us for the treatment of autoimmune diseases, such as systemic lupus erythematosus, SLE, or lupus. We understand that MedImmune expects to file INDs on these two antibodies with the FDA before the end of 2006.

Under the terms of the collaboration with MedImmune, we received an upfront payment of $15.0 million and will receive potential milestone payments for product candidates placed into clinical development. MedImmune will be fully responsible for all development costs up to the point of initiating pivotal trials of any product candidates. At that point, we have a choice for each potential product candidate. We can elect to enter into a profit sharing arrangement in the U.S. If we choose profit sharing, we will pay our proportionate share of the future development costs and reimburse MedImmune for a proportionate share of MedImmune s previous development costs plus interest. If we elect to enter into the profit sharing arrangement, we will also have the option to enter into a co-promotion relationship with MedImmune in the U.S. In the alternative, we can elect to forego any further funding for the product candidates and MedImmune will be fully responsible for all costs of development and commercialization. In that case, we will be entitled to milestone payments and substantial royalties on any sales in the U.S.

Regardless of what we elect to do with respect to the U.S. market, in the rest of the world we are entitled to milestone payments and royalties on any product sales.

Our Collaborative Partnerships

We have continued to increase our access to novel therapeutic targets by establishing collaborations with other companies and institutions that have identified potential therapeutic targets or have created platforms for the identification of such targets. We actively seek opportunities to in-license and/or acquire such targets and intend to develop novel therapeutic products by producing fully human antibodies that interact with such targets. As of March 1, 2005, we had agreements with more than 25 collaborators with whom we plan to jointly develop and commercialize human antibody products. Typically, a collaborator will provide one or more target antigen(s), and we will generate and develop antibodies against the antigen(s) using our UltiMAb Human Antibody Development System. We and our collaborators typically agree to share equally the costs of clinical development and manufacturing as well as revenues, expenses and profits associated with any products arising under the collaboration. We believe this allows us to participate in the research and development of substantially more potential candidates than we could develop on our own if we bore the entire cost of development.

Our Licensing Partnerships

Our licensing partners typically obtain licenses to one or more of our antibody generating technologies which allow these partners to develop and commercialize antibody-based products using our technology. We could receive license fees, milestone payments and royalties on product sales in connection with each of these products. Under these licenses, there is usually an initial period during which our licensing partner may elect to enter into a research license for antibodies to a particular designated target. Subsequently, our partner may elect to obtain a commercial license for one or more specific monoclonal antibodies. In some cases, once a partner has obtained a commercial license for monoclonal antibodies to a given target, we can no longer license our human antibody technology to a different company for that particular target. As of March 1, 2005, we had more than 20 licensing partnerships with partners including industry leaders such as Amgen, Centocor, Pfizer, Eli Lilly, Human Genome Sciences, Abbott Laboratories, Novartis, Novo Nordisk and Schering AG.

The financial terms of our licensing partnerships typically include license fees and a series of milestone payments commencing upon initiation of clinical trials and continuing through to commercialization. These fees and milestones may total up to $7.0 to $10.0 million per antibody if the antibody receives approval from the FDA and equivalent foreign agencies. A licensing partnership may involve multiple antibodies. Under these partnerships, we will also receive royalties on any product sales. In some cases, our partners reimburse us for research and development activities we conduct on their behalf. Generally, under the terms of these agreements, our partners are responsible for all costs of product development, manufacturing and commercialization of any products.

In September 2004, we entered into a series of agreements with Pfizer. The first agreement, or the Pfizer Amendment, amended our existing collaborative research and license and royalty agreements with Pfizer to provide for the discovery and development of up to 50 antibody products over ten years. The second and third agreements were a sublicense by us to Pfizer and a cross-license, or together, the Pfizer Licenses, of certain patents and patent applications solely relating to our respective anti-CTLA-4 antibody programs. The fourth agreement was a stock purchase agreement also related to the anti-CTLA-4 programs. Pursuant to certain of these agreements, Pfizer made a total initial cash payment to us of $80.0 million and purchased, through its wholly-owned subsidiary Pfizer Overseas Pharmaceuticals, a total of 4,827,808 unregistered shares of our common stock at a purchase price equal to $6.21 per share for an aggregate purchase price of $30.0 million at a small premium to market price at the time we entered into the collaboration. The shares were issued in a private placement pursuant to the exemption from

registration provided by Section 4(2) of the Securities Act of 1933, as amended. Pfizer also agreed to a two-year lock-up period with respect to any sales of such stock. In addition, we have no future obligation to register such stock.

Under the Pfizer Amendment, we expect to use our UltiMAb Human Antibody Development System to generate product candidates to disease-associated targets identified by Pfizer. We will receive standard market rates for performing these antibody-making services. The product candidates generated by the collaboration will then be transferred to Pfizer, which will be fully responsible for the worldwide development and commercialization of such product candidates, including the payment of all costs and expenses related thereto. We have no future payment obligations relating to the development and commercialization of these product candidates. We have the potential to receive research funding, license fees and milestone payments (if certain development milestones are met), as well as royalties on any commercial sales of the products.

We and Pfizer have retained all rights to our respective separate anti-CTLA-4 products. Pursuant to the Pfizer Licenses, which are non-exclusive, we have the potential to receive milestones and royalty payments based upon commercial sales of any Pfizer anti-CTLA-4 antibody product. In contrast, we have no future payment obligations to Pfizer in connection with any anti-CTLA-4 product we may develop. Both we and Pfizer are independently pursuing the clinical testing of antibodies to CTLA-4, including our MDX-010 and Pfizer s CP-675,206, which was not generated using our UltiMab technology.

Kirin and Other Technology Licenses

Effective September 4, 2002, we entered into a collaboration and license agreement with Kirin, which provides for us to exchange with Kirin certain cross-licenses for each other s technology for the development and commercialization of human antibody products. Pursuant to a letter of intent that was superceded by the collaboration and license agreement, we and Kirin developed the KM-Mouse, a unique crossbred mouse which combines the traits of our HuMAb-Mouse with Kirin s TC Mouse . Under the collaboration and license agreement, we are exchanging cross-licenses with Kirin with respect to the KM-Mouse and other antibody-generating mice. In addition, certain of the cross-licenses granted under the collaboration and license agreement are subject to license, milestone and royalty payments by one party to the other. We are aware of one anti-TRAIL-R2 antibody (HGS-TR2J), currently in Phase I clinical trials, which is being developed by HGS pursuant to a license with Kirin. We expect to receive royalties on sales of this product, should commercialization occur.

Through December 31, 2004, we had not made any milestone payments to Kirin, although approximately $1.9 million has been accrued as of December 31, 2004 representing a payment due Kirin as a result of our collaboration with Pfizer, and had made licensing and other payments of approximately $0.5 million. Based on a total of two products we are developing which use or we believe may use Kirin technology and that (i) are currently in clinical trials, or (ii) we anticipate may enter clinical trials through the end of 2006, we may be required to make milestone payments to Kirin aggregating up to approximately $8.5 million with respect to such products, or a maximum of approximately $4.25 million per product. Our future milestone payment obligations to Kirin may or may not be triggered, and may vary in size, depending on a number of variables, almost all of which are currently unknown, including the following:

- whether or not a decision is made to request a license from Kirin;
- the type of license requested (research or commercial);
- the success and timing of development efforts and clinical trials of product candidates covered by any such licenses;
- the type of product developed (payment obligations differ depending on whether a product is an *ex vivo* therapeutic, *in vivo* therapeutic, research reagent or diagnostic); and

- other financial provisions of the Kirin agreement that provide for variations in fee levels and netting of certain payments over specified periods of time that may impact the total amount potentially payable to Kirin for any particular license fee or milestone payment.

Whether we may be obligated to make milestone payments to Kirin in the future is subject to the success of our efforts with respect to products we are developing that utilize the Kirin technology and, accordingly, is inherently uncertain.

Unless terminated earlier, the collaboration and license agreement expires on December 31, 2014. The collaboration and license agreement can be terminated by either party in the event of a material breach by the other party if the breach is not cured during a specified cure period. In addition, either party may terminate any commercial license with respect to a specific biologic target granted to it by the other party under the agreement at any time.

In addition to our collaboration with Kirin, we have entered into a number of other agreements that contain licenses of third-party technology which may be used together with our own platform technologies for the generation, development and/or manufacture of our antibody products. In addition, we have entered into other third-party agreements that contain licenses associated with antibody products that target specific antigens. Many of these agreements contain milestone payments that become due with respect to products using/targeting the licensed technology/antigen only if and when certain specified pre-commercialization events occur. Not all of our products currently under development trigger such milestone payments. Through December 31, 2004, we had made milestone payments of approximately $0.3 million under these agreements. In addition, under the agreements we currently have in place (other than with Kirin), based on a total of five products we are developing for which milestones are potentially due and that (i) are now in clinical trials, or (ii) which we anticipate may enter clinical trials before the end of 2006, we may be obligated to make future milestone payments aggregating up to approximately $22.5 million with respect to such products. In general, potential milestone payments for our antibody products may or may not be triggered under these licenses, and may vary in size, depending on a number of variables, almost all of which are currently uncertain. Typically, the events that trigger these payments per product include:

- Submission of IND(s) or foreign equivalents;
- Commencement of Phase I, Phase II and/or Phase III clinical trials or foreign equivalents;
- Submission of BLA(s) or foreign equivalents; and
- Receipt of marketing approval(s) to sell products in a particular country or region.

In addition, the licenses above may trigger royalty payments in connection with the commercialization of certain of our products. To date, we have not made any royalty payments on sales of our products and believe we are at least a few years away from selling any products that would require us to make any such royalty payments. Whether we will be obligated to make milestone or royalty payments in the future is subject to the success of our product development efforts and, accordingly, is inherently uncertain.

Significant Partner Revenue

Revenue from partners representing 10% or more of total revenues for the years ended December 31, 2002, 2003 and 2004 is as follows:

Partner	2002	2003	2004
Genmab	37 %	48 %	26 %
Pfizer			20 %
Amgen	3 %	15 %	8 %
Lilly	11 %	7 %	6 %
IDM	36 %		

Further information regarding revenues from partners is included in Notes 10 through 12 to the Consolidated Financial Statements.

Strategic Investments

Genmab

In February 1999, we and a group of unrelated third party investors formed Genmab, a Danish biotechnology company, to develop and commercialize a portfolio of fully human antibodies derived from our HuMAb-Mouse technology. Initially, the investor group invested approximately DKK 35.4 million or $5.3 million (based on the then current exchange rate of $1.00 = DKK 6.73), and received approximately 44% of Genmab s share capital. At the same time, we contributed a license to our human antibody technology for producing antibodies to particular targets in exchange for comparable consideration of approximately 44% of Genmab s share capital. During Genmab s initial 12 months of operation, the investor group invested an additional DKK 49.0 million or $7.0 million (based on the then current exchange rate of $1.00 = DKK 6.99) for additional equity in Genmab. In connection therewith, we expanded our license to provide Genmab with broader rights to our human antibody technology in exchange for further equity, thereby maintaining our level of ownership in Genmab s share capital. Specifically, in exchange for equity, we granted Genmab 16 fully paid-up commercial licenses for antibody products. In addition, in May 2000, Genmab completed a private placement in which it received approximately DKK 321.0 million or $38.4 million (based on the then current exchange rate of $1.00 = DKK 8.35) from the original investor group and additional new investors. In connection therewith, we made an additional cash investment of $18.0 million in order to maintain our approximate 44% ownership interest in Genmab. In August 2000, we received additional equity in connection with the Genomics Agreement (as described below) valued at $2.0 million (based upon the recently completed private placement), representing payment for the first year which increased our equity interest in Genmab to approximately 45%.

In August 2000, we entered into a binding memorandum of understanding, or the Genomics Agreement, with Genmab, pursuant to which we granted Genmab rights to make available our transgenic mouse technologies for multi-target (five or more targets) genomics partnerships to certain pharmaceutical and biotechnology companies whose headquarters are located in Europe. Under the terms of the Genomics Agreement, Genmab may make available our human antibody technology (a) for large multi-target (five or more targets) partnerships to any Europe-based company except for: (i) certain Medarex partners, including Novartis, Merck KGaA, Schering, Aventis Behring, Immuno-Design Molecules S/A, or IDM, and Scil Biomedicals GmbH; and (ii) any European based pharmaceutical company with worldwide revenues in excess of $1 billion in 1999, provided, however, that Genmab may make available our human antibody technology to Sanofi/Synthélabo and Boehringer Ingelheim, and (b) for non-large multi-target (less than five targets) partnerships, to any company worldwide. We also have the right to participate in Genmab s large multi-target (five or more targets) partnerships, thereby sharing in certain costs and commercial benefits. We retain all rights to make available our technology to companies headquartered outside of Europe and to all companies for non-large multi-target (less than five targets) partnerships in Europe. Certain license fees, milestones and royalties due to us under our previously existing agreement with Genmab were reduced. The Genomics Agreement also provides that, under certain circumstances, we must negotiate in good faith to manufacture antibodies for Genmab s partnerships. Finally, the Genomics Agreement grants Genmab certain rights to access technologies acquired by us from each of Biosite Incorporated and Kirin, respectively.

The Genomics Agreement has an initial term of five years with a right exercisable by Genmab to extend the term for an additional two years. For each year of the agreement and during the term of any extension, we will receive $2.0 million per year from Genmab. At Genmab s option, these amounts may be paid in either cash or capital stock. During each of the years ended December 31, 2002, 2003 and 2004, the

Company recognized $2.0 million of revenue from this agreement. The initial term of this agreement expires in August 2005.

In October 2000, Genmab became a publicly listed company on the Copenhagen Stock Exchange. As a result of raising the equivalent of $187.0 million (based on the then current exchange rate) and subsequent investments in Genmab by other parties, our ownership interest in Genmab decreased to approximately 32%. In July 2004, Genmab completed a private placement of 5.6 million shares of its stock, resulting in a further reduction in our ownership interest. As of December 31, 2004, our ownership interest in Genmab was approximately 24.7%. We currently account for our investment in Genmab under the equity method of accounting.

IDM

During the second half of the 1990s, the focus of our business shifted from humanized and murine monoclonal antibody-based products to fully human antibody development. As a result, in July 2000, we entered into an agreement with Immuno-Design Molecules, S.A., or IDM, whereby we licensed to IDM certain of our humanized and murine antibodies in exchange for equity units in IDM. Under the agreement, IDM acquired worldwide rights to the use of our MDX-210 anti-HER-2 product in connection with cell therapy. IDM also acquired the right to receive royalty payments from third party sales of MDX-210 in Europe, outside the field of cell therapy. Additionally, IDM acquired certain rights in all fields to additional products which we are not actively developing at this time.

As a result of this transaction, we recorded a gain from the transfer of this technology of approximately $40.5 million (based upon an independent valuation) as non-cash contract revenue over a two year period ending in September 2002 for financial reporting purposes (see Note 12 to the Consolidated Financial Statements). In October 2000, we participated in a private placement of equity interests in IDM and purchased additional equity of approximately $5.2 million. Our current equity position in IDM is approximately 8%. In the event that we exercise certain warrants held by us to purchase convertible or redeemable bonds of IDM and such bonds are converted or redeemed, our equity position in IDM would be approximately 23%, based on the shares of IDM currently outstanding. These warrants are exercisable between September 2002 and September 2010, and such bonds may be converted or redeemed within six months of such exercise.

Celldex

We are in the process of a possible initial public offering of a portion of the common stock of our wholly-owned subsidiary Celldex Therapeutics, Inc. As part of this transaction, we have assigned or licensed to Celldex certain intellectual property related to our vaccine technology, including the rights to MDX-1307, one of our product candidates for the treatment of cancer, as well as the IND associated with this product which became effective in February 2004. If the offering is completed, we anticipate that we will continue to hold approximately 70% of the outstanding shares of common stock of Celldex. We cannot assure you that this transaction will be consummated.

In January 2005, Celldex entered into an asset purchase agreement to acquire substantially all of the assets of Alteris Therapeutics, Inc., a Pennsylvania based private biotechnology company. Through its strategic acquisition of the Alteris assets, Celldex will acquire the following assets:

- An exclusive worldwide non-royalty bearing, fully paid-up license to the patents covering a validated proprietary cancer antigen EGFRvIII for use in vaccine and immunization approaches to prevent, inhibit and treat tumor formation and progression;

- The exclusive rights to commercialize ALT-110, a therapeutic cancer vaccine based on the EGFRvIII cancer antigen that is currently being studied by a number of academic institutions in an investigator-initiated Phase II clinical trial for brain cancer and an investigator-initiated Phase I clinical trial for various other cancers; and

- An exclusive worldwide fee and royalty bearing license to the patent applications covering the Rapid Identification of Alternative Splicing system, or RIAS, a target discovery platform technology.

The acquisition of the Alteris assets is subject to the completion of Celldex s initial public offering and certain other standard closing conditions. A majority of the Alteris stockholders have agreed to vote in favor of the acquisition, subject to their fiduciary obligations.

Our Human Antibody Technology

The UltiMAb Technology Platform

Antibodies are natural proteins produced in the human body by B cells and serve as an important defense against disease. Human B cells produce millions of different types of antibodies, all with varying shapes that cause them to attach to and, as a result, neutralize different disease targets. For example, certain antibodies seek out and attach to viruses, bacteria and diseased cells, making them susceptible for destruction by the human immune system. Others attach to specific disease targets and block their interaction with other molecules.

Our solution to making antibodies with fully human protein sequences is to use transgenic strains of mice in which mouse antibody gene expression is suppressed and effectively replaced with human antibody gene expression. Because our mice contain genes encoding human antibodies, we believe the antibodies we generate are more likely to have favorable safety profiles and be eliminated less rapidly from the human body, potentially reducing the frequency and amount of dosing required to affect disease targets. Additionally, our fully human antibodies do not require any humanization, a process that at times has proven to be challenging and time consuming, and can result in antibodies with lowered binding affinities for their respective targets. Our human antibody technology includes (i) our HuMAb-Mouse technology, (ii) Kirin s TC Mouse technology, and (iii) the KM-Mouse technology, a crossbred mouse that combines the characteristics of our HuMAb-Mouse with those of the TC Mouse. In total these technologies constitute our UltiMAb Human Antibody Development System.

Our HuMAb-Mouse technology refers to transgenic mice in which the mouse genes for creating antibodies have been disrupted and functionally replaced by human antibody genes. Our HuMAb-Mouse transgenic strains contain key gene sequences from unrearranged human antibody genes that code for both the heavy and light chains of human antibodies. Because genes determine what proteins are made, our transgenic mice make human antibody proteins. We have thus created mice that have the ability to make fully human monoclonal antibodies. This result avoids the need to humanize murine monoclonal antibodies, and because the human genes in our HuMAb-Mouse are stable, they are passed on to offspring of the mice. Mice can, therefore, be bred indefinitely at relatively low cost and without additional genetic engineering. Our HuMAb-Mouse can generate fully human antibodies with affinities in the picomolar range, as high as 10^{12}.

Through our collaboration with Kirin, we have access to the Kirin TC Mouse, which contains complete sets of the variable and constant genes found in the corresponding natural human immunoglobulin loci, including all heavy chain classes that encode all isotypes (IgG1-4, IgA1-2, IgD, IgM and IgE). The TC Mouse also has the ability to make fully human monoclonal antibodies. Together with Kirin, we have developed the KM-Mouse, a crossbred mouse that combines the characteristics of our HuMAb-Mouse with those of Kirin s TC Mouse, retaining the capability to produce all human antibody isotypes with an immune response we believe previously unseen in any human antibody producing mouse system.

To further enhance our ability to create products from genomics research, we have also coupled the UltiMAb Human Antibody Development System with other technologies, such as our proprietary toxin

technology for creating antibody toxin conjugates, some of which we acquired from Corixa Corporation in 2002. Our toxin program includes small molecules known as duocarmycins, which have been designed to overcome multi-drug resistance. We believe this program provides us with a platform for generating cytotoxic drugs that specifically target various cancers.

The UltiMAb Advantage

Our unique technology platform constitutes what we believe to be the most complete technology solution available in the marketplace for generating fully human antibodies and enables us to produce antibodies that we believe set the industry standard in that they are (i) 100% human, (ii) of a very high affinity, and (iii) can be produced and manufactured relatively quickly and efficiently.

We believe that our human antibody technologies offer the following advantages over other antibody technologies:

- *Fully Human Antibodies*. Unlike humanization techniques, our UltiMAb Human Antibody Development System generates antibodies with 100% human protein sequences, which we believe will permit the development of products with a favorable safety profile. Additionally, we believe fully human antibody-based products are likely to be eliminated less rapidly from the human body, potentially reducing the frequency and amount of dosing.

