2004 Targeted Genetics Annual Report

COMMITMENT

EXECUTION

PROGRESS

MOMENTUM

OUR VISION

Discover, develop and deliver molecular medicines to treat and prevent diseases with significant unmet medical need

OUR APPROACH

Focus on significant product development opportunities that leverage our extensive capabilities in the development, manufacturing and commercialization of gene delivery technologies

Dear Fellow Shareholders:

A Commitment to Commercializing
Novel Therapies
for Serious Diseases

Targeted Genetics is committed to discovering and delivering molecular medicines to treat or prevent diseases with significant unmet medical need. In 2004 we continued to focus our resources on important product opportunities that leverage our extensive capabilities and experience in the development and manufacturing of products based on gene delivery technologies. Toward this end, we started 2004 with two key objectives: to advance the clinical development of our three core programs and to leverage our leading adeno-associated virus (AAV) capabilities into new product-focused opportunities with significant revenue-generating potential. I am very pleased to report that we achieved both objectives in 2004 and we are positioned to advance our most promising programs in 2005.

Having said that, unfortunately the past months have not been without a product disappointment. Throughout 2004 we continued enrollment, dosing and follow-up of patients with mild to moderate cystic fibrosis (CF) in our Phase II trial of tgAAVCF. This double-blind, placebo-controlled study was designed to evaluate the impact of repeated doses of tgAAVCF on lung function, inflammation and biologic markers. In March 2005, we reported preliminary data indicating that the study failed to meet its primary endpoint of improving lung function compared with placebo. Based on these results, we have decided not to continue development of tgAAVCF.

I would like to take this opportunity to thank the Cystic Fibrosis Foundation, the members of the CF medical community and, most of all, CF patients and their families, for their support of our efforts to develop a new approach to treating this disease. We remain optimistic that continued advances in science and medicine will result in new CF therapies that will make a difference in the lives of those living with the disease.

Despite this setback, we remain committed to developing gene-based therapies because we believe in their enormous potential to treat serious diseases. The timelines for successfully commercializing breakthrough technologies, such as monoclonal antibodies and targeted cancer therapies, have always been longer than the investment, medical and patient communities would like. However, companies that have held the course, innovated around the

INDICATION	RESEARCH PRECLINICAL PHASE 1 PHASE 2 PHASE 3	GENE
AIDS		HIV gag/pro and others
INFLAMMATORY ARTHRITIS		TNFR:Fc
HYPERLIPIDEMIA		VLDLr
CONGESTIVE HEART FAILURE		Serca2a
HUNTINGTON'S DISEASE		HTT RNAi

challenges and remained focused on addressing clinical needs have been rewarded commercially and by their ability to make a positive impact on the lives of patients and their families.

As pioneers in the field of gene-based therapies, we have had to cross many frontiers. We have successfully navigated much of the difficult terrain faced by those at the leading edge of biomedical science, and I am proud that we have played a part in setting the manufacturing and regulatory standards for the clinical evaluation of AAV-based product candidates. We know that there are other challenges that must be overcome, but the unmet medical needs of so many patients inspire us to rise above them. We believe that persistence and pragmatism in our continued development of gene-based therapies will benefit our shareholders, our company and, most importantly, the many patients who face the daily struggle of living with serious illness.

Executing Our Clinical Development Programs

Although we were disappointed that the results of the most recent Phase II CF trial did not support the continued development of tgAAVCF, we believe that our programs in HIV/AIDS prophylaxis and inflammatory arthritis have important clinical and commercial potential. Throughout 2004 we advanced the clinical development of both programs.

In late 2004, we completed enrollment and dosing in the European arm of a dose-escalation Phase I safety trial of tgAAC09, our AAV-based vaccine against HIV/AIDS. Preliminary results from this portion of the study, which were reported in February 2005, demonstrated that the vaccine candidate met the safety endpoint and was well tolerated in healthy volunteers who were uninfected with HIV. These data provide a solid foundation on which to expand our HIV/AIDS vaccine program to include higher doses, evaluate the effects of sequential doses of the vaccine (prime-boost) on immune responses and explore the use of vectors based on AAV serotype 1.

Already in 2005 we have made significant advances in our HIV/AIDS vaccine program. In February, in collaboration with the International AIDS Vaccine Initiative (IAVI) and researchers at Columbus Children's Research Institute (CCRI) and The Children's Hospital of Philadelphia (CHOP), we announced the expansion of the Phase I trial to India. This is an important location in which to evaluate tgAAC09 because the vaccine is targeted against the clade C strain of HIV, which is prevalent in India and other parts of the developing world.

In 2004 we initiated a Phase I trial of tgAAC94 in patients with inflammatory arthritis, including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. The double-blind, placebo-controlled, dose-escalating trial will assess safety, and we will also collect data on molecular markers of gene expression following a single injection of tgAAC94 or placebo into the affected joint. This study is ongoing at eight sites in the United States and Canada.

tgAAC94 is designed for injection directly into affected joints of those suffering from inflammatory arthritis, a chronic disease that causes pain, stiffness, swelling and loss of function in the joints. tgAAC94 utilizes our AAV vector capabilities to deliver a DNA sequence encoding an inhibitor of TNF-a, an inflammatory molecule that has been validated as a therapeutic target. Anti-TNF therapies have been very successful in treating inflammatory arthritis and other inflammatory autoimmune diseases. However, 15 to 40 percent of patients with rheumatoid arthritis, a type of inflammatory arthritis, who are currently treated with these therapies have one or more joints that do not respond to treatment. We believe that tgAAC94 may serve as a potential alternative or supplement to these therapies in patients with various types of inflammatory arthritis who have one or more joints that do not respond to systemic protein therapy.

In June 2004, we presented positive preclinical data from studies of tgAAC94 at the 7th annual meeting of the American Society of Gene Therapy. These studies evaluated multiple routes of administering tgAAC94 and demonstrated complete suppression of inflammatory arthritis over three months of study in an animal model of the disease. We are encouraged by the preclinical data generated to date in this program and are looking forward to reporting preliminary results of the ongoing Phase I trial in mid-2005.

Continued Progress in Business and Corporate Development

I am proud of our accomplishments in advancing three clinical development programs on time and within budget. This success reflects our growing expertise in the manufacture and clinical development of AAV-based product candidates and highlights our leadership in the area of AAV-based therapies. This leadership position continues to provide us with new and exciting opportunities to leverage our manufacturing and product development infrastructure into additional revenue-generating, product-focused collaborations. Our efforts to leverage our AAV capabilities in 2004 resulted in the formation of two exciting collaborations, which were announced in January of 2005.

The first of these collaborations is with Celladon and is focused on developing AAV-based therapies for congestive heart failure (CHF) utilizing Celladon's portfolio of genes and gene variants. Simultaneous with the initiation of this collaboration, Enterprise Partners and Venrock Associates, venture capital funds that have invested in Celladon, made a $6 million common stock investment in Targeted Genetics. Approximately $2 million of this funding will support the work we do within the collaboration and $4 million may be applied to our other programs.

CHF is a serious condition in which the heart loses its ability to pump blood efficiently. According to the National Heart, Lung and Blood Institute, about 5 million people in the United States alone have heart failure, and another 550,000 new cases are diagnosed each year. CHF contributes to or causes about 300,000 deaths annually. There is currently no cure for CHF. The second collaboration is with Sirna Therapeutics, a leader in ribonucleic acid (RNA) inhibition technologies. We are working with Sirna to utilize our AAV vectors to deliver small inhibitory RNAs targeted against the Huntington's disease (HD) gene. HD is a devastating, degenerative brain disorder for which there is, at present, no effective treatment or cure. According to the National Institute of Neurological Disorders and Stroke, 30,000 people in the United States alone have HD, and at least another 150,000 are at risk for developing the disease.

Sirna's scientific advisor and collaborator, Dr. Beverly Davidson at the University of Iowa, has published data demonstrating that the delivery of small inhibitory RNA using an AAV vector efficiently inhibited gene expression in an animal model of spinocerebellar ataxia 1, a member of a class of inherited human neurodegenerative diseases that includes HD.

We believe that these two collaborations validate our position as the leader in AAV manufacturing and product development, and we intend to continue to pursue such relationships throughout 2005.

We recognize that a significant factor in our ability to advance our programs and create value for patients and investors is predicated on the disciplined management of our financial resources. In 2004 we took several steps to strengthen our financial position. In January we announced a three-year extension of our collaboration with IAVI and CCRI. We earned $8.3 million in revenue from IAVI under this collaboration in 2004 and expect to receive up to an additional $5.6 million in funding to support the program in 2005. We issued $25.5 million of common stock in a public offering in February 2004, and received an additional $6 million in December of 2004 through the sale of common stock to Enterprise Partners and Venrock Associates in conjunction with the Celladon collaboration.

As part of our effort to focus our financial resources on our core product development programs, we announced in June 2004 the sale of our majority-owned cell therapy subsidiary, CellExSys, to Chromos Molecular Systems. The sale provided a mechanism to accelerate the development of a promising body of cell therapy assets while enabling Targeted Genetics and the other CellExSys shareholders to have a long-term investment in the potential success of CellExSys' product development efforts.