- *High Affinity Antibodies.* Our human antibody technology takes advantage of the human body s natural affinity maturation process (whereby antibodies evolve over time to have higher affinity to targets), creating antibodies that can have affinities up to 1,000 times higher than the chimeric or humanized antibodies now approved for sale in the U.S.. Our high affinity antibodies have been generated against a wide range of target antigens. Our human antibodies are produced without the need for any subsequent engineering to make them more human a process that at times has proven to be challenging and time consuming. Thus, we reduce the risk that an antibody s structure and function will be altered between the time of the selection of the initial antibody and the time the final version of the antibody is placed into production.

- *Rapid Development Capabilities.* By combining our technology for creating fully human antibodies with our in-house development and clinical supply manufacturing expertise, we believe that we can rapidly progress from immunization to the clinic.

- *Diverse Selection of Antibodies Responding to Many Disease Targets.* We believe that our technology has the potential to generate high affinity human antibodies of all isotypes and subclasses that recognize more antigen structures. In addition, we have been able to create large panels of monoclonal antibodies to many potentially medically relevant antigens. For a given antigen target, the ability to select a product candidate from a pool of multiple antibodies could be important in selecting the optimal antibody product candidate for development.

- *Flexibility for Our Partners.* Our human antibody technology can be used either in our laboratories or in the laboratories of our partners. This provides our partners with the flexibility to incorporate our technology into their research and development programs or to contract with us to produce the antibodies.

- *Greater Certainty of Intellectual Property Rights.* We are not aware of any licenses required to create fully human antibodies using our UltiMAb technology platform to a target owned by the user except under patents currently owned or licensed by us. In contrast, various entities hold patents that may cover the chimerization or humanization of monoclonal antibodies. In addition, several companies and academic institutions have developed phage libraries for the creation of monoclonal antibodies, and a number of companies and academic research centers have received patents that may apply to the creation of phage-derived monoclonal antibodies.

Our Research, Development and Manufacturing of Human Antibodies

Our product development efforts are supported by our experience in both generating and developing numerous human antibodies and in manufacturing clinical supply materials. We believe this experience, together with increased access to novel therapeutic targets, will allow us to rapidly generate and develop a large, diverse pipeline of fully human antibody products. We intend to develop some of these product candidates for our own account and some in collaboration with other companies, leveraging their respective research and development resources.

Our antibody generation resources include highly trained teams of scientists in our research facilities located in Milpitas and Sunnyvale, California, as well as in Annandale and Bloomsbury, New Jersey, that work with our UltiMAb Human Antibody Development System to generate antibodies for our own development and for our partners. These scientists are experienced in molecular biology, protein chemistry, animal biology, pharmacology, toxicology and process science/formulation. Other development resources include in-house medical professionals with product development expertise in oncology, infectious diseases, rheumatology, immunology and pulmonology, and consulting arrangements with leading academic researchers.

In addition to our experience in generating antibodies, we have considerable experience in clinical development and clinical supply antibody manufacturing. To facilitate the development and commercialization of antibody-based products for us and for our partners, we have assembled a team of experienced scientific, production and regulatory personnel. This team operates in Bloomsbury, New Jersey, and in our clinical trial material manufacturing facility in Annandale, New Jersey.

Our Bloomsbury, New Jersey, research and development facility is situated on approximately 135 acres of land and currently contains space for approximately 165,000 square feet of laboratory and office space. We completed a renovation of these facilities in 2004 and currently use approximately 100,000 square feet in these facilities, accommodating approximately 225 employees engaged in antibody research, development and manufacturing.

We lease approximately 45,000 square feet of laboratory, clinical trial production and office space in Annandale, New Jersey, where we manufacture antibody products for use in clinical development and clinical trials conducted by us and by certain of our partners. Our Annandale facility currently has the capacity to develop up to 15 new antibody projects per year and operates in all respects in accordance with current good manufacturing practices, or cGMP, regulatory requirements for the manufacturing of clinical trial materials. We believe that our existing facility in Annandale is adequate for the production of materials for clinical trials of our products and for providing the support we offer to our partners in connection with our human antibody technology in the near-term. We are currently negotiating with third-party manufacturers to establish clinical and commercial supply contracts necessary for our future production requirements. In September 2003, we entered into a clinical supply agreement with Lonza Group Ltd. with respect to MDX-010 and MDX-060, and, together with our partner BMS, we are pursuing ongoing discussions with respect to terms of a commercial supply agreement for MDX-010. We do not currently have the capability to manufacture our products under development in large commercial quantities and have no experience in commercial-scale manufacturing.

Our Cross License Agreement With Abgenix

In 1994, prior to our acquisition of GenPharm International, Inc., Abgenix, Inc. and related entities brought a lawsuit against GenPharm relating to intellectual property issues involved in creating transgenic mice capable of generating fully human antibodies. GenPharm filed counterclaims, and the litigation was settled in March 1997 upon the execution of a patent cross-license and settlement agreement. Under the terms of this agreement, GenPharm granted a license, on a non-exclusive basis, to certain patents, patent applications, third party licenses and inventions pertaining to the development and use of certain

transgenic rodents, including mice, that produce fully human antibodies. In exchange for this license, GenPharm received payments in 1997, and after our acquisition of GenPharm, we received payments, including interest, from Abgenix and its related parties, which totaled approximately $38.6 million. Neither Abgenix nor any of its related entities have any further payment obligations to us under the agreement. Neither we nor GenPharm were required to make any payments to Abgenix or any related entity under the terms of the agreement. The agreement also provides us with a non-exclusive license to certain intellectual property held by Abgenix.

Intellectual Property

Proprietary protection for our products, processes and know-how is important to our business. Our policy is to file patent applications to protect technology, inventions, and improvements that we consider important to the development of our business. We also rely upon trade secrets, know-how and continuing technological innovation to develop and maintain our competitive position. We plan to aggressively prosecute and defend our patents and proprietary technology.

Currently, we hold a total of 60 issued patents in the U.S., and over 140 issued patents in foreign countries with respect to our HuMAb-Mouse technology and products, our bispecific molecule technology and products, and to our other technology and products.

Of these, 16 of our issued patents and allowed patent applications in the U.S. and 26 of our issued patents in foreign countries, including European countries, Japan, Korea, New Zealand and Australia, among others, relate to various aspects of our HuMAb-Mouse technology and products. These patents, almost all of which are in the same patent family, claim the transgene, the transgenic mouse, methods of obtaining high affinity antibodies, and compositions of matter for high affinity antibodies, among others. These patents have expiration dates beginning in 2008. We also have more than 150 related pending U.S. and foreign patent applications directed to various aspects of our HuMAb-Mouse technology and products. These include patent applications describing several of our particular human antibody product candidates, such as our anti-PSMA, anti-CTLA-4 and anti-CD30 product candidates.

Additionally, we hold exclusive and non-exclusive licenses to various pertinent technologies relating to our HuMAb-Mouse technology. For example, these technologies include microinjection of transgene DNA, homologous recombination, chromosome transfer, yeast artificial chromosome transgene technology and other relevant technologies. We also hold an exclusive sub-license to intellectual property created at the University of California relating to aspects of our anti-CTLA-4 antibody product and have licenses from BMS and Pfizer concerning other intellectual property related to our anti-CTLA-4 product. We have a license from the U.S. Public Health Service with respect to MDX-1379. We have a license from medac GmbH relating to certain aspects of our anti-CD30 antibody product. We have been assigned patent rights from Northwest Biotherapeutics, Inc. relating to aspects of our anti-PSMA antibody product and have a non-exclusive license from Millennium Pharmaceuticals, Inc. relating to aspects of our anti-PSMA antibody product. We have been assigned patent rights relating to our anti-interferon alpha receptor antibody product by Nufarm, B.V., Medisup International N.V., Pharma Pacific Pty. Ltd and Laboratorie European de Biotechnologie. We have acquired patent rights relating to our anti-IP-10 antibody product through our acquisition of Ability Biomedical. In addition, we have acquired patent rights from Corixa relating to tumor-activated prodrugs and Ultra-Potent Toxins.

We own registrations for the following trademarks in the listed jurisdications: Medarex® in the U.S., the European Union, Canada, Australia and Switzerland; HuMAb-Mouse®, KM-Mouse®, UltiMAb Human Antibody Development System®, and Putting the Immune System to Work® in the U.S. and European Union; GenPharm® and Trans-Phage Technology® in the U.S.; and UltiMAb® in the European Union.

Regulatory Issues

General

The production, distribution and marketing of products employing our technology, and our research and development activities, are subject to extensive governmental regulation in the U.S. and in other countries. In the U.S., our products are regulated both as drugs and as biological products and are subject to the Federal Food, Drug, and Cosmetic Act, as amended, the Public Health Service Act, also as amended, and the regulations promulgated under these statutes, as well as to other federal, state, and local statutes and regulations. These laws, and similar laws outside the U.S., govern the clinical and non-clinical testing, manufacture, safety, effectiveness, approval, labeling, distribution, sale, import, export, storage, record keeping, reporting, advertising and promotion of our products. Product development and approval within this regulatory framework, if successful, will take many years and involve the expenditure of substantial resources. Violations of regulatory requirements at any stage may result in various adverse consequences, including FDA s and other health authorities delay in approving or refusal to approve a product. Violations of regulatory requirements also may result in enforcement actions, including withdrawal of approval, labeling restrictions, seizure of products, fines, injunctions and/or civil or criminal penalties.

The following paragraphs provide further information on certain legal and regulatory issues with a particular potential to affect our operations or the future marketing of products employing our technology.

Research, Development, and Product Approval Process. The research, development, and approval process in the U.S. and elsewhere is intensive and rigorous, and generally takes many years. The typical process required by the FDA before a therapeutic drug or biological product may be marketed in the U.S. includes:

- submission to the FDA of an application for an IND, which must become effective before human clinical trials may commence;

- preliminary human clinical studies to evaluate the drug or biologic and its manner of use; adequate and well-controlled human clinical trials to establish (i) for a drug, whether it is safe and effective for its intended uses, and (ii) for a biological product, whether it is also pure and potent;

- FDA review of whether the facility in which the drug or biologic is manufactured, processed, packed or held meets standards designed to assure the product s continued quality; and

- submission of an appropriate product application to the FDA, and approval of the application by the FDA.

During preclinical testing, studies are performed with respect to the chemical and physical properties of candidate formulations, and are subject to good laboratory practices requirements. Biological testing is typically done in animal models to demonstrate the activity of the compound against the targeted disease or condition and to assess the apparent effects of the new product candidate on various organ systems, as well as its relative therapeutic effectiveness and safety. An IND must be submitted to the FDA and become effective before studies in humans may commence.

Clinical trial programs in humans generally follow a three-phase process. Typically, Phase I studies are conducted in small numbers of healthy volunteers or, on occasion, in patients afflicted with the target disease, to determine the metabolic and pharmacological action of the product candidate in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. In Phase II, studies are generally conducted in larger groups of patients having the target disease or condition in order to validate the clinical endpoint, and to obtain preliminary data on the effectiveness of the product candidate and optimal dosing. This phase also helps determine further the safety profile of the product candidate. In Phase III, large-scale clinical trials are generally conducted in hundreds of patients having

the target disease or condition to provide sufficient data for the statistical proof of effectiveness and safety of the product candidate as required by U.S. and foreign regulatory agencies.

In the case of products for cancer and certain other life-threatening diseases, the initial human testing may be done in patients with the disease rather than in healthy volunteers. Because these patients are already afflicted with the target disease or condition, it is possible that such studies will provide results traditionally obtained in Phase II studies. These studies are often referred to as Phase I/II studies. Notwithstanding the foregoing, even if patients participate in initial human testing and a Phase I/II study carried out, the sponsor is still responsible for obtaining all the data usually obtained in both Phase I and Phase II studies.

Before proceeding with a study, sponsors may seek a written agreement from the FDA regarding the design, size, and conduct of a clinical trial. This is known as a Special Protocol Assessment, or SPA. We and BMS are developing MDX-010 in combination with MDX-1379 under an SPA for the treatment of certain severe types of melanoma. Among other things, SPAs can cover clinical studies for pivotal trials whose data will form the primary basis to establish a product s efficacy. Where the FDA agrees to an SPA, the agreement may not be changed by either the sponsor or the FDA except if the sponsor and the FDA agree to a change, or a senior FDA official determines that a substantial scientific issue essential to determining the safety or effectiveness of the product was identified after the testing began. SPAs thus help establish up-front agreement with the FDA about the adequacy of the design of a clinical trial to support a regulatory approval, but the agreement is not binding if new circumstances arise. There is no guarantee that a study will ultimately be adequate to support an approval even if the study is subject to an SPA.

U.S. law requires that studies conducted to support approval for product marketing be adequate and well controlled. In general, this means that either a placebo or a product already approved for the treatment of the disease or condition under study must be used as a reference control. Studies must also be conducted in compliance with good clinical practice, or GCP, requirements, and informed consent must be obtained from all study subjects.

The clinical trial process for a new compound can take 10 years or more to complete, and there can be no assurance that the data collected will be in compliance with GCP requirements, will demonstrate that the product is safe or effective, or, in the case of a biologic product, pure and potent as well, or will provide sufficient data to support FDA approval of the product. The FDA may prevent clinical trials from beginning or may place clinical trials on hold at any point in this process if, among other reasons, it concludes that clinical subjects are being exposed to an unacceptable health risk. Trials may also be prevented from beginning or may be terminated by institutional (in most cases, hospital) review boards, who must review and approve all research involving human subjects. Side effects or adverse events that are reported during clinical trials can delay, impede, or prevent marketing authorization. Similarly, adverse events that are reported after marketing authorization can result in additional limitations being placed on a product s use and, potentially, withdrawal of the product from the market. Any adverse event, either before or after marketing authorization, can result in product liability claims against the company.

During the course of, and following the completion of clinical trials, the data are analyzed to determine whether the trials successfully demonstrated safety and effectiveness, and whether a product approval application may be submitted. In the U.S., if the product is regulated as a drug, a New Drug Application, or NDA, must be submitted and approved before commercial marketing may begin. If the product, such as an antibody, is regulated as a biologic, a Biologic License Application, or BLA, must be submitted and approved before commercial marketing may begin. The FDA Center for Drug Evaluation and Research, or CDER, has responsibility for the review and approval of drugs, and also has responsibility for the review and approval of certain therapeutic biologics such as antibodies, cytokines, growth factors, enzymes, interferons and certain proteins. The FDA Center for Biologics Evaluation and Research, or CBER, has responsibility for other biologics, including vaccines. Based on this distribution of

responsibility, we expect that most of our products will be reviewed by CDER. The NDA or BLA must include a substantial amount of data and other information concerning the safety and effectiveness (and, in the case of a biologic, purity and potency) of the compound from laboratory, animal and human clinical testing, as well as data and information on manufacturing, product stability, and proposed product labeling.

Each domestic and foreign biopharmaceutical manufacturing establishment, including any contract manufacturers we may decide to use, must be listed in the NDA or BLA and must be registered with the FDA. The application will not be approved until the FDA conducts a manufacturing inspection, approves the applicable manufacturing process for the drug or biological product, and determines that the facility is in compliance with current good manufacturing practice, or cGMP, requirements. If the manufacturing facilities and processes fail to pass the FDA inspection, we will not receive approval to market these products.

Under the Prescription Drug User Fee Act, as amended, the FDA receives fees for reviewing a BLA or NDA and supplements thereto, as well as annual fees for commercial manufacturing establishments and for approved products. These fees can be significant. The NDA or BLA review fee alone can exceed $0.67 million, although certain limited deferrals, waivers and reductions may be available.

Under applicable laws and FDA regulations, each NDA or BLA submitted for FDA approval is usually reviewed for administrative completeness and reviewability within 45 to 60 days following submission of the application. If deemed complete, the FDA will file the NDA or BLA, thereby triggering substantive review of the application. The FDA can refuse to file any NDA or BLA that it deems incomplete or not properly reviewable. If the FDA refuses to file an application, the FDA will retain 25% of the user fee as a penalty. The FDA has established performance goals for the review of NDAs and BLAs six months for priority applications and 10 months for regular applications. However, the FDA is not legally required to complete its review within these periods and these performance goals may change over time. Moreover, the outcome of the review, even if generally favorable, typically is not an actual approval but an action letter that describes additional work that must be done before the application can be approved. The FDA s review of an application may involve review and recommendations by an independent FDA advisory committee. Even if the FDA approves a product, it may limit the approved therapeutic uses for the product as described in the product labeling, require that warning statements be included in the product labeling, require that additional studies be conducted following approval as a condition of the approval, impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval.

Significant legal and regulatory requirements also apply after FDA approval to market under an NDA or BLA. These include, among other things, requirements related to adverse event and other reporting, product advertising and promotion, and ongoing adherence to cGMPs, as well as the need to submit appropriate new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. The FDA also enforces the requirements of the Prescription Drug Marketing Act, or PDMA, which, among other things, imposes various requirements in connection with the distribution of product samples to physicians.

The regulatory framework applicable to the production, distribution, marketing, sale and/or reimbursement of our products may change significantly from the current descriptions provided herein in the time that it may take for any of our products to reach a point at which an NDA or BLA is approved.

Overall research, development and approval times depend on a number of factors, including the period of review at the FDA, the number of questions posed by the FDA during review, how long it takes to respond to the FDA questions, the severity or life-threatening nature of the disease in question, the availability of alternative treatments, the availability of clinical investigators and eligible patients, the rate of enrollment of patients in clinical trials and the risks and benefits demonstrated in the clinical trials.

Treatment IND Status. Treatment INDs are used to make new drugs and biologic products available to desperately ill patients as early in the drug development process as possible, before general marketing is approved and begins. The FDA may allow an investigational drug to be used under a treatment IND if there is preliminary evidence of the drug s efficacy and the drug is intended to treat a serious or life-threatening disease for which no comparable or satisfactory alternative therapy exists. We or our collaborative partners may be able to recover some of the costs of production, manufacture, research, development and handling prior to market approval if patients are allowed to be charged for the product used in such studies. There are specific conditions that must be met before a sponsor may charge for an investigational product, including notifying the FDA in writing in advance. The FDA may notify the sponsor that it is not authorized to charge for the product.

Drugs and Biologics for Serious or Life-Threatening Illnesses. The Federal Food, Drug and Cosmetic Act, as amended, and FDA regulations provide certain mechanisms for the accelerated Fast Track approval of products intended to treat serious or life-threatening illnesses which have been studied for safety and effectiveness and which demonstrate the potential to address unmet medical needs. The procedures permit early consultation and commitment from the FDA regarding the preclinical and clinical studies necessary to gain marketing approval. Provisions of this regulatory framework also permit, in certain cases, NDAs or BLAs to be approved on the basis of valid surrogate markers of product effectiveness, thus accelerating the normal approval process. MDX-010 in combination with MDX-1379 has been granted Fast Track status for the treatment of high risk Stage II, Stage III and Stage IV melanoma. Genmab s HuMax-CD4 has been granted Fast Track status for the treatment of CTCL. Certain other products employing our human antibody technology might also qualify for this accelerated regulatory procedure. However, we cannot make assurances that the FDA will agree, and, even if the FDA agrees that these products qualify for accelerated approval procedures, the FDA may deny approval of our drugs or may require that additional studies be required before approval. The FDA would also likely require us to perform post-approval, or Phase IV, studies as a condition of such early approval. In addition, the FDA may impose restrictions on distribution and/or promotion in connection with any accelerated approval, and may withdraw approval if post-approval studies do not confirm the intended clinical benefit or safety of the product. Special rules would also apply to the submission to FDA of advertising and promotional materials prior to use.

Orphan Drugs. Under the Orphan Drug Act, special incentives exist for companies to develop products for rare diseases or conditions, which are defined to include those diseases or conditions that affect fewer than 200,000 people in the U.S. Companies may request that FDA grant a drug orphan designation prior to approval. Products designated as orphan drugs are eligible for special grant funding for research and development, FDA assistance with the review of clinical trial protocols, potential tax credits for research, reduced filing fees for marketing applications, and a special seven-year period of market exclusivity after marketing approval. Orphan drug exclusivity prevents FDA approval of applications by others for the same drug and the designated orphan disease or condition. FDA may approve a subsequent application from another person if FDA determines that the application is for a different drug or different use, or if FDA determines that the subsequent product is clinically superior, or that the holder of the initial orphan drug approval cannot assure the availability of sufficient quantities of the drug to meet the public s need. A grant of an orphan designation is not a guarantee that a product will be approved. If a sponsor receives orphan drug exclusivity upon approval, there can be no assurance that the exclusivity will prevent another entity from receiving approval for the same or a similar drug for the same or other uses.

Other U.S. Regulatory Requirements

In the U.S., the research, manufacturing, distribution, sale, and promotion of drug and biological products are potentially subject to regulation by various federal, state and local authorities in addition to

the FDA, including the Centers for Medicare and Medicaid Services (formerly the Health Care Financing Administration), other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice and individual U.S. Attorney offices within the Department of Justice, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended, the False Claims Act, also as amended, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veterans Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Moreover, we are now, and may become subject to, additional federal, state and local laws, regulations and policies relating to safe working conditions, laboratory practices, the experimental use of animals, and/or the use, storage, handling, transportation and disposal of human tissue, waste and hazardous substances, including radioactive and toxic materials and infectious disease agents used in conjunction with our research work.

Foreign Regulatory Requirements

We and our collaborative partners are subject to widely varying foreign regulations, which may be quite different from those of the FDA, governing clinical trials, product registration and approval, and pharmaceutical sales. Whether or not FDA approval has been obtained, we must obtain a separate approval for a product by the comparable regulatory authorities of foreign countries prior to the commencement of product marketing in these countries. In certain countries, regulatory authorities also establish pricing and reimbursement criteria. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. In addition, under current U.S. law, there are significant restrictions on the export of products not approved by the FDA, depending on the country involved and the status of the product in that country.

Reimbursement and Pricing Controls

In many of the markets where we or our collaborative partners would commercialize a product following regulatory approval, the prices of pharmaceutical products are subject to direct price controls (by law) and to drug reimbursement programs with varying price control mechanisms. Public and private health care payors control costs and influence drug pricing through a variety of mechanisms, including through negotiating discounts with the manufacturers and through the use of tiered formularies and other mechanisms that provide preferential access to certain drugs over others within a therapeutic class. Payors also set other criteria to govern the uses of a drug that will be deemed medically appropriate and therefore reimbursed or otherwise covered. In particular, many public and private health care payors limit reimbursement and coverage to the uses of a drug that are either approved by the FDA or that are supported by other appropriate evidence (for example, published medical literature) and appear in a recognized drug compendium. Drug compendia are publications that summarize the available medical evidence for particular drug products and identify which uses of a drug are supported or not supported by the available evidence, whether or not such uses have been approved by the FDA. For example, in the case of Medicare coverage for physician-administered oncology drugs, the Omnibus Budget Reconciliation Act of 1993, or OBRA 93, with certain exceptions, prohibits Medicare carriers from refusing to cover unapproved uses of an FDA-approved drug if the unapproved use is supported by one or more citations in the American Hospital Formulary Service Drug Information, the American Medical Association Drug

Evaluations, or the U.S. Pharmacopoeia Drug Information. Another commonly cited compendium, for example under Medicaid, is the DRUGDEX Information System.

Competition

We face competition in several different forms. Our human antibody generation activities currently face competition from several companies and from other technologies. In addition, the actual products being developed by us or by our partners also face actual and potential competition.

The development of biotechnology and pharmaceutical products is a highly competitive business subject to rapid technological change. We know of many pharmaceutical and biotechnology companies conducting research or development on therapeutic monoclonal antibody products. Many of these companies have commenced clinical trials with, and several have successfully commercialized, antibody products. Some of these companies are also pursuing product development efforts for the same disease areas or against the same biological targets as we or our partners are pursuing.

We face competition from many companies that provide the services of generating monoclonal antibodies for antibody-based therapeutics. One competitor with respect to our human antibody technology is Abgenix. As a result of the cross-licensing agreement with GenPharm (our wholly owned subsidiary since 1997), Abgenix offers to potential partners the use of its transgenic mouse known as XenoMouse to generate fully human monoclonal antibodies. In addition, we have entered into agreements with each of Kirin and Genmab, respectively, which grant these companies licenses to our proprietary transgenic mouse technology platform, enabling them to compete with us in offering antibody generation and development services in certain markets. Certain of our other partners who have licensed our transgenic mouse technology also could compete with us with respect to the development of certain antibodies. Other companies are also developing, or have developed technologies for generating human or partially human antibodies. For example, Xenerex Biosciences (a subsidiary of Avanir Pharmaceuticals) and XTL Biopharmaceuticals Ltd. each have developed technology that, according to Xenerex and XTL, will allow them to generate fully human monoclonal antibodies in functionally modified mice. Several companies are developing, or have developed, technologies not involving animal immunization that result in libraries composed of numerous human antibody sequences. For example, phage and yeast display technology is being used by companies such as Cambridge Antibody Technology Group plc, or CAT, Dyax Corp., Genetastix Corporation and MorphoSys AG to develop therapeutic products comprising human antibody sequences. Companies such as Johnson & Johnson, MedImmune, Amgen, Biogen Idec, Inc., Novartis, Genentech, Inc., Protein Design Labs, Inc., Abbott Laboratories and Wyeth have generated therapeutic antibody-based products that are currently in development or on the market and are derived from recombinant DNA that comprise human antibody sequences. Numerous additional companies are developing therapeutic products comprising human antibody components.

We are aware of several pharmaceutical and biotechnology companies actively engaged in research and development of antibody-based products that have commenced clinical trials with, or have successfully commercialized, antibody products. Some of these companies, such as Pfizer, ImClone Systems Incorporated, Johnson & Johnson, Wyeth, Amgen, Abbott, UCB Pharma, Biogen Idec, Abgenix, CAT, MorphoSys AG, Tanox, Inc., Genentech, Human Genome Sciences, Millennium and Protein Design Labs are addressing diseases and disease indications that are being targeted by us and certain of our partners. For example, Pfizer is developing CP-675,206, an antibody to CTLA-4, in potential competition with our product candidate, MDX-010. Several of these companies are also licensees of our transgenic mouse technology. Many of these companies and institutions, either alone or together with their partners, have substantially greater financial resources and larger research and development divisions than we have. In addition, many of these competitors, either alone or together with their partners, have substantially greater experience than us in developing pharmaceutical products, undertaking preclinical testing and human clinical trials, obtaining FDA and other regulatory approvals of such products and the manufacturing and

marketing of such products. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA or European Union marketing approval and commercializing products more rapidly than us.

Other technologies can also be applied to the treatment of the diseases that we or our partners are pursuing. For example, immunoconjugates monoclonal antibodies linked to toxins or radioactive isotopes are being developed by others. In addition, the application of recombinant DNA technology to develop potential products consisting of proteins (such as growth factors, hormones, enzymes, receptor fragments and fusion proteins, or cytokines) that do not occur normally in the body, or occur only in small amounts, has been underway for some time. Included in this group are interleukins such as IL-2 and IL-11, interferons alpha, beta and gamma, colony stimulating factors such as G-CSF and GM-CSF, clotting factors, growth hormones, erythropoeitin, DNAse, tPA, glucocerebrosidase, PDGF, and a number of other biological response modifiers. Continuing development of new chemical entities and other drugs by large pharmaceutical companies also carries with it the potential for discovery of agents for treating disease indications targeted by drugs that we or our partners are developing.

Marketing

Our potential products may be marketed and sold in several possible ways, depending on the product, including: solely by us, jointly by us and our collaborative partners, or solely by or on behalf of our licensing partners. Marketing and sales rights with respect to MDX-010 are subject to the terms of our collaboration with BMS. We believe that a small sales force could successfully introduce and detail certain of our potential products that have concentrated marketplaces. Other products, however, may require a larger sales force. Currently, we have no sales force. We may develop our own internal sales force for these products if they proceed to commercialization.

We acknowledge that the successful marketing of some of our potential products is beyond the capabilities of all but the largest pharmaceutical organizations. For this reason, we along with our collaborative partners may license to major pharmaceutical companies individual products serving large markets or those that will be widely distributed and/or detailed geographically, if the products are approved by the FDA. Our collaboration with BMS is an example of this kind of relationship.

Employees

As of December 31, 2004, we employed 435 regular, full and part-time employees, of whom approximately 363 are engaged in research and development activities. There are 72 employees involved in business development, legal, finance and other administrative functions. None of our employees is covered by a collective bargaining agreement. We have entered into employment contracts with certain of our executive officers. Our success will depend in large part upon our ability to attract and retain employees. We face competition for employees from other companies, research and academic institutions, government agencies and other organizations. We believe we maintain good relations with our employees.

Available Information

We were incorporated in the State of New Jersey on July 8, 1987. Our principal executive offices are located at 707 State Road, Princeton, New Jersey 08540. Our telephone number is (609) 430-2880.

We file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission, or SEC. You may read and copy our reports, proxy statements and other information at the SEC s public reference room at Room 1024, 450 Fifth Street N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available at the SEC s web site at *www.sec.gov*. In

addition, you can read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street N.W., Washington, D.C. 20006.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website on the World Wide Web at www.medarex.com, by contacting the Investor Relations Department at our corporate offices by calling (609) 430-2880 or by sending an e-mail message to *information@medarex.com*. You can direct requests for literature to the information request section on our website.

FORWARD LOOKING INFORMATION AND RISK FACTORS THAT MAY AFFECT FUTURE RESULTS

This Annual Report contains forward-looking statements within the meaning of Sections 27A and 21E of the Securities Exchange Act of 1934, as amended, including statements regarding our expectations, beliefs, intentions, or strategies regarding the future. Statements preceded by, followed by or that otherwise include the words believes , expects , anticipates , intends , estimates , plans , forecasts , is likely to , proj similar expressions or future conditional verbs such as should , would , may , and could are generally forward-looking in nature and not historica facts. Forward-looking statements include, without limitation, statements in this section, and in the sections entitled Management s Discussion and Analysis of Financial Condition and Results of Operations, Business and elsewhere in this Annual Report regarding, among other things, uncertainties relating to our technology; history of operating losses and anticipation of future losses; uncertainty of product development; need for additional capital and uncertainty of change; uncertainty of patent and proprietary rights; management of growth, and risks of acquiring new technologies; uncertainties related to clinical trials; government regulation and uncertainty of obtaining regulatory approval; dependence on key personnel; dependence on research collaborators and scientific advisors; uncertainty of health care reform measures and third-party reimbursement and risk of product liability. All forward-looking statements included in this Annual Report are based on information available to us as of the date hereof, and we do not assume any obligation to update any such forward-looking statements. Our actual results may differ materially from the results discussed in the forward-looking statements. Among the factors that could cause actual results to differ materially are the factors detailed below. Accordingly, in addition to the other information in this Annual Report, the following factors should be considered carefully. References to our products, business, financial results or financial condition should be considered to refer to us and our subsidiaries unless the context otherwise requires.

Our product candidates have not been and may not ever be approved for sale and/or commercialized, and many are in early stages of development.

Our human antibody technology is a new approach to the generation of antibody-based therapeutic products. Active product candidates employing our human antibody technology have not moved beyond clinical development. Based on public disclosures, regulatory applications, including INDs, have been submitted to the FDA or comparable foreign authorities, for 22 product candidates derived from our UltiMAb platform. To date, neither we nor our partners have any product candidates employing our human antibody technology that have been approved for sale by the FDA or comparable foreign authorities and/or commercialized. In addition, we are not aware of any commercialized fully human monoclonal antibody therapeutic products that have been generated from any technologies similar to ours. Product candidates employing our human antibody technology may not advance beyond clinical development or demonstrate clinical safety and effectiveness.

Our human antibody technology may not generate antibodies against all the antigens to which it is exposed in an efficient and timely manner, if at all. If our human antibody technology fails to generate

antibody product candidates, or if we or our partners do not succeed in the development of products employing our antibody technology, those product candidates may not be approved or commercialized and our business, financial condition and results of operations may be materially harmed.

Successful development of our products is uncertain. To date, no revenues have been generated from the commercial sale of our products and our products may not generate revenues in the future.

Our development of current and future product candidates is subject to the risks of failure inherent in the development of new pharmaceutical products and products based on new technologies. These risks include:

- delays in product development, clinical testing or manufacturing;
- unplanned expenditures in product development, clinical testing or manufacturing;
- failure in clinical trials or failure to receive regulatory approvals;
- emergence of superior or equivalent products;
- inability to manufacture on our own, or through others, product candidates on a commercial scale;
- inability to market products due to third-party proprietary rights;
- election by our partners not to pursue product development;
- failure by our partners to develop products successfully; and
- failure to achieve market acceptance.

In certain instances, we have experienced delays in our product development and clinical testing as a result of slower than anticipated patient recruitment. In a number of instances, we have terminated the development of certain products in the early stages of human clinical testing due to a lack of effectiveness. In addition, we determined not to continue the development of one late-stage product candidate due to both a lack of effectiveness and unforeseen safety issues that arose in clinical testing. This product did not employ our core fully human antibody technology.

Because of these risks, our research and development efforts or those of our partners may not result in any commercially viable products. If a significant portion of these development efforts are not successfully completed, required regulatory approvals are not obtained or any approved products are not commercially successful, our business, financial condition and results of operations may be materially harmed.

Because we and our partners have not begun commercial sales of our products, our revenue and profit potential are unproven and our limited operating history makes it difficult for an investor to evaluate our business and prospects. Our technology may not result in any meaningful benefits to our current or potential partners. No revenues have been generated from the commercial sale of our products, and our products may not generate revenues in the future. Further, due to our limited operating history, we have difficulty accurately forecasting our revenue. Our business and prospects should be considered in light of the heightened risks and unexpected expenses and problems we may face as a company in an early stage of development in a new and rapidly evolving industry.

We have incurred large operating losses and we anticipate that these losses will continue.

We have incurred large operating losses and we anticipate that these losses will continue for the foreseeable future. In particular, as of December 31, 2004, we had an accumulated deficit of approximately $599.4 million. Our net loss was $186.5 million for the year ended December 31, 2004. Our losses have resulted principally from:

- research and development costs relating to the development of our technology and antibody product candidates;
- costs associated with the establishment of our laboratory and manufacturing facilities and manufacturing of products; and
- general and administrative costs relating to our operations.

We intend to continue to make significant investments in:

- research and development;
- preclinical testing and clinical trials;
- establishing new collaborations; and
- new technologies.

In addition, we may be obligated to make milestone payments on certain of our products as they progress through the clinical trial process.

We do not know when or if we or our partners will complete any pending or future product development efforts, receive regulatory approval or successfully commercialize any approved products.

We may continue to incur substantial operating losses even if our revenues increase. As a result, we cannot predict the extent of future losses or the time required for us to achieve profitability, if at all.

Our operating results may vary significantly from period-to-period, which may result in a decrease in the price of our securities.

Our future revenues and operating results are expected to vary significantly from period-to-period due to a number of factors. Many of these factors are outside of our control. These factors include:

- the timing of the commencement, completion or termination of partnership agreements;
- the introduction of new products and services by us, our partners or our competitors;
- delays in, or termination of, preclinical testing and clinical trials;
- changes in regulatory requirements for clinical trials;
- costs and expenses associated with preclinical testing and clinical trials;
- the timing of regulatory approvals, if any;
- sales and marketing expenses; and
- the amount and timing of operating costs and capital expenditures relating to the expansion of our business operations and facilities.

Period-to-period comparisons of our results of operations may not be relied upon as an indication of future performance.

It is possible that in some future periods, our operating results may be below expectations of analysts and investors. If this happens, the price of our securities may decrease.

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We may need substantial additional funding. We may not be able to obtain sufficient funds to grow our business or continue our operations.

We will continue to expend substantial resources for research and development, including costs associated with developing our antibody technology and conducting preclinical testing and clinical trials. Our future capital requirements will depend on a number of factors, including, by way of example:

- the size and complexity of research and development programs;
- the scope and results of preclinical testing and clinical trials;
- the retention of existing and establishment of further partnerships, if any;
- continued scientific progress in our research and development programs;
- the time and expense involved in seeking regulatory approvals;
- competing technological and market developments;
- the time and expense of filing and prosecuting patent applications and enforcing patent claims; and
- the cost of establishing manufacturing capabilities, conducting commercialization activities and arrangements and in-licensing products.

We believe our current sources of liquidity will be sufficient to meet our near term operating, debt service and capital requirements for at least the next 24 months. To the extent our 2.25% convertible senior notes due in 2011 are converted into shares of our common stock on or before their maturity date, we will have use of that portion of the principal amount of the notes to fund our on-going operations. In any event, we may require additional financing within this time frame and may raise funds through public or private financings, line of credit arrangements, collaborative relationships and/or other methods. The use of cash on hand or other financial alternatives will depend on several factors including, but not limited to, the future success of our products in clinical development, the prevailing interest rate environment, and access to the capital markets. We may be unable to raise sufficient funds to complete development of any of our product candidates, to continue operations or to repay our debt obligations at maturity. As a result, we may face delay, reduction or elimination of research and development programs or preclinical or clinical trials, in which case our business, financial condition or results of operations may be materially harmed.

We have a significant amount of debt and may have insufficient cash to satisfy our debt service obligations. In addition, the amount of our debt could impede our operations and flexibility.

We have $150.0 million in aggregate principal amount of our 2.25% convertible senior notes outstanding, which, unless converted to shares of our common stock or redeemed, will mature in 2011. Our ability to make payments on these notes and our other obligations will depend on our future operating performance and ability to generate cash and may also depend on our ability to obtain additional debt or equity financing. Generally, during the last five years, our operating cash flows were negative and insufficient to cover our fixed charges. Our ability to generate sufficient operating cash flow to service our indebtedness, including the notes, and fund our operating requirements will depend on our ability, alone or with others, to successfully develop, manufacture, and obtain required regulatory approvals and market our product candidates, as well as other factors, including general economic, financial, competitive, legislative and regulatory conditions, some of which are beyond our control. If we are unable to generate sufficient operating cash flow to service our indebtedness and fund our operating requirements, we may need to obtain additional debt or equity financing to do so, which may not be available to us on satisfactory terms or at all. In addition, if new indebtedness is incurred, the risks relating to our ability to service our indebtedness that we face could intensify.

Even if we are able to meet our debt service obligations, the amount of debt we have could adversely affect us in a number of ways, including by:

- limiting our ability to obtain any necessary financing in the future for working capital, capital expenditures, debt service requirements or other purposes;
- limiting our flexibility in planning for, or reacting to, changes in our business;
- placing us at a competitive disadvantage relative to our competitors who have lower levels of debt;
- making us more vulnerable to a downturn in our business or the economy generally; and
- requiring us to use a substantial portion of our cash to pay principal and interest on our debt, instead of applying those funds to other purposes such as working capital and capital expenditures.

Clinical trials required for our product candidates are expensive and time-consuming, and their outcome is uncertain.

In order to obtain FDA approval to market a new drug product, we or our partners must demonstrate proof of safety and efficacy in humans. To meet these requirements, we or our partners will have to conduct extensive preclinical testing and adequate and well-controlled clinical trials. Conducting clinical trials is a lengthy, time-consuming and expensive process. The length of time may vary substantially according to the type, complexity, novelty and intended use of the product candidate, and often can be several years or more per trial. Delays associated with products for which we are directly conducting preclinical or clinical trials may cause us to incur additional operating expenses. Moreover, we will continue to be affected by delays associated with the preclinical testing and clinical trials of certain product candidates conducted by our partners over which we have no control. The commencement and rate of completion of clinical trials may be delayed by many factors, including, for example:

- the inability to manufacture sufficient quantities of qualified materials under current good manufacturing practices, or cGMPs, for use in clinical trials;
- the need or desire to modify our manufacturing processes;
- slower than expected rates of patient recruitment;
- the inability to adequately observe patients after treatment;
- changes in regulatory requirements for clinical trials;
- the lack of effectiveness during the clinical trials;
- unforeseen safety issues;
- delays, suspension, or termination of the clinical trials due to the institutional review board responsible for overseeing the study at a particular study site; and
- government or regulatory delays or clinical holds requiring suspension or termination of the trials.

Even if we obtain positive results from preclinical or clinical trials, we may not achieve the same success in future trials. Clinical trials may not demonstrate statistically sufficient safety and effectiveness to obtain the requisite regulatory approvals for product candidates employing our human antibody technology. In a number of instances, we have terminated the development of certain products in the early stages of human clinical testing due to a lack of effectiveness. In addition, we have determined not to continue the development of one late-stage product candidate due to both a lack of effectiveness and

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unforeseen safety issues that arose in clinical testing. This product did not employ our core fully human antibody technology.

Generally, our clinical trials, including our melanoma trials, are conducted in patients with serious life-threatening diseases for whom conventional treatments have been unsuccessful or for whom no conventional treatment exists, and in some cases, our product is used in combination with approved therapies that themselves have significant adverse event profiles. During the course of treatment, these patients could suffer adverse medical events or die for reasons that may or may not be related to our products. The most common adverse events associated with our trials of MDX-010 have consisted of flu-like symptoms such as fever, chills and nausea. These events were expected and generally responded to standard medical therapy. In addition, some patients have experienced anticipated drug-related ABEs, such as diarrhea, rash, reduced pituitary function, colitis and increased liver enzymes, ranging from mild in most cases to severe in a very small number of instances. Other than a very small number of fatalities, which may or may not be attributable to our product candidate, most ABEs resolved with treatment. We cannot assure you that additional safety issues will not arise with respect to our products in the future.

To date, we have experienced slower than expected rates of patient recruitment in certain of our clinical trials. As a result, in certain instances, we have experienced delays in our product development and clinical testing. In addition, data obtained from clinical trials of our products to date have been insufficient to demonstrate safety and efficacy under applicable FDA guidelines. As a result, these data will not support an application for regulatory approval without further clinical trials. Clinical trials that we conduct or that third-parties conduct on our behalf may not demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for any of our product candidates. We expect to commence new clinical trials from time to time in the course of our business as our product development work continues. The failure of clinical trials to demonstrate safety and effectiveness for our desired indications could harm the development of that product candidate as well as other product candidates. Any change in, or termination of, our clinical trials could materially harm our business, financial condition and results of operations.