Finally, we continued to expand our portfolio of intellectual property. Key highlights in this area include the signing of an exclusive license with the National Institutes of Health for patents that cover the use of the AAV inverted terminal repeat (ITR) as a promoter sequence in AAV vectors. We also added a patent to

our portfolio that covers AAV vectors containing sequences from AAV serotype 1. The patent was issued to University of Pennsylvania and is exclusively licensed to Targeted Genetics. We believe that these patents will support our ongoing efforts to develop AAV-based therapies.

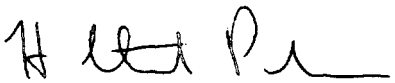
Maintaining Our Momentum

Our accomplishments in 2004 create a new set of goals for Targeted Genetics in 2005. In our inflammatory arthritis program, we expect to report data from the ongoing Phase I trial by mid-year and will utilize that data to determine the next steps in the clinical development of this very exciting product candidate. In our HIV/AIDS vaccine program, we are working to complete the Phase I trial in Europe and India, including the protocol extension that will assess the impact of a boost dose.

As always, we will continue to look for opportunities to leverage our technology assets, manufacturing capabilities and gene therapy product development expertise to create additional value for our shareholders. Targeted Genetics has generated proof of concept data in several other diseases, including hemophilia and cancer, and while not within our current development focus, we believe that these programs provide opportunities for establishing out-licensing agreements or partnerships that may provide us with additional revenue or sources of funding. We also continue to seek partnership opportunities for our AAV manufacturing capabilities and our other gene delivery technologies. As we seek to capitalize on new opportunities, we also remain committed to managing our financial resources to support our long-term product development programs.

2004 was a very productive year and I would like to thank everyone on the Targeted Genetics team for their ongoing commitment to helping us achieve our goals and for the enthusiasm they bring to their jobs each day. I believe we have the team we need to realize the commercial and clinical potential of our product candidates. I also would like to thank you, our shareholders, for your ongoing support and for sharing our vision of improving the treatment of diseases with significant unmet medical need. I look forward to sharing our progress with you in the months ahead.

Sincerely,



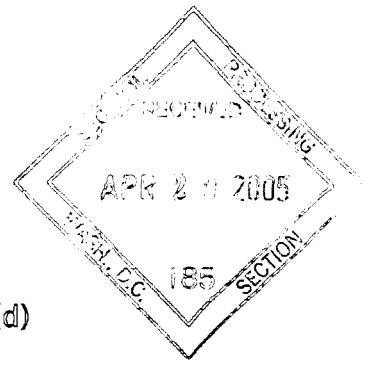
H. Stewart Parker
President and Chief Executive Officer

FOR ADDITIONAL INFORMATION ABOUT TARGETED GENETICS, PLEASE VIEW OUR ONLINE ANNUAL REPORT AT

www.targetedgenetics.com/2004AR

Form 10-K

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

OR

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

For the transition period from to

Commission File Number No. 0-23930

TARGETED GENETICS CORPORATION

(Exact name of Registrant as specified in its charter)

Washington	91-1549568
(State of Incorporation)	*(IRS Employer Identification No.)*

1100 Olive Way, Suite 100
Seattle, WA 98101
(Address of principal executive offices, including, zip code)

(206) 623-7612
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:
None
Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $0.01 Par Value

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 ☑ No ☐

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

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

The aggregate market value of common stock held by non-affiliates of the Registrant as of June 30, 2004 was approximately $88 million based on the closing price of $1.59 per share of the Registrant's common stock as listed on the NASDAQ SmallCap Market.

Indicate the number of shares outstanding of each of the Registrant's classes of common stock as of March 1, 2005

Title of Class	Number of Shares
Common Stock, $0.01 par value	85,628,244

DOCUMENTS INCORPORATED BY REFERENCE

(1) The information required by Part III of this report, to the extent not set forth in this report, is incorporated by reference from the Proxy Statement for the Annual Meeting of Shareholders to be held on May 26, 2005. The definitive proxy statement will be filed with the Securities and Exchange Commission within 120 days after December 31, 2004, the end of the fiscal year to which this report relates.

TARGETED GENETICS CORPORATION
ANNUAL REPORT ON FORM 10-K

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PART I

Item 1. *Business*

This annual report on Form 10-K contains forward-looking statements that involve risks and uncertainties. Forward-looking statements include statements about our product development and commercialization goals and expectations, potential market opportunities, our plans for and anticipated results of our clinical development activities and the potential advantage of our product candidates, and other statements that are not historical facts. Words such as "may," "can be," "may depend," "will," "believes," "estimates," "expects," "anticipates," "plans," "projects," *"intends," or statements concerning "potential" or "opportunity" and other words of similar meaning or the negative thereof may identify forward-looking statements, but the absence of these words does not mean that the statement is not forward-looking. In making these statements, we rely on a number of assumptions and make predictions about the future. Our actual results could differ materially from those stated in or implied by forward-looking statements for a number of reasons, including the risks described in the section entitled "Factors Affecting Our Operating Results, Our Business and Our Stock Price" in Part II, Item 7 of this annual report.*

You should not unduly rely on these forward-looking statements, which speak only as of the date of this annual report. We undertake no obligation to publicly revise any forward-looking statement after the date of this annual report to reflect circumstances or events occurring after the date of this annual report or to conform the statement to actual results or changes in our expectations. You should, however, review the factors, risks and other information we provide in the reports we file from time to time with the Securities and Exchange Commission, or SEC.

Business Overview

Targeted Genetics Corporation develops gene therapy products and technologies for treating both acquired and inherited diseases. Our gene therapy product candidates are designed to treat disease by regulating cellular function at a genetic level. This involves introducing genetic material into target cells and expressing it in a manner that provides the desired effect. We have assembled a broad base of proprietary intellectual property that we believe gives us the potential to address the significant diseases that are the primary focus of our business. Our proprietary intellectual property includes genes, methods of transferring genetic material into cells, processes to manufacture our AAV-based product candidates and other proprietary technologies and processes related to our lead product development candidates. In addition, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will enable us to develop products based on our proprietary intellectual property.

Gene therapy products involve the use of delivery vehicles, called vectors, to place genetic material into target cells. Our proprietary vector technologies include both viral and synthetic vectors. Our viral vector development activities, which use modified viruses to deliver genetic material into cells, focus primarily on adeno-associated virus, or AAV, a virus that has not been associated with any human disease or illness. We believe that AAV provides a number of safety and gene delivery advantages over other viruses for several potential gene therapy products, including each of our product candidates currently under development. Our synthetic vectors deliver genetic material into cells using lipids, which are fatty, water-insoluble organic substances that can promote gene uptake through cell membranes. We believe that synthetic vectors may provide a number of gene delivery advantages for repeated, efficient delivery of therapeutic genetic material into rapidly dividing cells, such as certain types of tumor cells. Although all of our current product development candidates utilize AAV as the delivery vector, we believe that possessing capabilities in both viral and synthetic approaches provides advantages in our corporate partnering efforts and increases the range of our potential products that may reach the market.

Our most advanced product candidate is tgAAVCF for treating cystic fibrosis. tgAAVCF is being evaluated in a second Phase II clinical trial that was initiated in July 2003. We designed this trial to enroll up to 100 patients and are conducting it in collaboration with the Cystic Fibrosis Foundation, or CF Foundation. In June 2004, we announced that an independent data monitoring committee, or DMC, met for a scheduled interim analysis of this Phase II clinical trial. Based upon its review, the DMC recommended continuation of the study as planned. The DMC provided its recommendation based upon safety parameters and an analysis of whether or not there was a chance that, upon full patient enrollment, the study could show a statistically significant positive impact on lung function measurements in patients treated with tgAAVCF compared to placebo. We expect to present data from the trial in mid to late March of 2005. The primary endpoint in this trial is an improvement in lung function 30 days following initial administration of tgAAVCF. We are also looking for improvement in lung function at day 90, which is 60 days following the administration of a second dose of tgAAVCF, to assess whether any improvement in lung function can be sustained. Review of the primary endpoint, safety and secondary endpoints in the trial will become the basis for determining how, or if, to continue development of tgAAVCF. This second Phase II trial follows an initial Phase II repeat dosing trial for which we announced final data in June 2003. Data from this trial showed a good safety profile and indicated a statistically significant improvement in lung function at day 30 and a decrease in levels of an inflammatory cytokine at day 14 in patients treated with tgAAVCF when compared to placebo.