Success in early clinical trials may not be indicative of results obtained in later trials.

Results of our early clinical trials and those of our partners using our human antibody technology are based on a limited number of patients and may, upon review, be revised or negated by authorities or by later stage clinical results. Historically, the results from preclinical testing and early clinical trials have often not been predictive of results obtained in later clinical trials. A number of new drugs and biologics have shown promising results in initial clinical trials, but subsequently failed to establish sufficient safety and effectiveness data to obtain necessary regulatory approvals. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval.

In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development. For example, the FDA has moved several product categories previously regulated by the agency s Center for Biologics Evaluation and Research, or CBER, to the agency s Center for Drug Evaluation and Research, or CDER. These product categories include antibodies as well as cytokines, growth factors, enzymes, interferons and certain proteins. FDA has also recently announced a planned reorganization within CDER to create a new consolidated office for the review of oncology therapies. Oncology therapies are currently reviewed by different offices within CDER. The effect that these reorganizations at the FDA will have on clinical trials and product approval outcomes or timing is uncertain, but could cause delays or other currently unforeseeable effects.

Product candidates employing our antibody technology may fail to gain market acceptance.

Even if clinical trials demonstrate the safety, effectiveness, potency and purity of products developed by us or our partners using our technology and all regulatory approvals have been obtained, product candidates employing our antibody technology may not gain market acceptance among physicians, patients, third-party payors and the medical community. For example, the current delivery systems for antibody-based therapeutic products are intravenous and subcutaneous injection, which are generally less well received by patients than tablet or capsule delivery. The degree of market acceptance of any product candidates employing our technology will depend on a number of factors, including, for example:

- establishment and demonstration of clinical efficacy, potency and safety, especially as compared to conventional treatments;
- cost-effectiveness;
- alternative treatment methods;
- reimbursement policies of government and third-party payors; and
- marketing and distribution support for our product candidates.

In addition, many of our activities involve genetic engineering in animals and animal testing, controversial subjects which have received adverse publicity from animal rights activists and various other interest groups. Such adverse publicity could decrease market acceptance of products employing our technology.

If products employing our technology do not achieve significant market acceptance, our business, financial condition and results of operations may be materially harmed.

The successful commercialization of our antibody products will depend on obtaining coverage and reimbursement for use of these products from third-party payors.

Sales of pharmaceutical products largely depend on the reimbursement of patients medical expenses by government health care programs and private health insurers. Without the financial support of the governments or third-party payors, the market for products employing our human antibody technology will be limited. These third-party payors are increasingly challenging the price and examining the cost effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of our products. Such studies may require us to dedicate a significant amount of resources. Our project candidates may not be considered cost-effective. Third-party payors may not reimburse sales of products employing our human antibody technology, or enable us or our partners to sell them at profitable prices.

Third-party payors control health care costs by limiting both coverage and the level of reimbursement for new health care products. In the future, the U.S. government may institute price controls and further limits on Medicare and Medicaid spending. Internationally, medical reimbursement systems vary with differing degrees of regulation. Pricing controls and reimbursement limitations could affect the payments we receive from sales of products generated using our human antibody technology. These variations could harm our ability and the ability of our partners to sell products generated using our human antibody technology in commercially acceptable quantities at profitable prices.

We may experience pressure to lower the prices of any prescription pharmaceutical products we are able to obtain approval for because of new and/or proposed federal legislation.

Federal legislation, enacted in December 2003, has added an outpatient prescription drug benefit to Medicare, effective January 2006. In the interim, Congress has established a discount drug card program

for Medicare beneficiaries. Both benefits will be provided primarily through private entities, which will attempt to negotiate price concessions from pharmaceutical manufacturers. These negotiations may increase pressures to lower prices. While the new law specifically prohibits the U.S. government from interfering in price negotiations between manufacturers and Medicare drug plan sponsors, some members of Congress are pursuing legislation that would permit the U.S. government to use its enormous purchasing power to demand discounts from pharmaceutical companies, thereby creating *de facto* price controls on prescription drugs. In addition, the new law contains triggers for Congressional consideration of cost containment measures for Medicare in the event Medicare cost increases exceed a certain level. These cost containment measures could include some sorts of limitations on prescription drug prices. The new legislation also modified the methodology used for reimbursement of physician administered and certain other drugs already covered under Medicare Part B. This new methodology would likely apply to certain of our products if and when commercialized. Experience with new reimbursement methodology is limited, and could be subject to change in the future. Our results of operations could be materially harmed by the different features of the Medicare prescription drug coverage legislation, by the potential effect of such legislation on amounts that private insurers will pay for our products and by other healthcare reforms that may be enacted or adopted in the future.

We may face increased competition from products imported from Canada or other countries.

Any products we are able to commercialize may be subject to competition from lower priced versions of such products and competing products from Canada, Mexico, and other countries where there are government price controls or other market dynamics that make the products lower priced. The ability of patients and other customers to obtain these lower priced imports has grown significantly as a result of the Internet, an expansion of pharmacies in Canada and elsewhere targeted to American purchasers, the increase in U.S.-based businesses affiliated with Canadian pharmacies marketing to American purchasers, and other factors. Many of these foreign imports are illegal under current law. However, the volume of imports is now significant due to the limited enforcement resources of the FDA and the U.S. Customs Service, and the pressure in the current political environment to permit the imports as a mechanism for expanding access to lower priced medicines.

In addition, in December 2003, federal legislation was enacted to change U.S. import laws and expand the ability to import lower priced versions of our and competing products from Canada, where there are government price controls. These changes to the import laws will not take effect unless and until the Secretary of Health and Human Services certifies that the changes will lead to substantial savings for consumers and will not create a public health safety issue. The previous Secretary of Health and Human Services determined that there was not a basis to make such a certification at this time. However, it is possible that a subsequent Secretary could make the certification in the future. In addition, legislative proposals have been made to implement the changes to the import laws without any certification, and to broaden permissible imports in other ways. Even if the changes to the import laws do not take effect, and other changes are not enacted, imports from Canada and elsewhere may continue to increase due to market and political forces, and the limited enforcement resources of the FDA, the Customs Service, and other government agencies. For example, state and local governments have suggested that they may import drugs from Canada for employees covered by state health plans or others, and some have already put such plans in place.

The importation of foreign products could adversely affect our profitability. This potential impact could become more significant in the future, and the impact could be even greater if there is a further change in the law or if state or local governments take further steps to import products from abroad.

Our manufacturing facilities may not continue to meet regulatory requirements and have limited capacity.

Before approving a new drug or biologic product, the FDA requires that the facilities at which the product will be manufactured are in compliance with current good manufacturing practices, or cGMP requirements. To be successful, our therapeutic products must be manufactured for development and, following approval, in commercial quantities, in compliance with regulatory requirements and at acceptable costs. While we believe our current facilities are adequate for the limited production of product candidates for clinical trials, our facilities are not adequate to produce sufficient quantities of any products for commercial sale.

If we are unable to establish and maintain a manufacturing facility or secure third-party manufacturing capacity within our planned time and cost parameters, the development and sales of our products and our financial performance may be materially harmed.

We may also encounter problems with the following:

- production yields;
- quality control and assurance;
- shortages of qualified personnel;
- compliance with FDA regulations, including the demonstration of purity and potency;
- changes in FDA requirements;
- production costs; and/or
- development of advanced manufacturing techniques and process controls.

We are aware of only a limited number of companies on a worldwide basis that operate manufacturing facilities in which our product candidates can be manufactured under cGMP regulations, a requirement for all pharmaceutical products. We are currently pursuing late-stage clinical and commercial supply agreements with cGMP-compliant third-party manufacturers with available capacity to meet our internal production timetables. We have entered into clinical supply agreements with Lonza Group Ltd. with respect to MDX-010 and MDX-060, and, together with our partner BMS, we are pursuing ongoing discussions with respect to terms of a commercial supply agreement for MDX-010. We do not currently have the capability to manufacture our products under development in large commercial quantities and have no experience in commercial-scale manufacturing. It would take a substantial period of time for a contract facility that has not been producing antibodies to begin producing antibodies under cGMP regulations. We cannot make assurances that we will be able to contract with such companies for clinical and/or commercial supply on acceptable terms or in a timely manner, if at all. Moreover, even if we are able to enter into clinical and/or commercial supply manufacturing arrangements with cGMP-compliant third-party manufacturers, we cannot assure you that such manufacturers will be able to produce products that are substantially equivalent to the product candidates that we have produced in our own facilities and used in our clinical trials. If such companies are not able to produce products that are substantially equivalent to our product candidates, the progress of our clinical trials and/or commercialization of our products may be delayed and our business, financial condition and results of operations may be materially harmed.

In addition, we and any third-party manufacturer will be required to register manufacturing facilities with the FDA and other regulatory authorities. The facilities will be subject to inspections confirming compliance with cGMP or other regulations. If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition and results of operations may be materially harmed.

We are, in part, dependent on our partners willingness and/or ability to devote resources to the development of product candidates or otherwise support our business as contemplated in our partnership agreements.

We depend, in part, on our partners to support our business, including the development of products generated through the use of our antibody technology. In particular, under the terms of our collaboration and co-promotion agreement with BMS, we have granted a license to commercialize our lead product candidate, MDX-010, to BMS for the treatment of a broad range of cancers. We have also granted to BMS a sub-license to MDX-1379 for use in combination with MDX-010 for the treatment of metastatic melanoma. The successful development and commercialization of MDX-010 is dependent, in large part, on the actions of BMS, which are outside of our control. The failure of BMS to act in accordance with its obligations under the collaboration and co-promotion agreement may cause us to incur substantial additional costs in order to develop and commercialize MDX-010, which could have a material adverse effect on our business.

We currently, or in the future may, rely on our partners to:

- access proprietary antigens for the development of product candidates;
- access skills and information that we do not possess;
- fund our research and development activities;
- manufacture products;
- fund and conduct preclinical testing and clinical trials;
- seek and obtain regulatory approvals for product candidates; and/or
- commercialize and market future products.

Our dependence on our partners subjects us to a number of risks, including:

- our partners have significant discretion whether to pursue planned activities;
- we cannot control the quantity and nature of the resources our partners may devote to product candidates;
- our partners may not develop products generated using our antibody technology as expected; and
- business combinations or significant changes in a partner s business strategy may adversely affect that partner s willingness or ability to continue to pursue these product candidates.

If we do not realize the contemplated benefits from our partners, our business, financial condition and results of operations may be materially harmed.

Our existing partnerships may be terminated, and we may not be able to establish additional partnerships.

Our licensing partners generally have the right to terminate our partnerships at any time. Our ability to continue our current partnerships and to enter into additional partnerships is dependent in large part on our ability to successfully demonstrate that our UltiMAb technology is an attractive method of developing fully human antibody therapeutic products. Existing or potential partners may pursue alternative technologies, including those of our competitors, or enter into other transactions that could make a collaboration with us less attractive to them. For example, if an existing partner purchases or is purchased by a company that is one of our competitors, that company could be less willing to continue its collaboration with us. In addition, a company that has a strategy of purchasing companies rather than entering into partnership arrangements might have less incentive to enter into a collaboration agreement with us. Moreover, disputes may arise with respect to the ownership of rights to any technology or products

developed with any current or future partner. Lengthy negotiations with potential new partners or disagreements between us and our partners may lead to delays or termination in the research, development or commercialization of product candidates. If we are not able to establish additional partnerships on terms that are favorable to us or if a significant number of our existing partnerships are terminated and we cannot replace them, we may be required to increase our internal product development and commercialization efforts. This would likely:

- limit the number of product candidates that we will be able to develop and commercialize;
- significantly increase our need for capital; and/or
- place additional strain on management s time.

Any of the above may materially harm our business, financial condition and results of operations.

Due to the size of our equity interest in Genmab, we must include a portion of its income and losses in our financial statements.

Due to the size of our equity interest in Genmab, we are currently required to account for our interest in Genmab under the equity method of accounting, which provides that we must include a portion of Genmab s income and losses equal to our percentage equity interest in Genmab in our consolidated financial statements. For the years ended December 31, 2002, 2003 and 2004, our share of Genmab s losses were approximately $19.6 million (excluding the $31.0 million impairment charge discussed below), $15.0 million and $19.8 million, respectively. As such, the current value of our equity interest in Genmab as determined by the equity method of accounting is $1.6 million, which we expect to be reduced to zero in the first quarter of 2005 and, accordingly, recognition of our share of Genmab s net losses will be suspended.

Our strategic investments in our partners whose securities are publicly traded expose us to equity price risk and, in addition, investments in our partners may be deemed impaired, which would affect our results of operations.

We have a number of strategic investments which expose us to equity price risk. These investments may become impaired which would adversely affect our results of operations.

We are exposed to equity price risk on our strategic investments in our publicly-traded partners, including Genmab and Amgen, Inc., and as part of our business strategy, we may choose to make additional similar investments in public companies in the future. As these investments are the result of strategic alliances with our collaborative partners, we typically do not attempt to reduce or eliminate our market exposure of these types of strategic investments. Under SFAS No. 115, Accounting for Certain Investments in Debt and Equity Securities, these investments are designated as available-for-sale and are reported at fair value on our consolidated balance sheet. Unrealized holding gains and losses on available-for-sale securities are generally excluded from earnings and reported within other comprehensive income which is a separate component of shareholders equity. Under our accounting policy, marketable equity securities are generally considered to be impaired if their fair value is less than our cost basis in such securities for more than six months, or some other period in light of the particular facts and circumstances surrounding the investment. If a decline in the fair value of available-for-sale securities is considered to be other than temporary, the cost basis of the security is written down to fair value as a new cost basis and the amount of the write-down is included in earnings as an impairment charge. For the year ended December 31, 2002, we recorded impairment charges of approximately $40.5 million (of which approximately $31.0 million related to Genmab) on our strategic investments in publicly traded companies. During the year ended December 31, 2003, no impairment charges were recorded related to the value of our investments in publicly traded companies. For the year ended December 31, 2004, we recorded impairment charges of $0.2 million on investments in partners whose securities are publicly traded. If we

deem these investments to be further impaired at the end of any future reporting period, we may incur additional impairment charges on these investments.

In addition, we have investments in several of our partners whose securities are not publicly traded, such as IDM. The value of our investments in these companies are inherently more difficult to estimate than our investments in publicly traded companies. We estimate the value of these investments by using information acquired from industry trends, the management of these companies, financial statements, and other external sources. Specifically, our determination of any potential impairment of the value of privately held securities includes an analysis of the following for each company on a periodic basis: review of interim and year-end financial statements, cash position and overall rate of cash used to support operations, the progress and development of technology and product platform, the per share value of subsequent financing and potential strategic alternatives. Based on the information acquired through these sources, we record an investment impairment charge when we believe an investment has experienced a decline in value that is considered to be other than temporary. For the years ended December 31, 2002, 2003 and 2004, we recorded impairment charges of approximately $2.4 million, $1.4 million and $7.1 million, respectively, on our investments in privately-held companies. Approximately $7.0 million of the 2004 impairment charge related to IDM. Future adverse changes in market conditions or adverse changes in operating results of these companies may also require an impairment charge in the future.

We are dependent on our key personnel.

We are highly dependent on the members of our scientific and management staff. If we are not able to retain any of these persons, our business may suffer. In particular, we depend on the services of Donald L. Drakeman, J.D., Ph.D., our President and Chief Executive Officer; Nils Lonberg, Ph.D., our Senior Vice President and Scientific Director; and Geoffrey M. Nichol, M.D., MBA., our Senior Vice President, Product Development. We maintain a key man life insurance policy for Dr. Drakeman in the amount of $2.0 million and maintain key man life insurance policies in the amount of $1.0 million for each of Dr. Lonberg and Dr. Nichol. We have entered into employment agreements with Dr. Drakeman and all of our other executive officers, which expire in January, 2007. Thereafter, all of these agreements are automatically renewed for successive one (1) year terms unless we or the employee elect not to renew.

For us to pursue product development, marketing and commercialization plans, we will need to hire additional qualified scientific personnel to perform research and development. We will also need to hire personnel with expertise in clinical testing, government regulation, manufacturing, sales and marketing, relevant law and finance. We may not be able to attract and retain personnel on acceptable terms, given the competition for such personnel among biotechnology, pharmaceutical and healthcare companies, universities and non-profit research institutions. If we are not able to attract and retain qualified personnel, our business, financial condition and results of operations may be materially harmed.

We depend on patents and proprietary rights.

Our success depends in part on our ability to:

- apply for, obtain, protect and enforce patents;
- protect trade secrets;
- operate without infringing upon the proprietary rights of others; and
- in-license certain technologies.

We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. We protect our proprietary position by filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the

development of our business. While a number of patents have been issued in the U.S. and Europe relating to our human antibody technology, we may not be able to obtain patent protection in other countries. Our pending patent applications, those we may file in the future, or those we may license from third parties, may not result in patents being issued or enforceable. The patent position of biotechnology companies involves complex legal and factual questions and, therefore, enforceability cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. Thus, any patents that we own or license from third parties may not provide sufficient protection against competitors. Also, patent rights may not provide us with proprietary protection or competitive advantages against competitors with similar technology. Furthermore, others may independently develop similar technologies or duplicate any technology that we have developed. The laws of foreign countries may not protect our intellectual property rights to the same extent as do the laws of the U.S.

In addition to patents, we rely on trade secrets and proprietary know-how. We seek protection, in part, through confidentiality and proprietary information agreements. These agreements may not provide protection or adequate remedies in the event of unauthorized use or disclosure of confidential and proprietary information, or breach of these agreements. Furthermore, our trade secrets may otherwise become known to, or be independently developed by, our competitors.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. In the event that our technologies may infringe on the patents or violate other proprietary rights of third parties, we and our partners may be prevented from pursuing product development, manufacturing or commercialization. Such a result may materially harm our business, financial condition and results of operations.

Third parties may allege our products infringe their patents or may challenge the validity of our patents and other intellectual property rights, resulting in litigation or other time-consuming and expensive proceedings which could deprive us of valuable products and/or rights.

If we become involved in any intellectual property litigation, interference or other judicial or administrative proceedings, we will incur substantial expense and the efforts of our technical and management personnel will be diverted. An adverse determination may subject us to significant liabilities or require us to seek licenses that may not be available from third parties on commercially favorable terms, if at all. Therefore, we and our partners may be restricted or prevented from manufacturing and selling products employing our human antibody technology, which would harm our business.

Even though we have received patents pertaining to the HuMAb-Mouse technology, this does not mean that we and our licensees of HuMAb-Mouse technology will have exclusive rights to antibodies against all targets that are made using this technology, or that we or our licensees will have the right to make, develop, use or sell such antibodies.

Our patents covering the HuMAb-Mouse technology include patents that cover particular human antibodies. These patents do not cover all human antibodies.

Our patents may not protect against the importation of products, such as antibodies, made using HuMAb-Mouse technology.

Moreover, other parties could have blocking patent rights to products made using HuMAb-Mouse technology, such as antibodies, and their production and uses, for instance because of a proprietary position covering the antibody or the antibody s target. For example, we are aware of certain U.S. and European patents held by third parties relating to particular targets for their human monoclonal antibodies, to human monoclonal antibodies against various targets and bispecific products, and the manufacture and use of such products. We are also aware of certain U.S. and foreign patents and patent applications held by third parties relating to anti-CD4 antibodies, such as HuMax-CD4, anti-CD30 antibodies, such as MDX-060, anti-EGFr antibodies, such as HuMax-EGFr, anti-PSMA antibodies, such

as MDX-070, anti-Type 1 IFN antibodies, such as MDX-1103, and antibody-antigen conjugates, such as MDX-1307/bHCG-VAC, as well as other antibody products under development by us.

We are also aware of a U.S. patent owned by Genentech, relating to the production of recombinant antibodies in host cells. We currently produce certain of our products and our partners products using recombinant antibodies from host cells and may choose to produce additional products in this manner. If any of our antibody products are produced in the manner claimed in this patent, then we may need to obtain a license, should one be available. We have a license to this patent from Genentech for our anti-CTLA-4 product candidate (MDX-010) but currently do not have licenses for any of our other antibody product candidates. If we desire a license for any of our other antibody product candidates and are unable to obtain a license on commercially reasonable terms or at all, we may be restricted in our ability to make recombinant antibodies using Genentech s techniques. In addition to the Genentech patent, we are also aware of certain U.S. patents held by third parties relating to antibody expression in particular types of host cells, including CHO cells, which may be relevant to our current or future manufacturing techniques.

If our antibody products (or those antibody products of our partners using our human antibody technology) or their commercial use or production meet all of the requirements of any of the claims of the aforementioned patents, or patents that may issue from the aforementioned patent applications, then we or our partners may need a license to one or more of these patents. Further, we are aware of a number of other third party patent applications that, if granted, with claims as currently drafted, may cover our and our partners current or planned activities. We intend to seek licenses to such patents when, in our judgment, such licenses are needed. If any licenses are required, there can be no assurance that we will be able to obtain any such license on commercially favorable terms, if at all, and if these licenses are not obtained, we might be prevented from using certain of our technologies for the generation of our recombinant human antibody products. Our failure to obtain a license to any technology that we may require may materially harm our business, financial condition and results of operations. We cannot assure you that our products and/or actions in developing or selling human antibody products will not infringe such patents.

In general, our patent protection may not prevent others from developing competitive products using our technology or other technologies. Similarly, others may obtain patents that could limit our ability and the ability of our partners to use, import, manufacture, market or sell products or impair our competitive position and the competitive position of our partners.

We do not have exclusive access to the patents underlying the HuMAb-Mouse. In March 1997, prior to our acquisition of GenPharm, GenPharm entered into a cross-license and settlement agreement with Abgenix, Cell Genesys, Inc., Xenotech, L.P. and Japan Tobacco, Inc., pursuant to which Abgenix and these entities paid us a total of approximately $38.6 million in exchange for a non-exclusive license to certain patents, patent applications, third-party licenses and inventions pertaining to the development and use of certain transgenic rodents, including mice, that produce fully human antibodies that are integral to our products and business. These patents, licenses and inventions form the basis of our HuMAb-Mouse technology. Our business may suffer from the competition of these entities, as well as if any of these entities breach the cross-license and settlement agreement.

We are not the exclusive owner of the technology underlying the KM-Mouse. Effective September 4, 2002, we entered into a collaboration and license agreement with Kirin, which provides for us to exchange certain cross-licenses for each other s technology for the development and commercialization of human antibody products made using the HuMAb-Mouse, the KM-Mouse and certain other antibody-generating mice. Kirin has certain rights to distribute and use such mice throughout the world. Our business may suffer as a consequence of competition from Kirin or if the collaboration and license agreement were breached or terminated for any reason.

We have had and may continue to face product liability claims related to the use or misuse of products developed by us or our partners.

The administration of drugs to humans, in clinical trials or after commercialization, may expose us to product liability claims. Consumers, healthcare producers or persons selling products based on our technology may be able to bring claims against us based on the use of our products in clinical trials and the sale of products based on our technology. Product liability claims may be expensive to defend and may result in large judgments against us. We have obtained limited product liability coverage for our clinical trials, under which coverage limits are $10 million per occurrence and $10 million in the aggregate. Although we believe these coverage limits are adequate, we cannot be certain that the insurance policies will be sufficient to cover all claims that may be made against us. We intend to increase our coverage limits as we progress into additional late-stage clinical trials and to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for products in development. Product liability insurance is expensive, difficult to obtain and may not be available in the future on acceptable terms.

In November 1998, we voluntarily suspended clinical trials for one of our products after some patients experienced serious adverse events, or SAEs. This product did not employ our core fully human antibody technology and we have determined not to pursue further development of this product. As a result of these SAEs, we received a small number of claims, of which five resulted in lawsuits being filed. All of these lawsuits have been settled for insubstantial amounts. We cannot make assurances that additional claims will not be filed against us relating to these SAEs or arising out of any other clinical trial we have conducted or will conduct in the future.

Generally, our clinical trials, including our melanoma trials, are conducted in patients with serious life-threatening diseases for whom conventional treatments have been unsuccessful or for whom no conventional treatment exists, and in some cases, our product is used in combination with approved therapies that themselves have significant adverse event profiles. During the course of treatment, these patients could suffer adverse medical events or die for reasons that may or may not be related to our products. The most common adverse events associated with our melanoma trials have consisted of flu-like symptoms such as fever, chills and nausea. These events were expected and generally responded to standard medical therapy. In addition, some patients have experienced anticipated drug-related autoimmune adverse events, such as diarrhea, rash, reduced pituitary function, colitis and increased liver enzymes, ranging from mild in most cases to severe in a very small number of instances. Almost all of these adverse events responded to medical therapy. In a very small number of instances, fatalities have occurred during the course of these trials such fatalities may or may not be attributable to our product. Any of these events could result in a product liability claim. Any such claims against us, regardless of their merit, could result in significant awards against us, which could materially harm our business, financial condition and results of operations.

We face intense competition and rapid technological change.

The development of biotechnology and pharmaceutical products is a highly competitive business subject to significant and rapid technological change. We face competition in several different forms. First, our human antibody generation activities currently face competition from several competitors with similar technology to ours as well as distinctly different technologies. The actual products being developed by us or by our partners also face actual and potential competition. Developments by our competitors may render our human antibody technology obsolete or non-competitive.

We are aware of several pharmaceutical and biotechnology companies that are actively engaged in research and development in areas related to antibody therapeutics. Some of these companies have commenced clinical trials of antibody products or have successfully commercialized antibody products. Many of these companies are addressing the same diseases and disease indications as we and our partners. Also, we compete with companies that offer antibody generation services to other companies that have

disease related target antigens. These competitors have specific expertise or technology related to monoclonal antibody development. We compete directly with Abgenix, with respect to the generation of fully human antibodies from transgenic mice. In addition, we have entered into agreements with each of Kirin and Genmab, respectively, that grant these companies licenses to our proprietary transgenic mouse technology platform, enabling them to compete with us in offering antibody generation and development services in certain markets. We have also entered into license agreements with Pfizer which enable it to compete with us in the generation and development of antibodies to CTLA-4. Xenerex Biosciences and XTL Biopharmaceutical, Ltd. have developed technology that, according to Xenerex and XTL, will allow them to generate fully human monoclonal antibodies in functionally modified mice. Numerous additional companies are developing therapeutic products comprising human antibody components. Furthermore, several companies are developing, or have developed, technologies that do not involve immunization of animals for creating antibodies comprising human antibody sequences. For example, phage and yeast display technology is being used by companies, such as Cambridge Antibody Technology Group plc, Dyax Corp., Genetastix Corporation and MorphoSys AG to develop therapeutic products comprising human antibody sequences. Companies such as Johnson & Johnson, MedImmune, Amgen, Biogen Idec Inc., Novartis, Genentech, Protein Design Labs, Inc., Wyeth, Abbott Laboratories and Corixa have generated therapeutic products that are currently in development or on the market and that are derived from recombinant DNA that comprise human antibody components.

Other technologies can also be applied to the treatment of the diseases that we or our partners are pursuing. For example, immunoconjugates monoclonal antibodies linked to toxins or radioactive isotopes are being developed by others. In addition, the application of recombinant DNA technology to develop potential products consisting of proteins (such as growth factors, hormones, enzymes, receptor fragments and fusion proteins, or cytokines) that do not occur normally in the body, or occur only in small amounts, has been underway for some time. Included in this group are interleukins such as IL-2 and IL-11, interferons alpha, beta and gamma, colony stimulating factors such as G-CSF and GM-CSF, clotting factors, growth hormones, erythropoeitin, DNAse, tPA, glucocerebrosidase, PDGF, and a number of other similar biological agents. Continuing development of new chemical entities and other drugs by large pharmaceutical companies carries with it the potential for discovery of agents for treating disease indications also targeted by drugs that we or our partners are developing.

Some of our competitors have received regulatory approval or are developing or testing product candidates that compete directly with product candidates employing our antibody technology. Many of these companies and institutions, either alone or together with their partners, have substantially greater financial resources and larger research and development staffs than we or some of our partners do. In addition, many of these competitors have significantly greater experience than we do in:

- developing products;
- undertaking preclinical testing and clinical trials;
- obtaining FDA and other regulatory approvals of products; and
- manufacturing and marketing products.

Accordingly, our competitors may obtain patent protection, receive FDA approval or commercialize products before we or our partners do. If we or our partners commence commercial product sales, we or our partners will be competing against companies with greater marketing and manufacturing capabilities, areas in which we and certain of our partners have limited or no experience.

We also face intense competition from other pharmaceutical and biotechnology companies to establish partnerships, as well as relationships with academic and research institutions, and to license proprietary technology from these institutions. These competitors, either alone or with their partners, may succeed in developing or licensing technologies or products that are more effective than ours.

We are subject to extensive and costly government regulation.

Product candidates employing our human antibody technology are subject to extensive and rigorous domestic government regulation including regulation by the FDA, the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments and their respective foreign equivalents. The FDA regulates the research, development, preclinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, storage, approval, advertising, promotion, sale, distribution, import, and export of biopharmaceutical products. The FDA regulates human antibodies as biologics, subject to a Biologic License Application, or BLA, under the Public Health Service Act, as amended. If products employing our human antibody technology are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not we have obtained FDA approval for a given product and its uses. Such foreign regulation may be equally or more demanding than corresponding U.S. regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive and uncertain. We or our partners must obtain and maintain regulatory authorization to conduct clinical trials. We or our partners must obtain regulatory approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires the submission of extensive preclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product s safety, efficacy, potency and purity for each intended use. The development and approval process takes many years, requires substantial resources, and may never lead to the approval of a product. Failure to obtain regulatory approvals, or delays in obtaining regulatory approvals may:

- adversely affect the successful commercialization of any drugs that we or our partners develop;
- impose additional costs on us or our partners;
- diminish any competitive advantages that we or our partners may attain; and
- adversely affect our receipt of revenues or royalties.

Even if we are able to obtain regulatory approval for a particular product, the approval may limit the indicated uses for the product, may otherwise limit our ability to promote, sell, and distribute the product, may require that we conduct costly post-marketing surveillance, and/or may require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, may require further regulatory review and approval. Once obtained, any approvals may be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue. If we, our partners or our contract manufacturers fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things:

- delays in the approval of applications or supplements to approved applications;
- refusal of a regulatory authority, including the FDA, to review pending market approval applications or supplements to approved applications;
- warning letters;
- fines;
- import and/or export restrictions;
- product recalls or seizures;
- injunctions;

- total or partial suspension of production;
- civil penalties;
- withdrawals of previously approved marketing applications or licenses;
- recommendations by the FDA or other regulatory authorities against governmental contracts; and
- criminal prosecutions.

In certain cases, we expect to rely on our partners to file Investigational New Drug applications, or INDs, with the FDA and to direct the regulatory approval process for products employing our human antibody technology. Our partners may not be able to conduct clinical testing or obtain necessary approvals from the FDA or other regulatory authorities for their product candidates employing our human antibody technology. If they fail to obtain required governmental approvals, our partners will be delayed or precluded from marketing these products. As a result, commercial use of products employing our technology will not occur and our business, financial condition and results of operations may be materially harmed.

We do not have, and may never obtain, the regulatory approvals we need to market our product candidates.

Following completion of clinical trials, the results are evaluated and, depending on the outcome, submitted to the FDA in the form of a BLA, or a New Drug Application, or NDA, in order to obtain FDA approval of the product and authorization to commence commercial marketing. In responding to a BLA or NDA, the FDA may require additional testing or information, may require that the product labeling be modified, may impose post-approval study or reporting requirements or other restrictions on product distribution, or may deny the application. The timing of final FDA review and action varies greatly, but can take years in some cases and often involves the input of an FDA advisory committee of outside experts. Product sales in the U.S. may commence only when a BLA or NDA is approved.

To date, we have not applied for or received the regulatory approvals required for the commercial sale of any of our products in the U.S. or in any foreign jurisdiction. None of our product candidates has been determined to be safe and effective, and we have not submitted an NDA or BLA to the FDA or an equivalent application to any foreign regulatory authorities for any of our product candidates. We have only limited experience in filing and pursuing applications necessary to obtain regulatory approval. As a result, it is possible that none of our product candidates will be approved for marketing.

Product candidates that appear promising in the early phases of development, such as in early human clinical trials, may fail to reach the market for a number of reasons, such as the product candidate did not demonstrate acceptable clinical trial results even though it demonstrated positive preclinical trial results; the product candidate was not effective in treating the specified disease or condition; the product candidate had harmful side effects on humans or presented unacceptable safety risks; the governing regulatory authorities (such as the FDA) denied approval to the product candidate altogether or denied a commercially important indicated use; the product candidate was not economical for us to manufacture; and/or the product candidate was not cost effective in light of alternative therapies. We cannot guarantee that we will ever be able to produce commercially successful products.

If we or our manufacturing partners do not comply with current good manufacturing practices requirements, we will not be able to commercialize our product candidates.

We will depend on our own manufacturing facilities and on those of our partners and other third parties to manufacture products generated through the use of our human antibody technology. Before commercializing a new drug, manufacturers must demonstrate compliance with the applicable current good manufacturing practices, or cGMP, requirements which include quality control and quality assurance

requirements as well as the maintenance of extensive records and documentation. Manufacturing facilities are subject to ongoing periodic inspection by the FDA and corresponding foreign and state authorities, including unannounced inspections, and must be licensed before they can be used in commercial manufacturing for products generated through the use of our technology. In addition, cGMP requirements are constantly evolving, and new or different requirements may apply in the future. We, our partners or third party contract manufacturers may not be able to comply with the applicable regulations. After regulatory approvals are obtained, the subsequent discovery of previously unknown problems, or the failure to maintain compliance with existing or new regulatory requirements, may result in restrictions on the marketing of a product, withdrawal of the product from the market, seizures, the shutdown of manufacturing facilities, injunctions, monetary fines and/or civil or criminal sanctions.

Even if approved, our products will be subject to extensive post-approval regulation.

Once a product is approved, numerous post-approval requirements apply. Among other things, the holder of an approved BLA or NDA is subject to periodic and other FDA monitoring and reporting obligations, including obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the BLA or NDA. Application holders must also submit advertising and other promotional material to the FDA and report on ongoing clinical trials.

Advertising and promotional materials must comply with FDA rules in addition to other potentially applicable federal and state laws. The distribution of product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act. Manufacturing facilities remain subject to FDA inspection and must continue to adhere to FDA s current good manufacturing practice requirements. Application holders must obtain FDA approval for product, manufacturing, and labeling changes, depending on the nature of the change. Sales, marketing, and scientific/educational grant programs must comply with the Medicare-Medicaid Anti-Fraud and Abuse Act, as amended, the False Claims Act, also as amended, and similar state laws. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Veteran s Health Care Act of 1992, as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Depending on the circumstances, failure to meet these post-approval requirements can result in criminal prosecution, fines or other penalties, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, or refusal to allow us to enter into supply contracts, including government contracts. In addition, even if we comply with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw a product approval.

If we are able to obtain approvals for our products, the law or FDA policy could change and expose us to competition from generic or follow-on versions of our products.

Under current U.S. law and FDA policy, generic versions of conventional chemical drug compounds, sometimes referred to as small molecule compounds, may be approved through an abbreviated approval process. In general terms, the generic applicant references an approved innovator product for which full clinical data demonstrating safety and effectiveness exist for the approved conditions of use. The generic applicant in turn need only demonstrate that its product has the same active ingredient(s), dosage form, strength, route of administration, and conditions of use (labeling) as the referenced innovator drug, and that the generic product is absorbed in the body at the same rate and to the same extent as the referenced innovator drug (this is known as bioequivalence). In addition, the generic application must contain information regarding the manufacturing processes and facilities that will be used to ensure product quality, and must contain certifications to patents listed with the FDA for the referenced innovator drug.

There is no such abbreviated approval process under current law for biological products approved under the Public Health Service Act through a BLA, such as monoclonal antibodies, cytokines, growth factors, enzymes, interferons and certain other proteins. However, various proposals have been made to establish an abbreviated approval process to permit approval of generic or follow-on versions of these types of biological products. The proposals include proposals for legislation, and proposals for FDA to extend its existing authority to this area. For example, some have proposed that FDA allow a generic or follow-on copy of certain therapeutic biologics to be approved under the Public Health Service Act or under an existing mechanism known as a 505(b)(2) application. A 505(b)(2) application is a form of a New Drug Application, or NDA, where the applicant does not have a right to reference some of the data being relied upon for approval. Under current regulations, 505(b)(2) applications can be used where the applicant is relying in part on published literature or on findings of safety or effectiveness in another company s NDA.

505(b)(2) has not been used to date for therapeutic biologic products. In addition, the use of 505(b)(2) applications even for conventional chemical drug products is the subject of an ongoing legal challenge. It is thus not clear what the permitted use of a 505(b)(2) application might be in the future for biologics products, or whether any other proposals on generic or follow-on biologics will be adopted. However, if the law is changed or if FDA somehow extends its existing authority in new ways, and third parties are permitted to obtain approvals of versions of our products through an abbreviated approval mechanism, and without conducting full clinical studies of their own, it could adversely effect our business. Such products would be significantly less costly than ours to bring to market, and could lead to the existence of multiple lower priced competitive products. This would substantially limit our ability to obtain a return on the investments we have made in those products.

Our operations involve hazardous materials and are subject to environmental, health and safety controls and regulations.

As a biopharmaceutical company, we are subject to environmental, health and safety laws and regulations, including those governing the use of hazardous materials. The cost of compliance with environmental, health and safety regulations may be substantial. Our business activities involve the controlled use of hazardous materials and we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident or environmental discharge, we may be held liable for any resulting damages, which may exceed our financial resources and may materially harm our business, financial condition and results of operations.

Our stock price may be volatile.

There has been significant volatility in the market prices of biotechnology companies securities. Various factors and events may have a significant impact on the market price of our common stock. These factors include, by way of example:

- fluctuations in our operating results;
- announcements of technological innovations or new commercial therapeutic products by us or our competitors;
- published reports by securities analysts;
- progress with clinical trials;
- governmental regulation;
- developments in patent or other proprietary rights;
- developments in our relationship with collaborative partners;

- public concern as to the safety and effectiveness of our products; and
- general market conditions.

During the two-year period ended December 31, 2004, the sale prices of our common stock ranged between $2.69 and $11.55. The trading price of our common stock has been, and could continue to be, subject to wide fluctuations in response to these or other factors, including the sale or attempted sale of a large amount of our common stock into the market. Broad market fluctuations may also adversely affect the market price of our common stock.

We have obligations to issue shares of our common stock in the future, which may have a dilutive effect on the shares of our common stock currently outstanding.

As of February 28, 2005, we had 14,394,964 shares of common stock reserved for issuance pursuant to options and other stock based awards which had been granted under our stock option plans having a weighted average exercise price of $7.88 per share and we had reserved 886,313 shares of common stock for issuance pursuant to future grants of options under our stock option plans. We have filed registration statements on Form S-8 under the Securities Act covering all of these shares. Shares issued pursuant to these plans, other than shares issued to affiliates, will be freely tradable in the open market. Shares held by affiliates may be sold pursuant to the requirements of Rule 144.

In addition, as of that date, there were 102,915 shares reserved for issuance pursuant to a deferred compensation plan. The shares reserved for the deferred compensation plan will be issued in various amounts over various periods of time during the next three years. We have filed a registration statement on Form S-8 under the Securities Act covering those shares. Shares issued pursuant to this plan, other than shares issued to affiliates, will be freely tradable in the open market. Shares held by affiliates may be sold pursuant to the requirements of Rule 144.

As of February 28, 2005, we had reserved 1,000,978 shares of common stock for issuance pursuant to our 2002 Employee Stock Purchase Plan. We have filed a registration statement on Form S-8 under the Securities Act covering all of those shares. All shares issued under this plan, other than shares issued to affiliates, will be freely tradable on the open market. Shares held by affiliates may be sold pursuant to the requirements of Rule 144.

The exercise of all or a portion of the outstanding options may result in a significant increase in the number of shares of our common stock that will be subject to trading on the NASDAQ National Market and the issuance and sale of the shares of our common stock upon the exercise thereof may have an adverse effect on the price of our common stock.

As of February 28, 2005, we had 10,936,935 shares of common stock reserved for the issuance pursuant to the conversion of the $150.0 million aggregate principal amount of our outstanding 2.25% Convertible Senior Notes due May 15, 2011. Holders of these notes may convert their notes into shares of common stock at any time prior to maturity or redemption by us at a conversion rate of 72.9129 shares per each $1,000 principal amount of the notes ($13.72 per share), subject to adjustment.

Future sales of our common stock or other securities could cause the market price of our common stock to decline.

As of February 28, 2005, we had 110,529,979 shares of common stock outstanding, of which 9,374,318 are restricted securities as that term is defined in Rule 144 under the Securities Act. Under certain circumstances, these restricted securities may be sold without registration pursuant to such rule. We are unable to predict the effect that sales made under Rule 144 or pursuant to any registration may have on the market price of our common stock. The sale of a significant number of additional securities, or even the possibility thereof, may lower the market price of our common stock.

We have filed a registration statement on Form S-3 under the Securities Act relating to 3,791,346 shares of common stock that may be offered by one of our shareholders. These shares of common stock are freely tradable without restriction or further registration under the Securities Act except for shares held by our affiliates, which will be subject to resale limitations of Rule 144.