We have two product candidates in Phase I clinical trials. The first is tgAAC09 which is an AAV-based prophylactic vaccine intended for use in high-risk populations in developing nations to protect against the progression of Human Immunodeficiency Virus, or HIV, infection to Acquired Immune Deficiency Syndrome, or AIDS. This product candidate is being developed in a collaboration with the International AIDS Vaccine Initiative, or IAVI, a non-profit organization, and The Columbus Children's Research Institute at Children's Hospital in Columbus, Ohio, or CCRI. In December 2003, IAVI initiated a Phase I dose-escalation safety trial of tgAAC09 in Europe. This trial was designed to enroll up to 50 healthy volunteers who are uninfected with HIV. Each participant in this trial received a single injection of the vaccine candidate or placebo. The primary objective of this study is to evaluate safety of tgAAC09; however, we are also assessing the ability of tgAAC09 to elicit an immune response against the expressed antigen. Preliminary results from this study were announced in February 2005 and suggest that tgAAC09 was safe and well-tolerated in this trial. Results also showed that at the doses evaluated in this initial trial, a single administration of tgAAC09 did not elicit a significant immune response. These results support further development of tgAAC09, including clinical evaluation at higher dose levels. We will continue to monitor these volunteers in accordance with our clinical trial protocol and plan to present additional data from this trial in the first half of 2005. The current Phase I clinical trial of tgAAC09 is the initial step in a comprehensive development strategy of this vaccine program. IAVI recently expanded the single-dose Phase I trial to include sites in India. The purpose of this study is to further evaluate the safety of the vaccine in the population that would participate in subsequent efficacy trials, assuming continued development of the vaccine candidates. Additionally, in a non-human primate study, it was demonstrated that antibody and T cell responses can be increased after a second dose, or boost, of tgAAC09 vaccine. Based on this preclinical data and upon receiving the necessary regulatory approvals, we plan to expand the European Phase I trial to evaluate the safety and immunogenicity of this vaccine after a second dose. Volunteers who had participated in the Phase I trial will be offered a second dose. After volunteers who receive a second dose of tgAAC09 have been monitored according to protocol, we will unblind the study results and plan to report the data from the entire study. While these clinical trials are underway, we continue to pursue the development of additional vaccine candidates, including vaccines based on different serotypes, or strains, of AAV believed to be more efficient delivery systems for gene-based vaccines to muscle. We also plan to pursue the development of vaccines that contain genetic material to express multiple proteins from HIV, a multivalent approach, which may have the most potential to inhibit HIV entry or replication and thus protect against AIDS progression. Pre-clinical studies of these vaccine approaches have demonstrated an ability to elicit an immune response at lower administration dose levels.

Our second product candidate in a Phase I clinical trial is an AAV-based product candidate for the treatment of inflammatory arthritis. In March 2004, we initiated a Phase I clinical trial in patients with rheumatoid arthritis. This dose-escalation safety trial was initially designed to enroll up to 32 patients with rheumatoid arthritis to be conducted in up to eight sites in the United States and Canada. In December 2004, we amended the clinical trial protocol to reduce the number of patients to be enrolled into the study to up to 24 patients and expanded the patient population to include patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. This protocol amendment was intended to accelerate patient accrual into the trial and to expand the population of patients that could be studied with this product candidate. Patients will be monitored primarily for safety and we expect to collect data on any improvements in arthritis signs and symptoms. We expect to complete patient accrual and dosing in this trial and to be able to present data from the trial in mid-2005.

We have established broad delivery capabilities and a development infrastructure that can be leveraged into several potential new areas in addition to our three programs in clinical development. We believe that this may enable us to establish new strategic or collaborative relationships with others, such as the collaboration that was initiated in December 2004 with Celladon Corporation, or Celladon, to pursue the development of AAV delivered products for the treatment of congestive heart failure and with Sirna Therapeutics, Inc. in January 2005 to pursue the development of AAV delivered products for Huntington's disease. We have developed processes to manufacture our potential products at a scale amenable to clinical development and expandable to large-scale production for advancing our potential products to commercialization. These methods are similar to the methods used to manufacture other biologics. As a result, we can pursue opportunities to utilize excess capacity, when such capacity exits, to manufacture biologics for other companies. For example, in March 2003, we entered into a manufacturing services agreement with GenVec, Inc., or GenVec, to manufacture clinical supply of GenVec's cancer product candidate, an adenoviral-based gene therapy product. This project was completed in 2004.

We believe that a wide range of diseases may potentially be treated, or prevented, with gene-based products, including cancer, genetic diseases and infectious diseases. We believe that there is also a significant opportunity to use gene-based products to treat diseases that are currently treated using proteins and monoclonal antibodies, or small molecule drugs. Some of these diseases may be more effectively treated by gene-based therapies due to their ability to provide a long-term or a localized method of treatment. Additionally, we believe that there are potential therapeutic applications where a gene-based approach to delivering a therapeutic protein may be preferred due to inherent difficulties in delivering the therapeutic protein itself. Our business strategy is to leverage our proprietary intellectual property and AAV development capabilities into multiple product development programs and collaborations to maximize our product opportunities. Using AAV gene delivery systems, we are developing product candidates across multiple diseases with the belief that gene-based therapies may provide a means to treat diseases not fully treatable with current biologic and pharmaceutical drugs. We believe that, if successful, our product candidates have significant market potential. Currently, there are no commercially available gene therapy products in the United States, Europe or other principal markets. We intend to pursue product development programs to enable us to demonstrate proof of concept and eventually commercialize gene-based therapeutics to address currently unmet medical needs in treating disease.

The development of pharmaceutical products, including our cystic fibrosis, AIDS vaccine and inflammatory arthritis product candidates, involves extensive preclinical development followed by human clinical trials that take several years or more to complete. The length of time required to completely develop any product candidate varies substantially according to the type, complexity and novelty of the product candidate, the intended use of the product candidate, and the degree of involvement by a development partner. Our commencement and rate of completion of clinical trials may vary or be delayed for many reasons, including those discussed in the section entitled "Factors Affecting Our Operating Results, Our Business and Our Stock Price" in Part II, Item 7 of this annual report.

Our business strategy includes:

Diverse product development pipeline. We have multiple product development programs in various stages of preclinical or clinical development. Each of these product candidates addresses a market where we believe that there is significant medical need for new or improved therapies. We have also been able to leverage our AAV development capabilities and manufacturing infrastructure into additional collaborations focused on the development of product candidates to treat congestive heart failure, Huntington's disease and hyperlipidemia.

We are currently focused on the following product development programs:

		Development Status					
Product Candidate	Indication	Research & Preclinical	Phase I	Phase II	Phase III	Gene	Delivery System
tgAAVCF	Cystic Fibrosis					CFTR	AAV
tgAAC09	AIDS					HIVgag/pro and others	AAV
tgAAC94	Inflammatory Arthritis					TNFR:Fc	AAV
-----	Hyperlipidemia					VLDLr	AAV
-----	Congestive Heart Failure					SERCA2a	AAV
-----	Huntington's Disease					HTT RNAi	AAV

Broad intellectual property portfolio. To date, we have filed or exclusively licensed over 400 patent or patent applications with the United States Patent and Trademark Office, or USPTO, including foreign counterparts of some of these applications in Europe, Japan and other countries. Of these patent applications, over 100 patents have been issued or allowed. This proprietary intellectual property includes genes, formulations, methods of transferring genetic material into cells, processes to manufacture and purify our gene delivery product candidates and other proprietary technologies and processes.

Significant development and manufacturing expertise. We have developed proprietary manufacturing process for our AAV-based products that utilize processes, operations and equipment common to the biopharmaceutical industry. These processes, operations and equipment are broadly applicable to the production of viral vectors for gene therapy as well as recombinant proteins and monoclonal antibodies. In addition, we have significant expertise in researching and developing gene delivery technologies, including expertise in quality assurance, quality control, general research, regulatory affairs and clinical affairs. We have an established manufacturing facility that complies with current Good Manufacturing Practices. It is our strategy to leverage these development and manufacturing capabilities into new collaboration opportunities which can broaden the application of our technology into additional product opportunities.

Multiple gene delivery systems to maximize product opportunities. Our experience indicates that different disease targets will require different methods of gene delivery. The best gene delivery method for a particular disease will depend on the gene to be delivered, the type of cell to be modified, the duration of gene expression desired and the need for *in vivo* (inside the body) or *ex vivo* (outside the body) delivery. Our primary viral vector development activities focus on AAV vectors, which we and others have shown to be efficient in transferring genetic material to a wide variety of target cells. Because AAV vectors can deliver genetic material in a way that allows for expression of genetic information for long periods of time, we believe that these vectors may have particular utility in treating chronic diseases, such as cystic fibrosis and arthritis, which require long-term expression of the gene that is delivered to the cell. Additionally, the efficient gene transfer in muscle by AAV vectors and the subsequent robust and durable immune response to the expressed foreign gene, may support the development of vaccines capable of conferring protection against a number of infectious diseases. Our synthetic vectors deliver genetic material using lipids. Lipid-based vectors may have advantages in certain applications, such as some types of cancer, in which insertion of genetic material into rapidly dividing cells and shorter-term gene expression may be desired. We believe that using both types of vectors gives us one of the broadest gene delivery technology platforms in the field, and ultimately will give us the flexibility to develop products addressing a much broader range of diseases than we could develop using any single gene delivery system. We also have rights to certain intellectual property

relating to adenoviruses, which can also be used to deliver genetic material into cells, and may have utility in settings where short-term and rapid gene expression is needed.

Programs Under Active Development

tgAAVCF for Cystic Fibrosis

Cystic fibrosis is one of the most common single-gene deficiencies particularly affecting the Caucasian population. According to the Cystic Fibrosis Foundation, CF afflicts approximately 30,000 people in the United States and 70,000 people worldwide. The disease is caused by a defective cystic fibrosis transmembrane regulator, or CFTR gene, which interferes with normal lung function and results in a buildup of mucus in the lungs, leading to chronic infections, scarring of the lung, loss of lung function and early patient death. Current treatments for cystic fibrosis relieve the symptoms of the disease, but do not cure the underlying genetic defect that causes the disease or stop its progression.

tgAAVCF, our cystic fibrosis product candidate, is comprised of a DNA sequence, or gene, that codes for a functional CFTR protein delivered in an AAV vector. The objective of this gene therapy is to deliver the CFTR gene to cells of the lung, which can then produce the protein that is missing in cystic fibrosis patients. Based on our research and development activities to date, we believe that tgAAVCF may be superior to other gene therapies for treating cystic fibrosis, because the drug appears to have a good safety profile and an ability to deliver the CFTR gene to the airway cells in the lung and support production of the missing protein over an extended period. tgAAVCF has been granted orphan drug status by the FDA, which provides for seven years of market exclusivity and certain tax credits.