In addition, we have filed a shelf registration statement on Form S-3 under the Securities Act relating to the sale of up to $294.59 million of any of the following securities:

- debt securities;
- preferred stock;
- common stock; or
- warrants to purchase debt securities, preferred stock or common stock.

We have also filed a registration statement on Form S-3 under the Securities Act that relates to the sale by certain selling securityholders of up to 7,214,345 shares of our common stock which were issued upon the conversion of our $125.0 million 4.25% Convertible Senior Notes due August 15, 2010 in connection with the provisional redemption of such notes in January 2005. These shares of common stock are freely tradable without restriction or further registration under the Securities Act except for shares held by our affiliates, which will be subject to the resale limitations of Rule 144. We also have filed a registration statement on Form S-3 under the Securities Act that relates to the sale by certain selling securityholders of up to 3,272,091 shares of our common stock which were issued on the conversion of all of our $21.986 million 4.25% Convertible Senior Notes due August 15, 2010, in connection with the provisional redemption of such notes in January 2005. These shares of common stock are freely tradable without restriction or further registration under the Securities Act except for shares held by our affiliates, which will be subject to the resale limitations of Rule 144. In connection therewith, we have agreed to use our best efforts to keep these registration statements continuously effective until the earliest of (i) the sale of all outstanding registrable securities registered under the registration statements; (ii) the expiration of the period referred to in Rule 144(k) of the Securities Act with respect to the notes held by non-affiliates of us; (iii) all the registrable securities have ceased to be outstanding (whether as a result of repurchase or otherwise); and (iv) two years after the respective effective dates of these registration statements.

We have filed a registration statement on Form S-3 under the Securities Act relating to our $150.0 million 2.25% Convertible Senior Notes due May 15, 2011, and up to 10,936,935 shares of our common stock which may be issued upon conversion of the notes. The notes and the shares of common stock are freely tradable without restriction or further registration under the Securities Act except for shares held by our affiliates, which will be subject to the resale limitations of Rule 144.

We have filed a registration statement on Form S-4 under the Securities Act to register shares of our common stock having a maximum aggregate offering price of $12.0 million. Such shares are freely tradable without restriction or further registration under the Securities Act. On August 5, 2004 we issued 731,823 shares of such common stock, valued at approximately $4.3 million to satisfy a portion of the purchase price in connection with the acquisition of Ability Biomedical Corporation. This registration statement on Form S-4 under the Securities Act remains available for the sale of up to $7.7 million of our common stock.

Upon the occurrence of certain change of control events of our company, we are required to offer to repurchase all of our debt, which may adversely affect our business and the price of our common stock.

Upon the occurrence of certain change of control events of our company, we are required to offer to repurchase all of our outstanding 2.25% Convertible Senior Notes due May 11, 2011. As of February 28, 2005, $150.0 million aggregate principal amount of these notes was outstanding. In each instance, we may pay the repurchase price in cash or, at our option, in common stock. These change of control events

include, without limitation, (i) the acquisition by any third party of at least 50% of our common stock; or (ii) our merger or consolidation with or into any other person, any merger or consolidation of another person into us or our sale or other disposal of all or substantially all of our assets, except in certain limited circumstances provided in the indentures relating to the notes. Such repurchase rights may be triggered at a time at which we do not have sufficient funds available to pay the repurchase price in cash or determine that payment in cash is otherwise inadvisable. In such event, the issuance of a significant number of additional shares of common stock in payment of the repurchase price may lower the market price of our common stock.

Our restated certificate of incorporation, amended and restated by-laws, shareholder rights plan and New Jersey law contain provisions that could delay or prevent an acquisition of our company even if the acquisition would be beneficial to our shareholders, and as a result, our management may be come entrenched and hard to replace.

In May 2001, our board of directors adopted a shareholder rights plan. The shareholder rights plan provides for a dividend of one preferred share purchase right on each outstanding share of our common stock. Each right entitles shareholders to buy 1/1000th of a share of our Series A junior participating preferred stock at an exercise price of $150.00. Each right will become exercisable following the tenth day after a person or group announces an acquisition of 20% or more of our common stock. We will be entitled to redeem the rights at $0.001 per right at any time on or before the close of business on the tenth day following acquisition by a person or group of 20% or more of our common stock.

The shareholder rights plan and certain provisions of our restated certificate of incorporation and amended and restated by-laws may have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. This could limit the price that certain investors might be willing to pay in the future for our common stock. The provisions of our restated certificate of incorporation and amended and restated by-laws include:

- a classified board of directors;
- a requirement that special meetings of shareholders be called only by our board of directors, chairman of the board, chief executive officer or president;
- advance notice requirements for shareholder proposals and nominations;
- limitations on the ability of shareholders to amend, alter or repeal our by-laws; and
- the authority of the board of directors to issue, without shareholder approval, preferred stock with such terms as the board of directors may determine.

We are also afforded the protections of the New Jersey Shareholders Protection Act. This New Jersey statute contains provisions that impose restrictions on shareholder action to acquire control of our company. The effect of the provisions of our shareholder rights plan, restated certificate of incorporation and amended and restated by-laws and New Jersey law may discourage third parties from acquiring control of our company. In addition, these measures may result in the entrenchment of our management and may prevent or frustrate any attempt by shareholders to replace or remove our current management.

We do not intend to pay cash dividends on our common stock in the foreseeable future.

We intend to retain any future earnings to finance the growth and development of our business, and we do not plan to pay cash dividends on our common stock in the foreseeable future.

Legislative and regulatory actions, NASDAQ rules and potential new accounting pronouncements may impact our future financial position or results of operations.

Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses. Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations and NASDAQ National Market rules, are creating uncertainty with respect to, among other things, the enforcement of these new standards and the potential effect thereof for companies such as ours. Investments required to comply with changes in SEC, NASDAQ and accounting rules may result in increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities.

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our financial position or results of operations. New pronouncements and varying interpretations of pronouncements have occurred with frequency and may occur in the future and we may make changes in our accounting policies in the future.

Item 2. Properties

The following is a description of our owned and leased properties:

Leased/Owned Properties

Location	Leased/Owned	Square Feet	Use	Lease Expiration Date
Annandale, New Jersey	Leased	45,000	Laboratory, Office	2008
Bloomsbury, New Jersey	Owned	165,000	Laboratory, Office	N/A
Milpitas, California	Owned	60,000	Laboratory, Office	N/A
Sunnyvale, California	Leased	37,000	Laboratory, Office	2009
Princeton, New Jersey	Leased	20,000	Corporate Headquarters, Office	2006

We believe that our existing owned and leased facilities are adequate for the production of materials for clinical trials of our current products and for providing the services we currently offer to our partners in connection with our human antibody technology.

Item 3. Legal Proceedings

In the ordinary course of our business, we are at times subject to various legal proceedings. We do not believe that any of our current legal proceedings, individually or in the aggregate, will have a material adverse effect on our operations or financial condition.

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

There were no matters submitted to a vote of security holders during the last quarter of the year ended December 31, 2004, through the solicitation of proxies or otherwise.

PART II

Item 5. Market for Registrant s Common Equity and Related Shareholder Matters

Our common stock is traded on the NASDAQ National Market under the symbol MEDX. The following table sets forth, during the periods indicated, the high and low sales prices per share of our common stock, as reported on the NASDAQ National Market:

	Common Stock Price	
	High	Low
Year ended December 31, 2003		
First Quarter	$ 4.36	$ 2.69
Second Quarter	$ 7.35	$ 3.15
Third Quarter	$ 7.67	$ 4.48
Fourth Quarter	$ 7.56	$ 5.78
Year ended December 31, 2004		
First Quarter	$ 9.93	$ 6.28
Second Quarter	$ 11.13	$ 6.51
Third Quarter	$ 8.41	$ 4.37
Fourth Quarter	$ 11.55	$ 7.06

The number of shares of our common stock outstanding as of February 28, 2005 was 110,529,979. As of February 28, 2005, there were approximately 600 record holders of our common stock. As of March 22, 2004, the record date for our last Annual Meeting of Shareholders held on May 19, 2004, there were approximately 600 record holders of common stock (which includes individual holders) and approximately 32,447 beneficial shareholders of our common stock.

We currently expect to retain our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

The information required herein will be reported in our definitive Proxy Statement for the Annual Meeting of Shareholders which we expect will be filed on or before April 29, 2005, and is incorporated herein by reference.

Item 6. Selected Consolidated Financial Data

	For the Year Ended December 31,				
	2000	2001	2002	2003	2004
	(Dollars in thousands, except per share data)				
Statement of Operations Data:					
Revenues:					
Sales	$ 264	$ 191	$ 176	$ 25	$
Contract and license revenues	19,619	37,140	24,552	5,833	9,119
Sales, contract and license revenues from Genmab	2,574	4,973	14,751	5,316	3,355
Total revenues	22,457	42,304	39,479	11,174	12,474
Costs and expenses:					
Cost of sales	1,189	642	8,327	3	
Research and development	33,942	38,626	82,626	95,459	122,007
General and administrative	18,142	19,344	22,852	21,727	24,314
Write-off of facility costs			11,294		
Acquisition of in-process technology			16,312	6,500	5,455
Total costs and expenses	53,273	58,612	141,411	123,689	151,776
Operating loss	(30,816)	(16,308)	(101,932)	(112,515)	(139,302)
Equity in net loss of affiliate	(353)	(7,334)	(50,625)	(14,997)	(19,791)
Interest and dividend income	21,158	24,728	18,495	12,342	7,145
Impairment loss on investments in partners			(11,886)	(1,400)	(7,309)
Additional (payments) receipts related to asset acquisition			(2,425)	(31)	16
Interest expense	(3)	(4,615)	(9,065)	(11,777)	(12,845)
Debt conversion expense					(10,151)
Net loss on extinguishment of debt					(4,241)
Gain on disposition of Genmab stock		1,442			
Loss before provision (benefit) for income taxes	(10,014)	(2,087)	(157,438)	(128,378)	(186,478)
Provision (benefit) for income taxes	(13,075)	600	103	69	31
Income (loss) before cumulative effect of change in accounting principle	3,061	(2,687)	(157,541)	(128,447)	(186,509)
Cumulative effect of change in accounting principle				(830)	
Net income (loss)	$ 3,061	$ (2,687)	$ (157,541)	$ (129,277)	$ (186,509)
Basic and diluted net income (loss) per share(1):					
Income (loss) before cumulative effect of change in accounting principle	$ 0.04	$ (0.04)	$ (2.09)	$ (1.64)	$ (2.29)
Cumulative effect of change in accounting principle				(0.01)	
Net income (loss)	$ 0.04	$ (0.04)	$ (2.09)	$ (1.65)	$ (2.29)
Weighted average common shares outstanding(1)					
basic	71,532	73,937	75,231	78,314	81,494
diluted	73,232	73,937	75,231	78,314	81,494

	December 31,				
	2000	2001	2002	2003	2004
	(Dollars in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 343,603	$ 466,952	$ 350,046	$ 358,458	$ 374,507
Working capital	329,807	447,326	339,480	350,437	341,110
Total assets	558,107	720,427	549,051	557,726	549,345
Long term obligations		175,000	175,000	300,000	296,986
Cash dividends declared per common share					
Accumulated deficit	(123,375)	(126,062)	(283,603)	(412,880)	(599,389)
Total shareholders equity	485,289	482,562	352,143	234,011	107,389

(1) Computed on the basis described in Note 2 to the Consolidated Financial Statements.

Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations

Certain statements made in this Annual Report on Form 10-K are forward-looking statements that are subject to risks and uncertainties that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include information concerning our future financial performance, business strategy, plans, goals and objectives. Statements preceded by, followed by or that otherwise include the words believes , expects , anticipates , intends , estimates , plans , forecasts , is likely to , projected and similar expressions or future conditional verbs such as should , would , may , and could are generally forward-looking in nature and not historical facts. You should not place undue reliance on any such forward-looking statements as such statements speak only as of the date on which they are made, and we might not update them to reflect changes that occur after the date they are made.

Overview

We are a biopharmaceutical company focused on the discovery, development and potential commercialization of fully human antibody-based therapeutic products. We believe that our UltiMAb Human Antibody Development System® enables us to rapidly create and develop such products for a wide range of diseases, including cancer, inflammation, autoimmune disorders and other life-threatening and debilitating diseases.

Currently, 22 antibody products generated from our UltiMAb Human Antibody Development System are in human clinical trials. These antibodies are designed to treat a wide range of diseases, such as cancer, rheumatoid arthritis and other inflammatory, autoimmune and infectious diseases. The most advanced of these products is MDX-010 (currently in Phase III, Phase II and Phase I clinical trials), which we are developing jointly with Bristol-Myers Squibb Company, or BMS, for the treatment of metastatic melanoma and other cancers. Four of these antibody products are fully owned by Medarex and its affiliates: MDX-060 for lymphomas (Phase II clinical trial), MDX-070 for prostate cancer (Phase II clinical trial), MDX-214 for cancer (Phase I/II clinical trial) and MDX-1307 for genitourinary and breast cancers (Phase I clinical trial). We are also developing MDX-066 (Phase I clinical trial) jointly with The Massachusetts Biologic Laboratories for the treatment of *Clostridium difficile* associated diarrhea. Another antibody, MDX-018 (Phase I/II clinical trial), is being jointly developed with Genmab A/S for autoimmune disease, and three are being developed separately by Genmab: HuMax -CD4 (Phase II clinical trials) for T-cell lymphomas, HuMax-EGFr (Phase I/II clinical trial) for head and neck cancer and HuMax-CD20 (Phase I/II clinical trial) for lymphomas. Genmab and Amgen, Inc. are developing AMG 714 (Phase II clinical trial) for rheumatoid arthritis. Additionally, other licensing partners, including Novartis Pharma AG, Eli Lilly and Company, and Centocor, Inc. (a subsidiary of Johnson & Johnson), are developing a total of ten antibody products, for inflammatory and/or autoimmune diseases and cancer, that are currently in early clinical trials. Human Genome Sciences, Inc. has also announced the initiation of a Phase I trial of one anticancer antibody product developed pursuant to a licensing agreement with our partner Kirin Brewery Co., Ltd. We and our partners also have a number of UltiMAb® product candidates in preclinical development. The preceding information regarding the clinical status of antibody products is based on our and our partners public disclosure and other publicly available information.

Our revenue is principally derived from licensing our fully human antibody technology to pharmaceutical and biotechnology companies. The terms of these license agreements typically include potential license fees and a series of potential milestone payments commencing upon the initiation of clinical trials and continuing through commercialization. These payments may total $7.0 million to $10.0 million per product if the antibody receives approval from the U.S. Food and Drug Administration, or FDA, and equivalent foreign agencies. In general, we are also entitled to receive royalties on product sales. Additional revenue may be earned from the sales to, and in some cases, the manufacturing of antibodies for, our partners, as well as from government grants.

Our most significant costs on an annual basis are research and development expenses and general and administrative expenses. Research and development expenses represent those costs that support the advancement of our product pipeline and primarily consist of personnel costs, facilities (including depreciation), research and laboratory supplies, funding of outside research, license and technology access fees, expenses related to antibody manufacturing and clinical trial expenses. We believe that continued investment in research and development is critical to attaining our strategic objectives. General and administrative expenses consist primarily of personnel expenses for executive, finance, legal and administrative personnel, professional fees and other general corporate expenses. We may be required to add personnel in the future and incur additional costs as we expand our business activities.

We have a history of operating losses and may not achieve profitability. As of December 31, 2004, we had an accumulated deficit of approximately $599.4 million. Over the next several years, we expect to incur substantial expenses as we continue to identify, develop and manufacture our potential products, invest in research, move forward with our product development and prepare to commercialize our product(s). Our commitment of resources to research and the continued development and potential commercialization of our product candidates will require substantial additional funds. Our operating expenses may also increase as we invest in research or acquire additional technologies, as additional potential product candidates are selected for clinical development and as some of our earlier stage product candidates move into later stage clinical development. In addition, we may incur significant milestone payment obligations as our products progress towards commercialization. In the absence of substantial revenues from new corporate collaborations or other sources, we will incur substantial operating losses and may be required to raise additional funds through debt or equity financings or delay, reduce or eliminate certain of our research and development programs.

Critical Accounting Policies

The methods, estimates and judgments we use in applying our most critical accounting policies have a significant impact on the results we report in our consolidated financial statements. We evaluate our estimates and judgments on an on-going basis. We base our estimates on historical experience and on assumptions that we believe to be reasonable under the circumstances. Our experience and assumptions form the basis for our judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may vary from what we anticipate and different assumptions or estimates about the future could materially change our reported results. We believe the following accounting policies are the most critical to us, in that they are important to the portrayal of our financial statements and they require our most difficult, subjective or complex judgments in the preparation of our consolidated financial statements.

Revenue Recognition

We receive payments from our customers and partners for the sale of antibodies, for licenses to our proprietary technology, for product development services and from the achievement of product development milestones. These payments are generally non-refundable and are reported as deferred revenue until they are recognizable as revenue. We follow the following principles in recognizing revenue:

- We sell antibodies primarily to partners in the United States and overseas. Revenue from these sales is recognized when the antibodies are shipped.

- We receive research fees from the licensing of our proprietary technologies for research and development performed by our customers and partners. Revenue from these research fees is recognized generally over the term of the respective license period beginning only after both the license period has begun and the technology has been delivered.

- We receive fees for product development services (including manufacturing) we perform for our customers and partners. These fees are recognized ratably over the entire period during which the services are performed.

- Revenue from milestone payments is recognized when each milestone is achieved and when collectibility of such milestone payment is assured. Milestone payments are triggered either by the results of our research efforts or by the efforts of our partners and include such events as submission of an Investigational New Drug Application, or IND, commencement of Phase I, II or III clinical trials, submission of a Biologic License Application, or BLA, and approval of a product. Milestone payments are substantially at risk at the inception of an agreement. Upon achievement of a milestone event, we have no future performance obligations relating to that event.

- Revenue arrangements that include multiple deliverables, are divided into separate units of accounting if the deliverables meet certain criteria, including whether the fair value of the delivered items can be determined and whether there is evidence of fair value of the undelivered items. In addition, the consideration is allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units of accounting.

Investments

Our investment policy calls for investments in fixed income high grade securities such as U.S. corporate debt securities, U.S. treasury obligations and money market funds for which we believe there is not a significant risk of loss. Our primary objectives for our investment portfolio are liquidity and safety of principal. Investments are made to achieve the highest rate of return consistent with these two objectives. However, in the course of our business, we have made and may continue to make investments in companies (both public and private) as part of our strategic collaborations. Investments in companies whose securities are publicly traded (other than Genmab) are classified as marketable securities on our consolidated balance sheets. The fair market value of investments in our partners whose securities are publicly traded represented approximately 1.5% of total marketable securities as of December 31, 2003 and approximately 0.9% of total marketable securities as of December 31, 2004.

Under SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities,* our marketable securities are classified as available-for-sale securities and are carried at fair value. Marketable securities will include those securities of debt and publicly traded equity securities accounted for under the cost method. These securities trade on listed exchanges; therefore, fair value is readily available. These securities are also subject to an impairment charge when we believe an investment has experienced a decline in value that is other than temporary. Under our accounting policy, a decline in the value of our investments is deemed to be other than temporary and such investments are generally considered to be impaired if their value is less than our cost basis for more than six (6) months, or some other applicable period in light of the facts and circumstances surrounding the investments.

In addition, in connection with our collaborative partnering business, we sometimes make strategic investments in the securities of companies that are privately held. Investments in our partners whose equity is not publicly traded are classified in separate line items in our consolidated balance sheet entitled Investments in IDM and Investments in, and advances to, other partners and were approximately $51.7 million as of December 31, 2004. These securities are carried at original investment cost and adjusted for other than temporary impairment charges, if any. Because these securities are not listed on a financial exchange, the value of these investments is inherently more difficult to estimate than investments in public companies. We value these investments by using information acquired from industry trends, the management of these companies, financial statements, and other external sources. Specifically, our determination of any potential impairment of the value of privately held securities includes an analysis of

the following for each company on a periodic basis: review of interim and year-end financial statements, cash position and overall rate of cash used to support operations, the progress and development of technology and product platform, the per share value of subsequent financings and potential strategic alternatives. Based on the information acquired through these sources, we record an investment impairment charge when we believe an investment has experienced a decline in value that is other than temporary.

Future adverse changes in market conditions or adverse changes in financial condition and/or operating results of the companies in which we invest that may not be reflected in an investment s current carrying value may also require an impairment charge in the future.

Valuation of Long-Lived and Intangible Assets

We assess the impairment of identifiable intangible assets and long-lived assets whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Factors we consider important that could trigger an impairment review include the following:

- a significant underperformance relative to expected historical or projected future operating results;
- a significant change in the manner of our use of the acquired asset or the strategy for our overall business; and/or
- a significant negative industry or economic trend.

When we determine that the carrying value of intangible assets or long-lived assets are not recoverable based upon the existence of one or more of the above indicators of impairment, we may be required to record impairment charges for these assets that have not been previously recorded.