In June 2003, we announced the final results of a Phase II clinical trial to explore the safety and potential for improvement in lung function after repeated doses of aerosolized tgAAVCF delivered to the lungs of cystic fibrosis patients. These final results indicated that tgAAVCF met its primary endpoint demonstrating safety and tolerability in this first-ever repeat dosing study for an AAV-gene therapy product to treat cystic fibrosis. In this trial, which was a randomized, double-blind, placebo-controlled clinical trial that included 37 patients with mild cystic fibrosis, patients received treatment at days 0, 30 and 60 of the trial. The results suggested that the aerosolized product, administered via nebulizer to the lung, was safe and well tolerated by patients. Following approvals from an independent data safety monitoring board, the entry criteria for patients included in the clinical trial was reduced successively from 18 years old to 15 years old to 12 years old. No clinically significant differences in adverse events or laboratory safety parameters between placebo and tgAAVCF-treated patients were observed. Patients were also monitored at regular intervals for overall lung function using FEV1, a standard measure of lung function, from two weeks before initial dosing through day 150 of the trial. Results from the trial indicated that patients receiving tgAAVCF showed a statistically significant improvement in FEV1 lung function at 30 days after treatment compared to patients receiving placebo. Levels of IL-8, a cytokine associated with inflammation, were lower in tgAAVCF-treated patients at 14 days after treatment compared to patients in the placebo group. Excellent gene transfer was also observed in all patients tested, as measured by DNA polymerase chain reaction, a method for amplifying a specific AAV-CFTR DNA sequence, on DNA from tissue samples removed from the lung. Gene expression was not observed within the level of detection by the assays used to measure gene expression and AAV-neutralizing antibody response occurred systemically and locally. There was no apparent correlation between the clinical response that patients receiving tgAAVCF experienced with the presence, or levels, of neutralizing antibodies to AAV. In a subset analysis of results from this study, we observed that 22% of the patients receiving tgAAVCF in this trial experienced a 5% or greater sustained improvement in lung function over the 90-day course of treatment. Similar results were not observed in patients receiving placebo in the trial.

In July 2003, we initiated a larger confirmatory Phase II clinical trial for this cystic fibrosis product candidate. This Phase II, double-blind, randomized, placebo-controlled study, is being conducted through the CF Foundation and its Therapeutics Development Network and includes semi-monthly evaluation of changes in lung function after repeat dosing of tgAAVCF. We are also assessing the impact of tgAAVCF on inflammation and biologic markers over time when compared to placebo.

The study will continue to monitor the safety and tolerability profile of the product candidate. A total of 100 patients, 12 years of age and older, will be evaluated, 50 in the treatment group and 50 in the placebo group. Study participants receive two doses of tgAAVCF delivered via a nebulizer at day 0 and day 30 of the study and will be evaluated for a total of 90 days. Study participants are monitored for safety for seven months after the last dose. In June 2004, we announced that an independent data monitoring committee, or DMC, met for a scheduled interim analysis of this Phase II clinical trial. Based upon its review, the DMC recommended continuation of the study as planned. The DMC provided its recommendation based upon safety parameters and an analysis of whether or not there was a chance that, upon full patient enrollment, the study could show a statistically significant positive impact on lung function measurements in patients treated with tgAAVCF compared to placebo. We expect to present data from the trial in mid to late March of 2005. The primary endpoint in this trial is an improvement in lung function 30 days following initial administration of tgAAVCF. We are also looking for improvement in lung function at day 90, which is 60 days following the administration of a second dose of tgAAVCF, to assess whether any improvement in lung function can be sustained. Review of the primary endpoint, safety and secondary endpoints in the trial will become the basis for determining how, or if, to continue development of tgAAVCF.

AIDS Vaccine

According to the World Health Organization, more than 40 million people worldwide suffer from AIDS or are infected with HIV, nearly all of whom are expected to die from AIDS-related complications within the next two decades. Approximately five million men, women and children worldwide were newly infected with HIV in 2003. More than 20 million people have died from AIDS, which now kills more people worldwide than any other infectious disease. While current drug therapies such as protease inhibitors and reverse transcriptase inhibitors have helped many patients with AIDS to manage their disease, these therapies have not been shown to be curative, have significant and often treatment-limiting side effects and are costly. We believe that a vaccine to protect against the progression of HIV infection to AIDS could have significant market potential. To date, no company has applied for regulatory approval of a prophylactic AIDS vaccine, although several vaccines are under clinical development.

We are collaborating with IAVI and CCRI to develop a vaccine to protect against the progression of HIV to AIDS. The vaccine utilizes our AAV vectors to deliver multiple HIV genes that express viral proteins. Under the terms of this collaboration, IAVI is funding work at Targeted Genetics and at CCRI focused on preclinical and clinical development of a vaccine candidate. IAVI coordinates, manages and funds the clinical development activities of vaccine candidates developed under the collaboration. We have the right to commercialize in industrialized countries any vaccine that may result from this development collaboration. Under the terms of the collaboration, we have a qualified right to manufacture the vaccine for non-industrialized nations for IAVI. The section below entitled "Research and Development Collaborations" provides a detailed description of this collaboration.

Under this vaccine approach, we use an AAV vector to deliver genetic material from the HIV genome to muscle cells in a healthy individual. The objective of this vaccine is to express HIV viral genes as proteins by the muscle cells. The HIV proteins are detected by the immune system to elicit a strong immune response against HIV without exposing the vaccinated individual to HIV. Based on our preclinical animal studies, we believe that an AAV-based vaccine containing HIV genes could allow for gene expression of HIV proteins *in vivo,* thereby eliciting a robust and sustained immune response. Further, data from studies in nonhuman primates suggest that this vaccine approach may hold significant promise by triggering both an antibody and a T-cell immune response. Monkeys immunized with AAV vectors carrying SIV genes, the primate equivalent of HIV, develop immune responses that provide protection against disease progression after challenge with a pathogenic SIV virus. These data and additional preclinical data support the Phase I clinical trials in humans.

In December 2003, IAVI initiated a Phase I dose-escalation safety trial of tgAAC09 in Europe. This trial was designed to enroll up to 50 healthy volunteers who are uninfected with HIV. Each participant in this trial received a single injection of the vaccine candidate or placebo. The primary objective of this study is to evaluate safety of tgAAC09; however, we are also assessing the ability of

tgAAC09 to elicit an immune response against the expressed antigen. Preliminary results from this study were announced in February 2005 and suggest that tgAAC09 was safe and well-tolerated in this trial. Results also showed that at the doses evaluated in this initial trial, a single administration of tgAAC09, did not elicit a significant immune response. These results support further development of tgAAC09, including clinical evaluation at higher dose levels. We will continue to monitor these volunteers in accordance with our clinical trial protocol and plan to present additional data from this trial in the first half of 2005.

The current Phase I clinical trial of tgAAC09 is the initial step in a comprehensive development strategy of this vaccine program. IAVI recently expanded the single-dose Phase I trial to include sites in India. The purpose of this study is to further evaluate the safety of the vaccine in the population that would participate in subsequent efficacy trials, assuming continued development of the vaccine candidates. Additionally, in a nonhuman primate study, it was demonstrated that antibody and T cell responses can be increased after a second dose, or boost, of tgAAC09 vaccine. Based on this preclinical data and upon receiving the necessary regulatory approvals, we plan to expand the European Phase I trial to evaluate the safety and immunogenicity of this vaccine after a second dose. Volunteers who had participated in the Phase I trial will be offered a second dose. After volunteers who receive a second dose of tgAAC09 have been monitored according to protocol, we will unblind the study results and plan to report the data from the entire study.

While these clinical trials are underway, we continue to pursue the development of additional vaccine candidates, including vaccines based on different serotypes, or strains, of AAV believed to be more efficient delivery systems for gene-based vaccines to muscle. We also plan to pursue the development of vaccines that contain genetic material to express multiple proteins from HIV, a multivalent approach, which may have the most potential to inhibit HIV entry or replication and thus protect against AIDS progression. Preclinical studies of these vaccine approaches have demonstrated an ability to elicit an immune response at lower administration dose levels.

Inflammatory Arthritis

Rheumatoid arthritis, or RA, is a chronic disease that causes pain, stiffness, swelling and loss of function in the joints and inflammation in other organs. According to the Arthritis Foundation, RA affects more than two million people in the United States, with disease onset occurring most frequently in people between the ages of 25 and 50. While the exact cause of the disease remains unknown, autoimmune and inflammatory processes lead to chronic and progressive joint damage. Researchers have found that the cytokine called tumor necrosis factor-alpha, or TNFα, plays a pivotal role in this disease process and have shown anti-TNFα therapies to be a valuable strategy to treat RA. Psoriatic arthritis, or PsA, and ankylosing spondylitis, or AS, are similar chronic inflammatory diseases mediated by TNFα. AS, a progressive inflammatory disease involving the spine and associated soft tissues, may also result in arthritis in the peripheral joints. All three forms of inflammatory arthritis (RA, PsA and AS) are currently treated with protein therapies such as Amgen Inc.'s etanercept; a variety of systemic treatments, including steroid and non-steroid anti-inflammatory drugs, and monoclonal antibody therapies such as Johnson and Johnson's infliximab and Abbott's adalimumab; and other drugs such as methotrexate and cyclosporine. According to the publication "Medical Advertising News", the estimated worldwide market for anti-TNFα therapies and other biologics for the treatment of rheumatoid arthritis is expected to reach $7 billion by 2011.

TNFα is a critical component of the inflammatory process launched as part of the immune response to a variety of perceived bodily threats such as infection, injury, and other disease. While anti-TNFα therapies are now widely used in the treatment of inflammatory arthritis, there are a number of patients on systemic anti-TNFα therapies who do not fully respond to those therapies and still have one or several joints that cause them pain or impact their daily lives. We are developing a locally delivered AAV-based anti-TNFα product as a potential supplement to systemic protein therapy for use in patients with inflammatory arthritis where one or several joints do not respond to systemic protein therapy. We believe that local administration of a DNA sequence encoding an anti-TNFα protein may be a potentially useful supplement to currently used drugs in a number of inflammatory conditions. The characteristics of AAV vectors make them well suited for delivery of genetic material to joints and

other local environments. In addition, a locally administered anti-TNFα therapy could also be useful in patients with a limited number of joints impacted by RA who may not require systemic therapy.

Our product candidate, tgAAC94, is comprised of an AAV vector that contains a gene that encodes the soluble anti-TNFα protein TNFR:Fc. In preclinical animal models, we have administered AAV-rat TNFR:Fc into rats with experimentally induced RA. Data from these animal studies have shown that a single injection of a vector carrying the soluble TNFR gene into the ankles of arthritic rats resulted in a significant reduction in ankle and hind paw swelling as measured by arthritis index scores. Data also suggest that animals treated in a single joint experienced a reduction in swelling in both the treated joint as well as the contra-lateral joint. Following injection to the joint, we observed beneficial results without accompanying elevated levels of systemic protein expression. These results suggest, at least in animal models, that a systemic benefit may be possible with this treatment approach from a localized injection.

In March 2004, we initiated a Phase I clinical trial in patients with rheumatoid arthritis. This dose-escalation safety trial was initially designed to enroll up to 32 patients with rheumatoid arthritis to be conducted in up to eight sites in the United States and Canada. In December 2004, we amended the clinical trial protocol to reduce the number of patients to be enrolled into the study to up to 24 patients and expanded the patient population to include patients with rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis. This protocol amendment was intended to accelerate patient accrual into the trial and to expand the population of patients that could be studied with this product candidate. Patients will be monitored primarily for safety and we expect to collect data on any improvements in arthritis signs and symptoms. We expect to complete patient accrual and dosing in this trial and present data from the trial in mid-2005.

Hyperlipidemia

We are exploring gene therapies for cardiovascular disease by applying our AAV vector technology to treating hyperlipidemia, the elevation of lipids, or fats, such as cholesterol in the bloodstream. Approximately four million people in the United States have a genetic predisposition to some form of hyperlipidemia, such as familial hypercholesterolemia, familial combined hyperlipidemia and polygenic hypercholesterolemia. Approximately 10% of these patients have severe forms of the disease and do not respond to standard drug therapy, such as statins. If untreated, disease progression can lead to morbidity and death from heart attack or stroke. As part of our acquisition of Genovo, Inc. in 2000, we acquired a product development program aimed at assessing the delivery of genetic material to treat dyslipidemia, a condition of increased levels of LDL-type cholesterol. We have an ongoing collaboration with an academic laboratory to assess the potential clinical utility of AAV vector product candidates for treating hyperlipidemia. We have exclusive rights to certain intellectual property related to the use of AAV-based gene therapy for treating hypercholesterolemia.

Congestive Heart Failure

In December 2004, we entered into a collaboration with Celladon to develop AAV delivered product candidates for congestive heart failure, or CHF, by applying our AAV vector technology to deliver genetic material that can impact the contractility of the heart muscle. It is estimated that approximately five million people in the United States have some form of CHF with approximately 550,000 new cases reported annually. CHF leads to approximately 300,000 deaths annually in the United States. Current therapies for patients with CHF include ACE inhibitors, beta blockers, implanted mechanical assist devices and others. The gene therapy-based approach is directed toward improving or restoring normal cardiac function by delivering genetic material that can impact the pathways that regulate contractility of the heart. We are producing and evaluating gene-based drug candidates with Celladon that utilize our AAV delivery platform to deliver the SERCA2a gene and phospholamban gene variants, both believed to play a central role in the contractility of the heart.

Huntington's Disease

In January 2005, we entered into a collaboration with Sirna Therapeutics, Inc., to develop a gene therapy product candidate for the treatment of Huntington's Disease, or HD. HD is a degenerative

brain disorder for which there is, at present, no effective treatment or cure. According to the National Institute of Neurological Disorders and Stroke, 30,000 people in the United States have HD, and at least another 150,000 are at risk for developing the disease. HD results from degeneration of neurons in certain areas of the brain. This degeneration causes uncontrolled movements, loss of intellectual faculties, and emotional disturbance. HD typically begins in mid-life, between the ages of 30 and 45, though onset may occur as early as the age of 2. Children who develop the juvenile form of the disease rarely live to adulthood. The focus of this collaboration will be the development of an AAV-vector encoding short interfering RNA, or siRNA, to inhibit gene expression of the huntingtin gene. RNAi is a mechanism used by cells to regulate the expression of genes and replication of viruses. The RNA interference mechanism uses siRNA to induce the destruction of target RNA using naturally occurring cellular protein machinery. Through this mechanism, our objective is to interfere with the expression of the huntingtin protein that is believed to be the cause of HD and stop or slow progression of the disease.

Programs Not Under Active Development

In addition to our core product development programs in cystic fibrosis, inflammatory arthritis, AIDS prophylaxis, hyperlipidemia, congestive heart failure and Huntington's disease, we have generated proof of concept data in several other diseases. We believe that several of these programs provide opportunities for establishing development partnerships that may provide us with additional revenue or sources of funding. We are not pursuing the further development of these programs unless and until we can secure other sources of funding for them.

Cancer

Cancer arises from the disruption of normal cell growth and division, which are regulated by cellular proteins and genes. E1A is a gene derived from a common virus called an adenovirus that appears to have several anti-tumor characteristics. We recognized that if E1A could be delivered into cancerous cells, its ability to influence gene expression might be useful in slowing the growth of tumors and sensitizing them to chemotherapeutic drugs or radiation. We have completed a series of clinical studies in which we delivered E1A using a synthetic delivery system called DC-Cholesterol. We have also pursued the development of new formulations of E1A, which we believe have the potential to target cancer cells when administered systemically. One of these formulations in preclinical development, tgLPD-E1A, uses LPD technology and results in the formation of stable DNA particles of a small and defined size encapsulated in a lipid shell. This formulation appears to significantly contribute to the stability of the compound and enables vector particles delivered via intravenous administration to travel throughout the body with greatly reduced rates of degradation, thus improving gene transfer efficiency. We believe that this condensed DNA delivery platform provides the basis for developing a systemic delivery system for administering E1A or other genetic material to tumors.

During 2002, we suspended further clinical development of our cancer program to focus our activities on our AAV-based development programs. We may resume development of our oncology program, but do not plan to do so until we can find other sources of funding for the program.

Hemophilia

Hemophilia is a hereditary disorder caused by the absence or severe deficiency of blood proteins that are essential for proper coagulation. In the case of hemophilia A the missing protein is Factor VIII and in the case of hemophilia B, the missing protein is Factor IX. Hemophilia patients face chronic and spontaneous, uncontrolled bleeding that can lead to restricted mobility, pain and, if left untreated, death. Serious, acute bleeding incidents are generally treated by administering either manufactured or naturally-derived coagulation proteins. Because both manufactured and naturally-derived coagulation proteins are expensive, protein therapy is generally limited to treating acute bleeding episodes in patients with hemophilia. Further, proteins derived from human serum may carry blood-borne pathogens such as HIV, Epstein Barr virus and hepatitis C.

We have generated proof of concept data for Factor VIII gene therapy in mouse models of hemophilia A and for Factor IX gene therapy in mouse and dog models of hemophilia B. In these models, the use of AAV vectors to deliver the Factor VIII or Factor IX gene resulted in decreased bleeding times for extended periods of time. We had been developing our Factor VIII gene therapy with Wyeth Pharmaceuticals, or Wyeth. However, in November 2002, Wyeth notified us of its decision to terminate our development collaboration. We entered into an agreement for the termination of the collaboration in February 2003. We have suspended further development of this program until we obtain other sources of funding.

Programs Developed by a Third Party

Interferon Beta

As part of our collaboration with Biogen, Inc., or Biogen, which concluded in 2003, we provided Biogen with limited manufacturing process development support for its product development program directed at treating glioma using an adenoviral vector to deliver the gene for interferon beta. Interferon beta is a potent stimulator of the immune system, and sustained expression of this protein at the site of brain tumors may help the body rid itself of cancer cells. Prior to the merger of Biogen and IDEC Pharmaceuticals in November 2003, Biogen had licensed its rights to this program to IDEC as part of a co-development agreement covering multiple oncology product development programs. Based on the initial results of clinical trials conducted by Biogen, the further development of this glioma product candidate was discontinued by Biogen to pursue development activities towards targeted indications in malignant pleural effusions and liver metastases of colorectal cancer. We are entitled to receive royalties on future product sales by Biogen of product commercialized based on adenoviral delivery of interferon beta.