Acquired In-Process Technology

In-Process Technology expense for significant technology acquisitions is determined based on an analysis using risk-adjusted cash flows expected to be generated by products that may result from in-process technologies which have been acquired. This analysis includes forecasting future cash flows that are expected to result from the progress made on each in-process project prior to the acquisition date. Cash flows are estimated by first forecasting, on a product-by-product basis, net revenues expected from the sales of the first generation of each in-process project and risk adjusting these revenues to reflect the probability of advancing to the next stage of the FDA approval process. The forecast data in the analysis is based on internal product level forecast information maintained by us in the ordinary course of business. The inputs used in analyzing In-Process Technology is based on assumptions, which we believe to be reasonable but which are inherently uncertain and unpredictable. These assumptions may be incomplete or inaccurate, and unanticipated events and circumstances may occur. Appropriate operating expenses are deducted from forecasted net revenues on a product-by-product basis to establish a forecast of net returns on the completed portion of the in-process technology. Finally, net returns are discounted to a present value using discount rates that incorporate the weighted average cost of capital relative to the biotech industry and us as well as product specific risks associated with the acquired in-process research and development products. The product specific risk factors include the product s phase of development, type of product candidate under development, likelihood of regulatory approval, manufacturing process capability, scientific rationale, preclinical safety and efficacy data, target product profile, and development plan. In addition to the product specific risk factors, a discount rate is used for the valuation, which represents a considerable risk premium to our weighted average cost of capital. The valuations used to estimate In-Process Technology require us to use significant estimates and assumptions that if changed, may result in a different valuation for In-Process Technology.

Results of Operations

Years Ended December 31, 2002, 2003 and 2004

Contract and License Revenues

Contract and license revenues totaled $24.6 million, $5.8 million and $9.1 million for the years ended December 31, 2002, 2003 and 2004, respectively. Contract and license revenues for 2003 decreased by $18.7 million or 76% as compared to 2002. This decrease relates principally to a decrease in revenue from Immuno-Design Molecules, S.A., or IDM, of $14.3 million as a result of the completion of the recognition of revenue associated with the transfer of technology to IDM in July 2000, as well as a decrease in revenue of $3.4 million from Eli Lilly and Company. Contract and license revenues for 2004 increased by $3.3 million or 56% as compared to 2003. This increase relates principally to approximately $2.4 million of revenue recognized from our collaboration agreement with Pfizer, Inc. which was executed in September 2004 and approximately $0.6 million of revenue from the National Institutes of Health in accordance with a grant we received in 2004. Because contract and license revenues depend to a large extent on the product development efforts of our partners and licensees, our year-to-year contract and license revenues can fluctuate significantly and are inherently difficult to predict.

Sales, Contract and License Revenues from Genmab

Sales, contract and license revenues from Genmab A/S were $14.8 million, $5.3 million and $3.4 million for the years ended December 31, 2002, 2003 and 2004, respectively. Sales, contract and license revenues from Genmab for 2003 decreased by $9.4 million or 64% as compared to 2002. In 2002 there were sales of MDX-CD4 and MDX-015 totaling $11.4 million in order to support Genmab s clinical trials. There were no sales of such material to Genmab in 2003 or 2004. The 2003 decrease was offset, in part, by increased contract and license revenues related principally to an increased number of research licenses and antibody exclusive licenses requested by and granted to Genmab. Sales, contract and license revenues from Genmab for 2004 decreased by $2.0 million or 37% as compared to 2003. This decrease relates principally to fewer research licenses and antibody exclusive licenses requested by and granted to Genmab.

Cost of Sales

Cost of sales were $8.3 million, $3 thousand and $0 for the years ended December 31, 2002, 2003 and 2004, respectively. Cost of sales in 2003 decreased by $8.3 million, as compared to 2002. The decrease is the result of no sales of MDX-CD4 and MDX-015 to Genmab in 2003 as discussed above.

Research and Development Expenses

Research and development expenses for our products in development were $82.6 million, $95.5 million and $122.0 million for the years ended December 31, 2002, 2003 and 2004, respectively. Research and development expenses in 2003 increased by $12.8 million, or 16% as compared to 2002 and research and development expenses in 2004 increased by $26.5 million, or 28% as compared to 2003. Historically, due to the relatively small number of our products in clinical trials, we have not accounted for our research and development expenses on a project-by-project basis and, therefore, we do not provide a breakdown of such historical information in that format. We have, historically, tracked our costs in the categories discussed below, namely, research and product development and by the types of costs as outlined below.

Our research costs consist of costs associated with the breeding, care and continued development of our HuMAb-Mouse and KM-Mouse, as well as costs associated with research and testing of our product candidates prior to reaching the preclinical stage. Such research costs primarily include personnel costs,

facilities (including depreciation), research supplies, funding of outside research and license and technology access fees.

Our product development costs consist of costs of preclinical development (including manufacturing) and conducting and administering clinical trials. Such product development costs also include personnel costs, facilities (including depreciation), supply expense related to antibody manufacturing and clinical trial expenses.

The following table sets forth a breakdown of our research and development expenses by those associated with research and those associated with product development for the periods indicated.

	Year Ended December 31,		
	2002	2003	2004
Research	$ 34,659	$ 37,495	$ 53,284
Product Development	47,967	57,964	68,723
Total	$ 82,626	$ 95,459	$ 122,007

Research Costs

Research costs in 2003 increased by $2.8 million, or 8% as compared to 2002. Research costs in 2004 increased by $15.8 million, or 42% as compared to 2003. The increases in research costs primarily relate to the following.

- Personnel costs in 2003 were $12.7 million, an increase of $2.6 million or 25% as compared to 2002. Personnel costs in 2004 were $13.2 million, an increase of $0.5 million or 3% as compared to 2003. The increased personnel costs are primarily attributable to staff needed to support higher levels of new product development opportunities, the continued development of our UltiMAb® system, and the performance of contract services for our collaborative partners. Personnel costs include primarily salary, benefits, payroll taxes and recruiting costs. We expect personnel costs to continue to increase as we continue to increase our research activities.

- An $8.5 million expense representing a liability to Gilead Sciences, Inc. for the reduction of future royalty obligations relating to certain intellectual property rights regarding anti-CTLA-4 product candidates in 2004 for which no comparable payments were made in 2002 and 2003. The total consideration of $8.5 million is being paid to Gilead in eight equal quarterly installments. The first two of these payments were made in 2004. As of December 31, 2004, approximately $6.4 million (six installments) remained due to Gilead under this obligation (see further discussion under the section herein entitled *Other Liquidity Matters*).

- Facility costs in 2003 were $7.5 million, an increase of $2.3 million or 44% as compared to 2002. Facility costs in 2004 were $8.7 million, an increase of $1.2 million or 15% as compared to 2003. The increase in facility costs primarily relates to the substantial investments made in our research facilities in recent years. As a result, depreciation, utilities, maintenance, property taxes and related expenses increased for 2003, as compared to 2002, and for 2004, as compared to 2003. We expect to incur increased facility costs as a result of continued capital expansion, renovations and replacements.

- License and technology access fees in 2003 were $3.1 million, a decrease of $4.1 million or 58% as compared to 2002. License and technology access fees in 2004 were $6.9 million, an increase of $3.8 million or 125% as compared to 2003. These costs represent fees paid to certain partners and research organizations in connection with certain of our collaboration and license agreements. Included in the 2004 costs are payments to diaDexus, Inc., Pharma Pacific Pty Ltd. and Kirin Brewery Co., Ltd., or Kirin, for licenses to certain technologies. We expect license fees, including funds paid to certain partners, to increase in the future.

Product Development Costs

Product development costs in 2003 increased by $10.0 million, or 21% as compared to 2002. Product development costs increased by $10.8 million in 2004, or 19% as compared to 2003. The increases in product development costs primarily relate to the following:

- Contract manufacturing costs in 2003 were $0.7 million, an increase of $0.7 million or 100% as compared to 2002. Contract manufacturing costs in 2004 were $8.1 million, an increase of $7.4 million or 1091% as compared to 2003. The increase in third party contract manufacturing costs primarily represents production and packaging expenses for a Phase III pivotal trial of MDX-010 in combination with MDX-1379, which began in the third quarter of 2004 and certain MDX-060 manufacturing costs. We expect costs to third party manufacturers will increase in the future in order to support the advancement of our clinical pipeline.

- Personnel costs in 2003 were $20.6 million, an increase of $2.5 million or 14% as compared to 2002. Personnel costs in 2004 were $22.9 million, an increase of $2.3 million or 11% as compared to 2003. The increased personnel costs are a result of the increased staff needed to support more extensive clinical trial activities primarily for MDX-010. Personnel costs primarily include salary, benefits, payroll taxes and recruiting costs. We expect personnel costs to continue to increase as we continue to increase our product development activities and progress our products through clinical trials.

- Facility costs in 2003 were $12.6 million, an increase of $1.8 million or 16% as compared to 2002. Facility costs in 2004 were $13.1 million, an increase of $0.5 million or 4% as compared to 2003. The increase in facility costs primarily relates to the substantial investments made in our product development facilities in recent years. As a result, depreciation, utilities, maintenance, property taxes and related expenses increased for each of 2003 and 2004, as compared to prior year periods. We expect to continue to incur increased facility costs as a result of continued capital expansion, renovations and replacements.

- Supply costs in 2003 were $5.7 million, a decrease of $4.3 million or 44% as compared to 2002. In 2002 we manufactured larger quantities of material for Phase I and Phase II clinical trials for ourselves and our partners resulting in a significant increase in supply costs. Supply costs in 2004 were $4.6 million, a decrease of $1.1 million or 19% as compared to 2003. In 2003 we completed a change to our method of production which resulted in comparatively lower supply costs in 2004. Included in these costs are materials and small equipment associated with the manufacture of material for clinical trials. We expect these costs to increase as we continue to expand our product development efforts and increase our clinical trial activities.

- Clinical research fees in 2003 were $4.7 million, an increase of $3.1 million or 190% as compared to 2002 primarily as a result of an increase in the number of ongoing clinical trials particularly for MDX-010 and MDX-060. Clinical research fees in 2004 were also $4.7 million, representing the conclusion of certain Phase II clinical trials for MDX-010 offset by the initiation of the Phase III clinical trial for MDX-010 in combination with MDX-1379 which began in the third quarter of 2004. Clinical research fees include clinical investigator site fees, external trial monitoring costs and data accumulation costs. We expect expenses related to clinical trials to increase in the future as we continue to develop our therapeutic product pipeline.

We expect product development costs to increase in the future as more of our products enter clinical trials. In addition, we may be obligated to make milestone payments on certain of our products as they progress through the clinical trial process. Completion of clinical trials may take several years or more. The length of time varies according to the type, complexity and intended use of the product candidate. We estimate that clinical trials of the type we generally conduct are typically completed over the following periods:

Clinical Phase	Estimated Completion Period
Phase I	1-2 Years
Phase II	1-2 Years
Phase III	2-4 Years

The duration and cost of clinical trials may vary significantly over the life of a particular project as a result of, among other things, the following factors:

- the length of time required to recruit qualified patients for clinical trials;
- the duration of patient dosing and follow-up in light of trial results;
- the number of clinical sites required for trials; and
- the number of patients that ultimately participate.

We continue to explore new collaborative arrangements that may affect future spending for research and development. As part of our partnering strategy, a significant portion of the research and development expenses incurred in connection with products using our technology is expected to be borne by our partners. We believe this allows us to participate in the research and development of substantially more potential product candidates than we could develop on our own if we bore the entire cost of development. Products using our technology are currently in various stages of development from preclinical to Phase III. The successful development of these product candidates is dependent on many factors, including among other things, the efforts of our partners, unforeseen delays in, or expenditures relating to, preclinical development, clinical testing, manufacturing or regulatory approval, failure to receive market acceptance, the emergence of competitive products and the inability to produce or market our products due to third-party proprietary rights.

General and Administrative Expenses

General and administrative expenses include compensation, professional services, consulting, travel and facilities (including depreciation) and other expenses related to legal, business development, finance, information systems and investor relations. General and administrative expenses totaled $22.9 million, $21.7 million and $24.3 million for the years ended December 31, 2002, 2003 and 2004, respectively. General and administrative expenses decreased by $1.1 million in 2003, or 5% as compared to 2002. The 2003 decrease was generally attributable to a reduction in legal fees of $2.3 million primarily as a result of the completion of the negotiation and execution of our collaboration and license agreement with Kirin in 2002, and decreased consulting fees of $0.6 million, partially offset by higher personnel costs of $1.5 million. General and administrative expenses increased by $2.6 million in 2004, or 12% as compared to 2003. The 2004 increase is primarily attributable to increased personnel costs of $1.1 million, and increased legal fees of $1.0 million primarily as a result of the completion of the negotiation and execution of a series of agreements with Pfizer and our collaboration and license agreement with BMS in 2004. General and administrative expenses are expected to increase in the future as our products are developed and we expand our business activities.

Write-off of Facility Costs

Write-off of facility costs in 2002 relates to a determination we made to delay indefinitely the planned construction of a large scale manufacturing facility at our Bloomsbury, New Jersey, location and to pursue late-stage clinical and commercial supply agreements with third party manufacturers with available capacity to meet our current internal production timetables. As a result of this decision, we recorded a charge of $11.3 million in 2002, representing the write-off of design, engineering and other pre-construction costs. We believe that our existing facility in Annandale, New Jersey, is adequate for the production of materials for clinical trials of our products and for providing support we offer our partners in connection with our human antibody technology in the near-term. In September 2003, we entered into a clinical supply agreement with Lonza Group Ltd. with respect to MDX-010 and MDX-060, and, together with our partner BMS, we are pursuing ongoing discussions with respect to terms of a commercial supply agreement for MDX-010.

Acquisition of In-Process Technology

Acquisition of in-process technology for the year ended December 31, 2002, related to our acquisition of certain assets (including certain preclinical product candidates and programs related to the research and development of therapeutic products for the treatment of autoimmune disorders, cancer and infectious diseases) of Corixa Corporation in May 2002. The total cost of the acquisition (including transaction costs), discussed more fully under the section herein entitled Liquidity and Capital Resources, was $21.4 million. Based upon an independent third-party valuation, in 2002, $16.3 million of the cost of the acquisition was charged to operations as acquisition of in-process technology.

Acquisition of in-process technology for the year ended December 31, 2003 related to an amended and restated license agreement with Kyowa Hakko Kogyo Co. Ltd., or the Kyowa License, that we entered into during the fourth quarter of 2003. Under the terms of the Kyowa License we received certain intellectual property rights relating to the development and commercialization of our Ultra-Potent Toxin technology. The Kyowa License was the result of a renegotiation of a pre-existing license agreement with respect to Ultra-Potent Toxin technology between Kyowa and Corixa, whose license agreement we acquired as part of the May 2002 asset acquisition. Upon the execution of the Kyowa License, we paid Kyowa a total of $4.0 million and also made a final payment to Corixa in the amount of $2.5 million.

Acquisition of in-process technology for the year ended December 31, 2004 related to our acquisition of all of the outstanding capital stock not already owned by us of Ability Biomedical Corporation, a privately held Canadian biotechnology company, in August 2004. The total cost of the acquisition (including transaction costs), discussed more fully under the section herein entitled Liquidity and Capital Resources, was $5.7 million, of which approximately $5.5 million of in-process research and development was determined not to be technologically feasible and had no alternative future uses at the time of acquisition, and, as a result, was charged to operations as acquisition of in-process technology during 2004.

Equity in Net Loss of Affiliate

Equity in net loss of affiliate represents our share of Genmab s net loss for the years ended December 31, 2002, 2003 and 2004. Genmab is an affiliated company and is accounted for using the equity method of accounting (see Note 12 to the Consolidated Financial Statements). The recognition of our share of Genmab s net losses reduces the carrying value, or basis, of our investment in Genmab. We expect that during the first quarter of 2005 the remaining basis of our investment in Genmab will be reduced to zero and, accordingly, recognition of our share of Genmab s net losses will be suspended.

Equity in net loss of affiliate was $50.6 million, $15.0 million and $19.8 million for the years ended December 31, 2002, 2003 and 2004, respectively. Equity in net loss of affiliate in 2003 decreased by $35.6 million or 70% as compared to 2002. Included in equity in net loss of affiliate for 2002 is in an impairment

loss on our investment in Genmab of $31.0 million resulting from an approximate 60% decrease in the market value of Genmab s stock following Genmab s September 24, 2002, press release in which it announced that its HuMax-CD4 product, a fully human antibody that targets CD4 receptors on cells known as T-cells was found not to be effective in combination with methotrexate in a Phase II study of 155 patients with active rheumatoid arthritis. We recorded the $31.0 million impairment charge in the third quarter of 2002 as a result of the decrease in the market price of the Genmab stock, which was deemed to be other than temporary at the time. If we deem our investment in Genmab to be further impaired at the end of any future period, we may incur an additional impairment charge on this investment. Excluding the impact of the impairment in 2002, equity in net loss of affiliate would have decreased by $4.6 million or 23% as compared to 2002. This decrease was the result of a decrease in Genmab s net loss for 2003, primarily as a result of the recognition of $10.5 million of milestone revenue by Genmab during 2003.

On July 6, 2004, Genmab completed a private placement of 5.6 million shares of its stock. As a result of this private placement, our ownership percentage of Genmab was reduced from approximately 30.9% to 24.7%. The difference between our proportionate share of the additional equity raised was approximately $9.7 million and was accounted for in accordance with APB Opinion No. 18, *The Equity Method of Accounting for Investment in Common Stock,* and Staff Accounting Bulletin No. 51, *Accounting for Sales of Stock by a Subsidiary* increasing our investment in Genmab and capital in excess of par value. Equity in net loss of affiliate in 2004 increased by $4.8 million or 32% as compared to 2003. This increase reflects an increase in Genmab s net loss as a result of its expanded research and development efforts offset, in part, by a reduction in our ownership percentage, resulting from the 2004 private placement, and therefore a reduction of our share of Genmab s net loss for the second half of 2004.

Interest and Dividend Income

Interest and dividend income consists primarily of interest earned from our cash, cash equivalents and marketable securities. Interest and dividend income was $18.5 million, $12.3 million and $7.1 million for the years ended December 31, 2002, 2003 and 2004, respectively. Interest and dividend income in 2003 decreased by $6.2 million, or 33% as compared to 2002. The decrease reflects lower returns on our investment portfolio and a reduction in the size of our average cash balances invested, which, on average, were also lower during the period. Interest and dividend income in 2004 decreased by $5.2 million, or 42% as compared to 2003. This decrease primarily relates to lower returns on our investment portfolio as well as increased amortization of premiums on debt securities. We anticipate lower interest and dividend income in the future as we continue to fund our operations and capital expenditures from our cash reserves.

Impairment Loss on Investments in Partners

In the course of our business we may make investments in companies (both public and private) as part of strategic collaborations. We recorded impairment charges of $9.5 million, $0 and $0.2 million for the years ended December 31, 2002, 2003 and 2004, respectively related to investments in certain of our partners (other than Genmab) whose securities are publicly traded. The 2002 impairment charge was the result of certain investments trading below their original cost basis for more than six months. The 2004 impairment charge was the result of losses on one of these investments which were considered to be other than temporary. If we deem these investments to be further impaired at the end of any future period, we may incur additional impairment charges on these investments.

In addition, we have investments in several partners whose securities are not publicly traded. Because these securities are not publicly traded, the value of these investments is inherently more difficult to estimate than investments in publicly traded companies. We recorded impairment charges of $2.4 million, $1.4 million and $7.1 million for the years ended December 31, 2002, 2003 and 2004, respectively, related to investments in certain of our partners whose securities are not publicly traded. The 2004 impairment

charge is primarily comprised of a $7.0 million impairment related to our investment in IDM. The amount of the IDM impairment charge was calculated as the difference between the per share price received by IDM in a December 2004 private placement of its equity securities and our cost basis. If we deem these investments to be further impaired at the end of any future period, we may incur additional impairment charges on these investments.

Additional Payments (Receipts) Related to Asset Acquisitions

Additional payments (receipts) related to asset acquisition of $2.4 million, $31 thousand and ($16) thousand for the years ended December 31, 2002, 2003 and 2004, respectively, represent net additional purchase payments (receipts) to Northwest Biotherapeutics, Millennium Pharmaceuticals and Corixa in 2002, to Northwest Biotherapeutics in 2003 and to Gilead, Pharma Pacific and Ability Biomedical shareholders in 2004. Pursuant to the terms of our agreements with these companies, under certain circumstances we were required to pay (or to receive) an amount equal to the difference between the proceeds received by these companies from the sale of any shares of our common stock delivered as payment of any installment of the purchase price of the assets and the total amount of the purchase price installment due under the agreements.