Gene Therapy

Overview. Gene therapy is an approach to treating or preventing genetic and acquired diseases that involves introducing genetic material into target cells to modulate disease conditions. To be transferred into cells, a gene is incorporated into a delivery system called a vector, which may be either viral or synthetic. The process of gene transfer can be accomplished *ex vivo,* whereby cells are genetically modified outside of the body and infused into the patient, or *in vivo,* whereby vectors are introduced directly into the patient's body.

Once delivered into the cell, the gene can express or direct production of the specific proteins encoded by the gene. Proteins are fundamental components of all living cells and are essential to controlling cellular structure, growth and function. Cells produce proteins from a set of genetic instructions encoded in DNA, which contain all the information necessary to control cellular biological processes. DNA is organized into segments called genes, with each gene containing the information required to express a protein. When a gene, or genetic material is expressed, the sequence of DNA is transcribed into RNA, which is then translated into a sequence of amino acids that constitutes the resulting protein.

An alteration in the gene, or an absence of specific genes, causes proteins to be over-produced, under-produced, or produced incorrectly, any of which events may cause disease. These diseases include cystic fibrosis, in which a defective protein is produced, inflammatory arthritis, in which an important protein is over-produced, and hemophilia, in which a protein is under-produced. Deficient or absent genes can also cause cells to incorrectly regulate gene expression, which can cause diseases such as certain types of cancer and inflammatory disease. Gene therapy may be used to treat disease by replacing the missing or defective gene to facilitate the normal protein production or gene regulation capabilities of cells. In addition, gene delivery may be used to enable cells to perform additional roles in the body. For example, by delivering DNA sequences that encode proteins that are usually not expressed in the target cell and conferring new function to these cells, gene therapy could enhance the ability of the immune system to fight infectious diseases or cancer. Gene therapy may also be used to inhibit production of undesirable proteins or viruses that cause disease, by suppressing expression of their related genes within cells.

A key factor in the progress of gene therapy has been the development of safer and more efficient methods of transferring genes into cells. A common gene delivery approach uses modified viruses to transfer the desired genetic material into a target cell. The use of viruses takes advantage of their natural ability to introduce genetic material into cells and, once present in the target cell, to use the cell's metabolic machinery to produce the desired protein. In some gene therapy applications, viruses are genetically modified to inhibit the ability of the virus to reproduce itself. Successful viral gene transfer for diseases requiring long-term gene expression involves meeting a number of essential technical requirements, including the ability of the vector to carry the desired genetic material, transfer the genetic material into a sufficient number of target cells and enable the delivered genetic material to persist in the host cell and produce proteins for a long duration. We are using viral vectors such as AAV for potential gene therapy applications requiring long-term gene expression.

AAV Viral Vectors. With our scientific collaborators, we have developed significant expertise in designing and using AAV vectors in gene therapy. We believe that our AAV vectors are particularly well suited for treating a number of diseases for the following reasons:

- AAV does not appear to cause human disease;
- our AAV vectors do not contain viral genes that could produce unwanted cellular immune responses leading to side effects or reduced efficacy;
- AAV vectors can introduce and express genetic material into non-dividing or slowly dividing cells;
- AAV vectors can persist in the host cell, generally without integration into the host cell genome, to provide relatively long-term gene expression; and
- our AAV vectors can be manufactured by methods commonly utilized in the manufacture of other biopharmaceutical products.

We are building our proprietary position in AAV-based technology through our development or acquisition of rights to inventions that:

- provide important enhancements to AAV vectors;
- demonstrate novel approaches to the use of AAV vectors for gene therapy; and
- establish new and improved methods for large-scale production of AAV vectors.

We have conducted preclinical experiments to assess the potential for using AAV vectors to deliver therapeutic genetic material to a variety of target cells, including joints, muscles, the lung, the liver and the cardiovascular system. We are currently developing three product candidates that utilize AAV as the delivery vector: a cystic fibrosis treatment, an AIDS vaccine and an arthritis treatment and have entered into collaborations focused on the development of other product candidates.

Synthetic Vectors. Synthetic vector systems generally consist of DNA incorporating the desired gene, combined with various compounds designed to enable the DNA to be taken up by the host cell. Synthetic *in vivo* gene delivery approaches include:

- injecting pure plasmid, or "naked," DNA in an aqueous solution;
- encapsulating genetic material into lipid carriers such as liposomes, which facilitate the entry of DNA into cells;
- combining negatively charged DNA with positively charged, or cationic, lipids; and
- directing DNA to receptors on target cells by combining the gene with molecules, or ligands, that bind to the receptors.

While we are not currently developing any product candidates using synthetic vectors, we have exclusive rights to a significant body of synthetic gene delivery technology based on cationic lipids. These synthetic vectors, such as DC-Cholesterol, are formulated by mixing negatively charged DNA with positively charged cationic lipids, which promotes uptake of genetic material by cells. These

vectors appear to have a good safety profile for use *in vivo.* We believe that synthetic vectors have several characteristics that make them particularly well-suited for treating certain diseases, including:

- ability to transfer relatively large segments of DNA;
- ability to deliver genetic material in rapidly dividing or non-dividing cells; and
- ability to target to specific cell receptors.

Cell Therapy

In 2000, we established CellExSys, Inc., CellExSys, a majority-owned subsidiary, to further develop our *ex vivo* cell therapy capabilities. We formed CellExSys to pursue opportunities to separately fund and develop our *ex vivo* cell therapy technologies which were no longer within our core focus of gene-based therapies. CellExSys' portfolio of intellectual property included patents and patent applications relating to modification of T-cells with chimeric receptors, the use of T-cells as gene delivery vehicles and other proprietary technologies related to cell therapy.

In July 2004, Chromos Molecular Systems, Inc., Chromos, acquired all of the outstanding shares of CellExSys through a merger between CellExSys and Chromos Inc., a wholly owned subsidiary of Chromos. Under the terms of the merger agreement, Chromos has issued to CellExSys shareholders 1,500,000 shares of Chromos common stock and a secured convertible debenture totaling approximately $3.4 million Canadian (approximately $2.5 million U.S. at the time of closing). The debenture bears annual interest of 2% and is payable in two annual installments on the first and second anniversary of the closing. The debenture is repayable by Chromos at its option in either cash or by the issuance of shares of Chromos common stock, assuming certain limited conditions are met by Chromos. In combination with the shares of Chromos common stock issued at closing, if the debenture is fully paid in shares of Chromos common stock, the shareholders of CellExSys would receive up to a total of 3.5 million shares of Chromos common stock. We owned approximately 79% of CellExSys at the time of the merger.

As a result of the merger, we recorded a gain totaling $1.0 million during 2004 and periodically monitor our investment in Chromos common stock and the debenture for impairment in value. For a limited period of time, we have agreed to provide certain transition services and assistance to CellExSys, which Chromos pays for on a monthly basis.

Research and Development Collaborations

We have entered into various collaborations with pharmaceutical and biotechnology companies, and a non-profit organization to develop several of our product candidates. Our collaborations typically provide us with reimbursement of research and development costs, together with funding through purchases of our equity securities, loans, payments of milestone fees or direct funding of clinical trial costs. If the product candidate covered by the collaboration is successfully commercialized, we are generally entitled to manufacturing and royalty-based revenue. Substantially all of our revenue, and substantially all of our expected revenue for the next several years, is derived from our product development collaborations. We have ongoing collaborations with IAVI, the CF Foundation, Celladon and Sirna.

International AIDS Vaccine Initiative

In 2000, we entered into a three year research collaboration with IAVI and CCRI to develop an AIDS vaccine for use in non-industrialized countries. Effective December 2003, this collaboration was extended through the end of 2006. In January 2005, the principal investigator at CCRI involved in our collaboration assumed a position at The Children's Hospital of Philadelphia and he will continue to participate in the collaboration. Under the terms of this public-private collaboration, IAVI funds work at Targeted Genetics and at CCRI focused on development and preclinical studies of a vaccine candidate. IAVI also coordinates and funds the cost of clinical trials conducted under the collaboration. We have the right to commercialize any vaccine that may result from this development collaboration in industrialized countries, and we have a qualified right, subject to IAVI's determination

that our prices are reasonable, to manufacture the vaccine for non-industrialized nations and sell it to IAVI at full cost of manufacturing plus a reasonable public sector profit.

The vaccines, which will utilize our AAV vectors to deliver selected HIV genes, are designed to elicit a protective immune response against HIV and prevent its progression to AIDS. We anticipate that these vaccines, if successfully developed, would be provided to the developing countries of the world through the public health sector which includes organizations such as the World Health Organization and IAVI. IAVI funds our development activities based upon an agreed upon annual work plan and budget. Under the terms of the agreement any of the parties can terminate this collaboration, without cause, with ninety days advance notice. If IAVI terminates the collaboration for certain reasons, including our failure to continue to develop an AIDS vaccine, IAVI has the right to develop and commercialize AIDS vaccines utilizing intellectual property owned by us for use in manufacturing and commercializing AIDS vaccines in the developing and developed world. IAVI however does not have this termination right if the reason for the termination is due to our failure to continue to develop an AIDS vaccine because IAVI has stopped funding the development program.

During 2005, we plan to coordinate efforts to complete the ongoing Phase I clinical trial of tgAAC09 and pursue the development of additional AIDS vaccine development candidates. We expect that these vaccine candidates will include vaccines which are based on different serotypes, or strains, of AAV which are believed to be more efficient delivery systems for gene-based vaccines to muscle. Additionally, we plan to pursue the development of vaccines that contain genetic material to express multiple proteins from HIV, a multivalent approach, which may have the most potential to inhibit HIV entry or replication and thus protect against AIDS progression. Through December 31, 2004, we have earned $20.3 million in research and development revenue from IAVI under this collaboration. Assuming full implementation of the program work plan, we expect to receive up to $5.6 million of research and development funding from IAVI in 2005.

Under the terms of the collaboration, IAVI has retained rights to ensure that any safe and efficacious AIDS vaccines developed as part of this collaboration will be distributed in developing countries at a reasonable price to be determined by IAVI. If we are not able or decline to produce the vaccine for developing countries in reasonable quantities and at a reasonable price, IAVI has rights that will allow IAVI to contract with other manufacturers to make the vaccines available at a reasonable price in those countries.

Cystic Fibrosis Foundation

In April 2003, we established a collaboration with the CF Foundation related to our current Phase II clinical trial for our product candidate for treating cystic fibrosis. The CF Foundation has agreed to provide funding of approximately $1.7 million directly to the sites conducting the study to cover their direct trial costs. In return for funding of the external trial costs by the CF Foundation, we have agreed to provide the CF Foundation with a multiple of their funding contribution from future sales of this product candidate, if the product candidate is commercialized. This agreement is limited to the current Phase II clinical trial.

Celladon Corporation

In December 2004, we established a collaboration with Celladon to develop AAV based approaches to treating congestive heart failure, or CHF. Under the collaboration, Celladon is providing its proprietary intellectual property including the SERCA2a gene or phospholamban variant genes that are believed to be capable of mediating the contractility of the heart muscle. We are contributing our propriety AAV technology for use in the field of CHF to deliver these and other genes of interest to the heart. In connection with the formation of this collaboration, we received $6 million cash from the sale of our common stock to investors of Celladon. The proceeds were recorded in equity at the fair value of the common stock which approximated market value. In connection with our collaboration agreement with Celladon, we have agreed to contribute up to $2 million to support development activities under the collaboration. Our contribution will consist primarily of internal development and manufacturing efforts at rates agreed to by the parties. Under this collaboration, we are entitled to

receive payments for our research and development efforts above $2 million, development milestones, royalties on sales and manufacturing profits on potential future products that result from the collaboration.

Sirna Therapeutics, Inc.

In January 2005, we established a collaboration with Sirna to develop AAV based approaches to treating Huntington's Disease. Under the collaboration, Sirna is providing its proprietary intellectual property surrounding siRNA thought to be capable of silencing the expression of the huntingtin protein, which is thought to cause this neurodegenerative disease. We are applying our proprietary AAV technology for use in this field to deliver siRNA's to the brain. We, and Sirna, have agreed to co-develop product candidates under the collaboration and to share the costs of development. We expect that a substantial portion of our development costs will consist primarily of internal development and manufacturing efforts. Similarly, we have agreed to share any potential future revenues that result from the collaboration with Sirna.

Former Collaborations

Biogen, Inc.

In connection with our acquisition of Genovo in 2000, we established a three-year, multiple-product development and commercialization collaboration with Biogen. This collaboration ended in September 2003 upon the completion of the development period.

Under this collaboration, Biogen paid us $8 million in research funding and upfront payments and $1 million per year in research and development funding over the initial three-year development period. Biogen also agreed to provide us with loans of up to $10 million and to purchase up to $10 million of our common stock under an equity purchase commitment, each at our discretion. During 2001, we borrowed $10 million from Biogen under the loan commitment. The loan is due in August 2006 and bears interest at the one-year LIBOR rate plus 1%, reset quarterly. In 2002, we raised $4.0 million through the sale of 5,804,673 shares of our common stock to Biogen at a price of $0.69 per share and in August 2003, we raised $4.8 million through the sale of 2,515,843 shares of our common stock to Biogen at a price of $1.91 per share. The equity purchase commitment with Biogen has expired.

Upon the completion of this development collaboration in September 2003, we recognized $2.6 million in revenue which represented the remainder of previously deferred payments received from Biogen. Through December 31, 2003, we earned $11.0 million in revenue from Biogen under this collaboration and have received $18.8 million in proceeds from the issuance of debt and equity securities.

Wyeth

In 2000, we entered into a collaboration with Wyeth to develop AAV vector-based gene therapy products for treating hemophilia A and, potentially, hemophilia B. In November 2002, Wyeth elected to terminate this hemophilia collaboration and related agreements. Under the terms of our agreements with Wyeth, all rights that we granted or otherwise extended to Wyeth related to the hemophilia technology have returned to us. In connection with the termination of our collaboration with Wyeth, we entered into a settlement agreement with Wyeth in 2003, and received $3.2 million in settlement of outstanding expenses that we incurred under the collaboration and as an early termination payment.

Through December 31, 2003, we earned $18.4 million in upfront fees, research and development revenue and termination fees from Wyeth under this collaboration.

Emerald Gene Systems, Ltd.

In 1999, we formed Emerald Gene Systems, Ltd., or Emerald, our joint venture with Elan International Services, Ltd., a wholly-owned subsidiary of Elan Corporation plc, or Elan. We and Elan formed Emerald to develop enhanced gene delivery systems. The initial three-year development period

for Emerald ended during 2002. Since 2002, Emerald has had no operating activities and was dissolved. We and Elan funded the expenses of Emerald in proportion to our respective ownership interests. Through the completion of Emerald's operating activities, we had provided $7.5 million of cash funding to the Emerald joint venture. Emerald reimbursed each company for the costs of research and development and related expenses, plus a profit percentage.

On March 31, 2004, we entered into a termination agreement with Elan. The termination agreement provided for, among other things, our acquisition of Elan's equity interest in Emerald, the termination of technology license agreements between Emerald and both Targeted Genetics and Elan in accordance with the original terms of those license agreements, the full conversion of the Series B preferred stock held by Elan into shares of our common stock, and certain restrictions under which Elan could sell its holdings in our common stock. Elan also waived its right to nominate a director to our board of directors. In accordance with the termination agreement, the Series B preferred stock was converted into 4.33 million shares of our common stock. Following conversion of the Series B preferred stock, Elan held approximately 12.1 million shares of our common stock. Under the termination agreement Elan is permitted to trade these shares of our common stock in quantities equal to 175% of the volume limitation set forth in Rule 144(e)(1) promulgated under the Securities Act of 1933, as amended, subject to certain exceptions.

Prior to the termination agreement with Elan, we owned 80.1% of Emerald's common stock and 80.1% of Emerald's preferred stock and Elan owned the remaining 19.9% of Emerald's common and preferred stock. The common stock of Emerald held by Elan was similar in all respects to the common stock held by us, except that the common shares held by Elan did not have voting rights, but have been converted into voting common shares at Elan's election. Although we held 100% of the voting stock, Elan and its subsidiaries had retained significant minority investor rights that are considered participating rights under the Financial Accounting Standards Board, or FASB, Emerging Issues Task Force, or EITF, Bulletin 96-16, *Investors' Accounting for an Investee When the Investor Has a Majority of the Voting Interest but the Minority Shareholder Has Certain Approval or Veto Rights.* Because Elan's participating rights prevented us from exercising control over Emerald, we did not consolidate the financial statements of Emerald until we became the 100% owner, but instead accounted for our investment in Emerald under the equity method of accounting.

As part of our agreements related to Emerald, Elan provided us funding as follows:

- Elan purchased $5 million of our common stock in 1999 upon execution of the joint venture agreements and purchased an additional $5 million of our common stock in 2000;
- During 2001 and 2002, we drew an aggregate amount of $7.9 million under a $12 million convertible note commitment by Elan to fund a portion of our investment in Emerald, which convertible note commitment has now expired. In 2003, we elected to convert the entire outstanding principal and interest under this note commitment, which totaled $9.4 million, into 5,203,244 shares of our common stock in accordance with the original terms of the note; and
- In 1999, upon execution of the joint venture agreements, Elan received shares of our Series B convertible preferred stock valued at $12 million in exchange for our 80.1% interest in Emerald.

We also had collaborations with Celltech Group plc and with Genzyme that both ended in 2002. Research and development expenses for our internally-funded research and development activities were $10.2 million in 2004, $10.1 million in 2003 and $14.7 million in 2002. Research and development expenses for our externally-funded research and development activities were $7.1 million in 2004, $7.1 million in 2003 and $14.7 million in 2002.

Licensing Arrangements

Alkermes, Inc.

In 1999, we entered into a license agreement with Alkermes, Inc., or Alkermes, in which we received exclusive rights to an issued patent and other pending patent applications related to AAV

vector manufacturing. The license broadly covers a manufacturing method that we believe is critical to making AAV-based products in a commercially viable, cost-effective manner. The license to this technology, developed by Children's Hospital in Columbus, Ohio, covers the use of cell lines for manufacturing AAV vectors in multiple disease areas. Under the terms of the license agreement, we issued to Alkermes 500,000 shares of our common stock and warrants to purchase 2,000,000 shares of our common stock, which warrants expire in June 2007 and June 2009. Alkermes will also receive milestone payments and royalties on the sale of any products manufactured using the licensed technology and is entitled to a portion of any sub-licensing payments that we may receive.