Interest Expense

Interest expense was primarily related to interest and amortization of issuance costs on our 4.50% Convertible Subordinated Notes issued in June 2001, or the 4.50% notes, our 4.25% Convertible Senior Notes issued in July 2003, or the 4.25% notes, and our 2.25% Senior Subordinated Notes issued in May 2004, or the 2.25% notes. Interest expense was $9.1 million, $11.8 million and $12.8 million for the years ended December 31, 2002, 2003 and 2004, respectively. Interest expense in 2003 increased by $2.7 million, or 30% as compared to 2002 reflecting the addition of approximately five months of accrued interest on our 4.25% notes. Interest expense in 2004 increased by $1.1 million, or 9% as compared to 2003. The increase reflects a full year of interest expense on our 4.25% notes and the addition of approximately seven months of interest expense on our 2.25% notes, offset, in part, by a decrease in interest expense resulting from the redemption, repurchase and cancellation of the 4.50% notes in June and July of 2004. The 2.25% Notes are due in May 2011 and interest is payable semi-annually on May 15 and November 15 of each year. We expect interest expense to decrease in the future as a result of the redemption, repurchase and cancellation of the 4.50% Notes and the January 2005 conversion of our 4.25% notes (see further explanation under the section entitled *Other Liquidity Matters*).

Debt Conversion Expense

Debt conversion expense of $10.2 million for the year ended December 31, 2004 related to the make-whole payment associated with the December 2004 decision calling for the redemption of our 4.25% notes. Such amount was accrued as of December 31, 2004 and was paid in January 2005 (see further information under the section entitled *Cash Provided By Financing Activities*). There were no comparable charges for the years ended December 31, 2002 and 2003.

Net Loss on Extinguishment of Debt

In connection with a private placement of $150.0 million of our 2.25% notes (see further discussion under the section entitled *Liquidity and Capital Resources*) we repurchased and redeemed $142.0 million in aggregate principal amount of our 4.50% notes for cancellation. As a result of this repurchase and cancellation we recorded a loss on the early extinguishment of debt of approximately $4.5 million for the year ended December 31, 2004.

In January 2004, we and certain holders of our 4.50% notes completed an exchange and cancellation of $33.0 million in aggregate principal amount of the 4.50% notes, for the issuance of $21.986 million in aggregate principal of a new series of 4.25% notes and in connection therewith, we recorded a gain of approximately $0.3 million for 2004. We calculated the gain in accordance with EITF 96-19, *Debtor s Accounting for a Modification or Exchange of Debt Instruments*. EITF 96-19 requires that the gain on the early extinguishment of debt be computed using the fair value of the newly issued convertible debt which, at the time of the debt exchange, was trading at a premium to the principal amount of the notes. We classified the premium associated with the newly issued 4.25% notes of approximately $10.2 million as capital in excess of par value in accordance with APB 14, *Accounting for Convertible Debt and Debt Issued with Stock Purchase Warrants*.

Provision for Income Taxes

Our provision for income taxes of $0.1 million, $0.1 million and $31 thousand for the years ended December 31, 2002, 2003 and 2004, respectively, relates primarily to the New Jersey alternative minimum tax assessment which became effective in 2002.

Cumulative Effect of a Change in Accounting Principle

Cumulative effect of a change in accounting principle for the year ended December 31, 2003 was $0.8 million. Effective January 1, 2003, we changed our method of accounting for asset retirement obligations in accordance with SFAS No. 143, *Accounting for Asset Retirement Obligations*. Previously, we were not required to recognize amounts related to asset retirement obligations. Under SFAS No. 143, we now recognize asset retirement obligations in the period in which they are incurred if a reasonable estimate of a fair value can be made. The associated asset retirement costs are capitalized as part of the carrying amount of the long-lived asset. The adoption of SFAS No. 143 resulted in an increase in net property, buildings and equipment of approximately $1.4 million, recognition of an asset retirement obligation liability of approximately $2.2 million and a cumulative effect of a change in accounting principle of approximately $0.8 million.

Liquidity and Capital Resources

We require cash to fund our operations, to make capital expenditures and strategic investments, and to pay debt service on our convertible notes. Since inception, we have financed our operations through the sale of our securities in public and private placements, sales of our products for research purposes, development and manufacturing services, technology transfer and license fees and milestone payments. We expect to continue to fund our cash requirements from these sources in the future. In 2002, 2003, and 2004, we received net proceeds of $301.1 million from sales of our equity and debt securities.

At December 31, 2003 and 2004, we had $358.5 million and $374.5 million, respectively, in cash, cash equivalents and marketable securities. We primarily invest our cash equivalents and marketable securities in highly liquid, interest-bearing, investment grade and government securities in order to preserve principal.

Cash Used in Operating Activities

Cash used in operating activities was $64.0 million, $89.3 million and $6.0 million for the years ended December 31, 2002, 2003 and 2004, respectively. This reflects an increase of $25.3 million in 2003 as compared to 2002 and a decrease of $83.3 million in 2004 as compared to 2003.

The 2003 increase was primarily due to higher research and development expenses (approximately $12.8 million) related to the development of our product pipeline, a decrease in interest and dividend income (approximately $6.2 million) due to lower interest rates as well as lower average cash balances and an increase in interest expense (approximately $2.7 million) representing the addition of approximately five months of interest on our 4.25% notes which were issued in July 2003. The 2004 decrease is primarily due to an increase in deferred contract revenue (approximately $99.1 million) resulting from the up-front payments associated with collaborations with each of Pfizer and MedImmune, offset in part, by higher research and development expenses (approximately $26.5 million). The increase in research and development expenses resulted primarily from higher personnel costs, expenses related to our facilities, third-party research and contract manufacturing costs, and the costs of clinical trials. All of these costs were higher as result of our increased clinical trial and product development activities.

We have incurred and will continue to incur significant costs in the area of research and development, including preclinical and clinical trials, as our products are developed. We plan to spend significant amounts to progress our current products through the clinical trial and commercialization process as well as to develop additional product candidates on our own or with our partners. As our products progress through the clinical trial process, we may be obligated to make significant milestone payments on certain of our products. We also expect to incur future facility costs as a result of our continued capital expansion, renovations and replacements, but at a reduced rate. To a lesser extent, we expect our general and administrative costs to increase as we expand our administrative and business development activities. Furthermore, we expect our investment income to decrease as we fund our future operations and capital expenditures from our cash reserves. We anticipate that our operating expenditures may be partially offset by revenues from partners for license fees, milestone payments, and development and manufacturing services.

Cash Provided by (Used in) Investing Activities

Net cash provided by investing activities was $93.9 million in 2002. Net cash used in investing activities was $22.6 million in 2003 and $33.8 million in 2004, respectively. Cash was provided by and used in investing activities primarily as follows:

- Capital expenditures of $43.7 million, $8.9 million and $9.1 million in 2002, 2003 and 2004, respectively. Capital spending in 2002 reflects an investment in building improvements related to the expansion of our Milpitas, California, facility as well as leasehold improvements and the purchase of machinery, equipment and furniture and fixtures for our Sunnyvale, California, facility, which we leased in July 2002. The capital expenditures in 2003 and 2004 reflect an investment in laboratory automation as well as the addition of machinery and equipment.

- Net sales of marketable securities were $136.7 million and $3.2 million in 2002 and 2003, respectively. The net sales of marketable securities in 2002 were primarily to fund operations and capital expenditures. The net sales of marketable securities in 2003 were the result of funding operations and capital expenditures offset by the net proceeds received ($121.2 million) from the sale of our 4.25% notes in July 2003.

- Net purchases of marketable securities in 2004 were $27.9 million. The 2004 net purchases were the result of the proceeds received from the Pfizer collaboration ($110.0 million), the MedImmune collaboration ($15.0 million) and the net proceeds ($145.2 million) received for the private placement of our 2.25% notes, offset in part, by sales of marketable securities ($242.6 million) to fund operations and capital expenditures as well as to repurchase and redeem our 4.50% notes as discussed further in the section entitled *Cash Provided by Financing Activities* .

We expect 2005 capital expenditures to be approximately $15.0 million representing the purchase of machinery and scientific equipment and additional investment in lab automation.

Cash Provided by Financing Activities

Cash provided by financing activities was $0.6 million, $123.0 million and $31.6 million in 2002, 2003 and 2004, respectively. In 2002, cash provided by financing activities consisted primarily of proceeds received from the issuance of stock under our employee stock purchase plan of $0.5 million. In 2003, cash provided by financing activities consisted primarily of $121.2 million in net proceeds received from the sale of our 4.25% notes in July 2003 and $0.9 million from the issuance of common stock under our employee stock purchase plan. In 2004, cash provided by financing activities consisted primarily of $145.2 million in net proceeds received from the sale of our 2.25% notes in May 2004 and $31.8 million from sales of common stock primarily to Pfizer ($30.0 million) and the issuance of common stock under our employee stock purchase plan ($1.1 million), offset in part, by the repurchase, redemption and cancellation of our 4.50% notes ($144.6 million).

In July 2003, we completed a private placement pursuant to Rule 144A of the Securities Act of 1933, as amended of $125 million in aggregate principal amount of our 4.25% notes to qualified institutional investors. The 4.25% notes were initially convertible into shares of our common stock at the rate of 148.8261 shares per each $1,000 principal amount of notes, which is equivalent to an initial conversion price of approximately $6.72 per share, subject to anti-dilution adjustments. Interest was payable on February 15 and August 15 of each year. The first interest payment was made on February 15, 2004.

The 4.25% notes were scheduled to mature on August 15, 2010 and were redeemable at our option on or after August 15, 2006, or earlier if the price of our common stock exceeded specified levels. We received net proceeds from the private placement of the 4.25% notes of approximately $121.2 million (after deducting the initial purchasers discounts and offering expenses). As of December 31, 2004, we had purchased U.S. Treasury security strips to collateralize the notes in an amount sufficient to pay the four interest payments due on the 4.25% notes in 2005 and 2006. Such amount has been classified as segregated securities in the current assets section of our December 31, 2004, consolidated balance sheet.

On January 14, 2005, we completed the provisional redemption of all of our 4.25% notes which was previously announced in December 2004. Holders of all of the outstanding 4.25% notes ($146.986 million) converted their notes into a total of 21,875,353 shares of our common stock prior to the redemption date. In connection with the redemption, we paid approximately $12.5 million in cash representing the make-whole payment of $10.2 million and accrued interest of $2.3 million. We accrued the $10.2 million make-whole payment in the quarter ended December 31, 2004, at the time the redemption was announced.

In January 2004, we and certain holders of our 4.50% notes completed an exchange and cancellation of $33.0 million in aggregate principal amount of the 4.50% notes, for the issuance of $21.986 million in aggregate principal of a new series of 4.25% notes due August 15, 2010. As a result of this exchange and cancellation, our total convertible debt was reduced by $11.014 million.

In May 2004, we completed a private placement pursuant to Rule 144A of the Securities Act of 1933, as amended, of $150.0 million in aggregate principal amount of our 2.25% notes to qualified institutional investors. The 2.25% notes are initially convertible into shares of our common stock at the rate of 72.9129 shares per each $1,000 principal amount of notes, which is equivalent to an initial conversion price of approximately $13.72 per share, subject to anti-dilution adjustments. Interest is payable on May 15 and November 15 of each year. The first interest payment was made on November 15, 2004.

The 2.25% notes mature on May 15, 2011 and are redeemable at our option on or after May 20, 2009. Holders of the 2.25% notes may require us to repurchase the notes if we undergo a change in control as defined in the indenture. We received net proceeds from the private placement of the 2.25% notes of approximately $145.2 million (after deducting the initial purchasers discounts and offering expenses). The costs of issuance of the 2.25% notes of approximately $4.8 million have been deferred and are being amortized over the term of the 2.25% notes. In May 2011, or earlier if we undergo a change in control, we

may be required to use a significant portion of our cash to repay the remaining balance ($150.0 million) of the 2.25% notes. If our cash is not sufficient to meet our obligations under the 2.25% notes, we would be required to seek additional financing.

In June 2001, we issued $175 million of our 4.50% notes. The 4.50% notes were scheduled to mature on July 1, 2006. Concurrent with the private placement of the 2.25% notes described above, we repurchased approximately $65.6 million in aggregate principal amount of our 4.50% notes for cancellation during the second quarter of 2004. On July 1, 2004, we completed the redemption and cancellation of the remaining balance of our 4.50% notes of approximately $76.4 million for approximately $77.7 million plus accrued interest of approximately $1.7 million.

Other Liquidity Matters

As of December 31, 2004, we had federal net operating loss (NOL) carryforwards of approximately $426.6 million. These NOL carryforwards will expire in the years 2005-2024 (as more fully described in Note 5 to the consolidated financial statements), if not utilized. During 2000 we determined that an ownership change under Section 382 of the Internal Revenue Code of 1986, as amended, occurred during 1998. The effect of this ownership change was the imposition of a $3.2 million annual limitation on the use of NOL carryforwards attributable to periods before the change. This annual limitation will result in the expiration of some NOL carryforward credits before utilization. At December 31, 2004 the amount of NOL subject to the limitation was $43.8 million and the amount not subject to limitation was $382.8 million.

In connection with our merger with Essex Medical Products in 1987, we are committed to pay to Essex Chemical Corporation, or Essex, 20% of our net after-tax income until a total of $1.0 million has been paid, contingent upon the occurrence of certain events. As the result of our net income in 2000 we accrued $0.7 million payable to Essex, which remains accrued at December 31, 2004. At our option, this obligation may be satisfied by the payment of shares of our common stock having a fair market value equal to the amount owed, provided such shares are registered for sale with the Securities and Exchange Commission.

Our wholly-owned subsidiary Celldex Therapeutics, Inc. has filed a registration statement with the Securities and Exchange Commission related to a proposed initial public offering of a portion of its common stock. As part of this transaction, we have assigned or licensed to Celldex certain intellectual property related to our vaccine technology, including the rights to MDX-1307, one of our product candidates for the treatment of cancer, as well as the IND associated with this product which became effective in February 2004. If the initial public offering is completed, we anticipate that we will continue to hold approximately 70% of the outstanding shares of common stock of Celldex. We cannot assure you that this transaction will be consummated.

In July 2004, we entered into an amendment to a collaboration and license agreement with Gilead, referred to herein as the Gilead Amendment. Under the terms of the Gilead Amendment, we agreed to pay Gilead a total of $8.5 million in eight equal quarterly installments of $1.063 million, payable at our election, in cash, registered shares of our common stock or a combination thereof, in exchange for (i) a reduction of certain future royalty payment obligations payable by us to Gilead, and (ii) an expansion of the scope of certain licenses from Gilead to us relating to certain intellectual property rights regarding anti-CTLA-4 products. The first of these payments was paid on August 2, 2004 through the issuance of 185,622 shares of our common stock to Gilead. The second payment was made on October 1, 2004 in cash. The third payment was made on January 3, 2005 in cash. The five remaining payments will be made on a quarterly basis, commencing on April 1, 2005 and ending on April 3, 2006. If we decide to make a quarterly installment payment in shares of our common stock, the number of shares of common stock subject to issuance for any installment will be determined by dividing (x) $1.063 million (less any cash paid in connection with the installment) by (y) the average of the closing sales prices of our common stock for

each of the trading days during the five-trading-day period ending on (and including) the trading day that is two trading days immediately prior to the applicable date of issuance as publicly reported by NASDAQ. In the event that, during the 60-day period following the applicable date of issuance of such common stock, Gilead sells all of the shares of our common stock delivered as part of an installment payment under the Gilead License and the proceeds of such sale are less than $1.063 million (less any cash paid in connection with such installment), we must pay the difference to Gilead in cash. If such sale proceeds exceed $1.063 million (less any cash paid in connection with such installment), Gilead must pay us 50% of any such excess in cash. In the event that, during any such 60-day period, Gilead does not sell all of the shares of our common stock comprising the installment, there will be no such adjustment. In August 2004, we paid Gilead approximately $0.1 million representing the difference between the proceeds received by Gilead upon the sale of the 185,622 shares of common stock and the initial payment of $1.063 million.

In August 2004, we completed the acquisition of all of the outstanding capital stock not already owned by us of Ability Biomedical. Pursuant to this transaction, we acquired Ability Biomedical s intellectual property related to IP-10, a protein believed to be associated with a variety of immune disorders, including multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, chronic obstructive pulmonary disease and type I diabetes.

Under the terms of the share purchase agreement with Ability Biomedical, we made cash payments totaling approximately $606 thousand and issued a total of 731,823 shares of our common stock valued at approximately $4.3 million in exchange for all of Ability Biomedical s issued and outstanding stock not already owned by us. During the 60-day period following an issuance of shares of our common stock to the Ability Biomedical shareholders in connection with the acquisition, certain of such shareholders sold all of the shares issued to them for an amount less than the amount due to them under the share purchase agreement while certain other shareholders sold shares issued to them for an amount greater than the amount due them under the share purchase agreement. In accordance with the share purchase agreement, we received approximately $0.1 million representing 50% of the difference between the actual proceeds received and the amount due under the share purchase agreement.

Upon achievement of certain development milestones with respect to our anti-IP-10 antibody program, but no later than September 4, 2007, we may be required to pay the former shareholders of Ability Biomedical an additional amount of approximately $3.68 million in cash and/or common stock subject to fluctuations in currency exchange rates. In lieu of such additional payment, we also have the option to revert to the original joint collaboration agreement with the former shareholders of Ability Biomedical whereby each party would be responsible for 50% of the costs associated with the anti-IP-10 antibody.

In September 2004, we entered into a series of agreements with Pfizer. The first agreement amended our existing collaborative research and license and royalty agreements with Pfizer to provide for the discovery and development of up to 50 antibody products over ten years. The second and third agreements were a sublicense from us to Pfizer and a cross-license of certain patents and patent applications, in each case solely relating to our respective anti-CTLA-4 antibody programs. The fourth agreement was a stock purchase agreement also related to the anti-CTLA-4 programs. Pursuant to certain of these agreements, Pfizer made a total initial cash payment to us of $80.0 million and purchased 4,827,808 shares of our common stock at a purchase price equal to $6.21 per share for an aggregate purchase price of $30.0 million. These shares were issued in a private placement and the per share price represented a premium to market price at the time we entered into the collaboration.

In November 2004, we announced a collaboration and co-promotion agreement and a related securities purchase agreement with BMS. This collaboration became effective in January 2005. Under the terms of the collaboration, we and BMS have each granted the other certain intellectual property licenses and product rights on a worldwide basis in order to enable us to collaborate in research and development

of certain therapeutic antibody-based products for the treatment of cancer and other diseases, and, in the event that further development work is successful, to commercialize any resulting products. In particular, the collaboration includes a grant by us to BMS of a license to commercialize MDX-010, a fully human antibody product developed using our UltiMAb Human Antibody Development System, that is antagonistic to CTLA-4. MDX-010 is currently under investigation for the treatment of a broad range of cancers and other diseases. The collaboration also includes the grant by us to BMS of a sub-license to MDX-1379, a gp100 peptide vaccine licensed by us from the U.S. Public Health Service, for use with MDX-010 for the treatment of metastatic melanoma. We and BMS are currently conducting a Phase III clinical trial with MDX-010 and MDX-1379 combination therapy in Stage III and Stage IV metastatic melanoma patients at multiple sites within the U.S.

As part of the collaboration, we and BMS have committed to an initial multi-year budget of approximately $192.0 million to fund the development of MDX-010 as a potential treatment for a broad range of cancers. BMS will be responsible for 65% of all development costs related to clinical trials intended to support regulatory approval in both the U.S. and Europe, with the remaining 35% to be paid by us. We and BMS will share equally the costs of any clinical trials of products intended solely for regulatory approval in the U.S., and BMS will be fully responsible for all development costs that relate solely to regulatory approval in Europe and other parts of the world.

Under the terms of the collaboration, we could receive up to $205.0 million from BMS if all regulatory milestones are met, plus up to an additional $275.0 million in sales-related milestones. We will also have the option to co-promote any products in the U.S., and, if we elect to exercise this option and have participated in the funding of the applicable Phase II clinical trial(s), we will receive 45% of any profits from commercial sales. In the event we choose not to exercise our co-promotion rights, BMS will have exclusive commercial rights in the U.S. and will pay us royalties on commercial sales. Outside the U.S., BMS will have exclusive commercial rights and will pay us royalties on commercial sales.

Pursuant to these agreements, BMS made an initial cash payment to us on January 21, 2005 of $25.0 million. In addition, BMS purchased a total of 2,879,223 unregistered shares of our common stock at a purchase price equal to $8.6829 per share for an aggregate purchase price of $25.0 million. These shares were issued in a private placement pursuant to the exemption from registration provided by Section 4(2) of the Securities Act of 1933. The purchase price represented a premium to the market price on the date we entered into the collaboration. BMS has agreed to a two-year lock-up period with respect to any sales of such stock. We have no future obligation to register such stock.

Contractual Obligations

Our material contractual obligations under lease, debt and research funding agreements for the next five years, and thereafter, as of December 31, 2004, are as follows:

	Payments Due by Period				
	Less Than 1 Year	**1-3 Years**	**4-5 Years**	**After 5 Years**	**&nbs**