Relationship with Amgen, Inc.

Targeted Genetics was formed in 1989 as a subsidiary of Immunex Corporation, a biopharmaceutical company developing recombinant proteins as therapeutics. In connection with our formation and the entering into of Gene Transfer Technology License Agreement, we issued Immunex shares of our preferred stock that were subsequently converted into 1,920,000 shares of our common stock. In exchange, we received rights from Immunex under a Gene Transfer Technology License Agreement, including an exclusive worldwide license to certain Immunex proprietary technology specifically applicable to gene therapy applications. The licensed technology relates to gene identification and cloning, panels of retroviral vectors, packaging cell technology, recombinant cytokines, DNA constructs, cell lines, promoter/enhancer elements and immunological assays. In July 2002, Immunex was acquired by Amgen, Inc. Our license to the Immunex technology was not affected by the acquisition and we retain all rights granted under the original license.

Prior to Amgen's acquisition of Immunex, we exchanged sporadic correspondence and engaged in discussions with Immunex regarding the terms, scope and possible amendment of the Gene Transfer Technology License Agreement. Some of these communications have included, among other things, differing views about our rights to the gene construct coding for TNFR:Fc used in the development of our inflammatory arthritis product candidate tgAAC94. These communications did not lead to either a final resolution or an active dispute regarding our differences with Immunex. Following Amgen's acquisition of Immunex, we communicated to Amgen our desire to resume discussions seeking clarification of our relationship with Amgen. Our subsequent communications with Amgen have not yet resulted in a resolution of our differences. In February 2004, in response to our January 2004 announcement that we had received regulatory approval for a Phase I clinical study for tgAAC94, Amgen sent a letter to us taking the position that we were not licensed, either exclusively or non-exclusively, under Immunex intellectual property covering TNFR:Fc or therapeutic uses for TNFR:Fc. We have responded with a letter confirming our confidence that the Gene Transfer Technology License Agreement gives us an exclusive worldwide license to use the gene construct coding for TNFR:Fc for gene therapy applications. We have had, and expect to have further, communications with Amgen regarding our differences. Notwithstanding our confidence, it is possible that a resolution of those differences, through litigation or otherwise, could cause delay or discontinuation of our development of tgAAC94 or our inability to commercialize any resulting product.

Patents and Proprietary Rights

Patents and licenses are important to our business. Our strategy is to file or license patent applications to protect technology, inventions and improvements to inventions that we consider important to developing our business. To date, we have filed or exclusively licensed over 400 patent or patent applications with the USPTO, including foreign counterparts of some of these applications in Europe, Japan and other countries. Of these patent applications, over 100 patents have been issued or allowed. This proprietary intellectual property includes genes, formulations, methods of transferring genetic material into cells, processes to manufacture and purify gene delivery product candidates and other proprietary technologies and processes. We also rely on unpatented proprietary technology such as trade secrets, know-how and continuing technological innovations to develop and maintain our competitive position.

The patent positions of pharmaceutical and biotechnology firms, including our patent positions, are uncertain and involve complex legal and factual questions for which important legal principles are

largely unresolved, particularly with regard to human therapeutic uses. Patent applications may not result in the issuance of patents, and the coverage claimed in a patent application may be significantly reduced before a patent is issued. If any patents are issued, the patents may be subjected to further proceedings limiting their scope, may not provide significant proprietary protection and may be circumvented or invalidated. Patent applications in the United States and other countries generally are not published until more than 18 months after they are filed, and because publication of discoveries in scientific or patent literature often lags behind actual discoveries, we cannot be sure that we were, or our licensor was, the first creator of inventions covered by pending patent applications or the first to file patent applications for these inventions.

We have licensed technology underlying several issued and pending patents. Among these are two key patents that relate to the use of AAV vectors for gene delivery, one of which we have exclusively licensed from the National Institutes of Health, or NIH, and the second from the University of Florida Research Foundation. In addition, we have acquired nonexclusive rights to the CFTR gene being delivered in our tgAAVCF product candidate for cystic fibrosis, which uses our proprietary AAV delivery technology to deliver a copy of the CFTR gene. Licensing of intellectual property critical to our business involves complex legal, business and scientific issues. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop or commercialize the affected product candidates. For example, in July 1997 the licensor of our licensed CFTR gene and related vector was notified that the USPTO had declared an interference proceeding to determine whether our licensor or an opposing party has the right to the patent application on the CFTR gene and related vector. Although we are not a party to the interference proceeding, its outcome could affect our license to the CFTR gene and related vector. If the USPTO or the U.S. Circuit Court of Appeals ultimately determines that our licensor does not have rights to both the CFTR gene and the vector, we believe that we will be subject to one of several outcomes:

- our licensor could agree to a settlement arrangement under which we continue to have rights to the gene and the vector at our current license royalties;
- the prevailing party could require us to pay increased license royalties to maintain our access to the gene, the vector or both, as applicable, which licensing royalties could be substantial; or
- we could lose our license to the gene, the vector or both.

If our licensor does not retain its right to the CFTR gene and the vector, and we cannot obtain access at a reasonable cost or develop or license a replacement gene and vector at a reasonable cost, we will be unable to commercialize our potential tgAAVCF product candidate. For a more detailed description of this risk, see the section entitled "Factors Affecting Our Operating Results, Our Business and Our Stock Price-Litigation involving intellectual property, product liability or other claims and product recalls could strain our resources, subject us to significant liability, damage our reputation or result in the invalidation of our proprietary rights" in Part II, Item 7 of this annual report.

In addition to patent protection, we rely on trade secret protection for our confidential and proprietary information and technology. To protect our trade secrets, we generally require our employees, consultants, scientific advisors and parties to collaborative agreements to execute confidentiality agreements. In the case of employees and consultants, the agreements also provide that all inventions resulting from work performed by them while employed by us will be our exclusive property. Despite these agreements, and other precautions we take to protect our trade secrets and other proprietary unpatented intellectual property, we may be unable to meaningfully protect our trade secrets and other intellectual property from unauthorized use or misappropriation by a third party. These agreements may not provide adequate remedies in the event of unauthorized use or disclosure of our confidential information. In addition, our competitors could obtain rights to our nonexclusively licensed proprietary technology or may independently develop substantially equivalent proprietary information and technology. If our competitors develop and market competing products using our unpatented or nonexclusively licensed intellectual property or substantially similar technology or processes, our products could suffer a reduction in sales or be forced out of the market.

A number of pharmaceutical and biotechnology companies and research and academic institutions have developed technologies, filed patent applications or received patents for technologies that may be related to our business. Some of these technologies, applications or patents may conflict with our technologies or patent applications. This conflict could limit the scope of any patents that we may obtain for our technologies or result in denial of our patent applications. In addition, if patents or patent applications that cover our activities are or have been issued to other companies, we may be required to either obtain a license from the owner or develop or obtain alternative technology. A license may not be available on acceptable terms, if at all, and we may be unable to develop or obtain alternative technology.

As the biotechnology industry expands and more patents are issued, the risk increases that our processes and potential products may give rise to claims that they infringe on the patents of others. These other parties could bring legal actions against us claiming damages and seeking to stop clinical testing, manufacturing and marketing of the affected product or use of the affected process. If we are found by a court to have infringed on the proprietary rights of others, we could also face potential liability for significant damages and be required to obtain a license to the proprietary technology at issue if we continue to commercialize. A required license may not be available on acceptable terms, if at all, which could impair our ability to commercialize our product candidates. Similarly, administrative proceedings, litigation or both may be necessary to enforce patents issued to us, to protect trade secrets or know-how owned by us or to determine the enforceability, scope and validity of the proprietary rights of others. This type of litigation, regardless of its merit, could result in substantial expense to us and significantly divert the efforts of our technical and management personnel. An adverse outcome could adversely affect our business.

Competition

A number of companies and institutions are developing or considering the development of gene therapy treatments, including other gene delivery companies, biotechnology companies, pharmaceutical companies, universities, research institutions, governmental agencies and other healthcare providers. In addition to competition from these sources, our potential products will compete with more traditional therapies for the diseases on which we focus, including pharmaceutical products, medical devices and surgery. If our product candidates become commercial gene therapy products, they may compete with other analogous protein or pharmaceutical therapies. As a result, disputes including lawsuits, demands, threats or patent challenges may arise in an effort to slow our development. We also compete with others to acquire products or technology from research institutions or universities.

Many of our competitors have substantially more financial and other resources, larger research and development staffs and more experience and capabilities in researching, developing and testing products in clinical trials, obtaining FDA and other regulatory approvals and manufacturing, marketing and distributing products. In addition, the competitive positions of other companies may be strengthened through collaborative relationships, such as those with large pharmaceutical companies or academic institutions. As a result, our competitors may develop, obtain patent protection for, receive FDA and other regulatory approvals for or commercialize products more rapidly than we do or may manufacture and market their products more successfully than we do. Our competitors' technologies and products may be more effective or economically feasible than our potential products. If we are successful in commercializing our products, we will be required to compete with respect to manufacturing efficiency and marketing capabilities, areas in which we have no experience. These developments could limit the prices we are able to charge for any products we are able to commercialize or render our products less competitive or obsolete.

Governmental Regulation

All of our potential products must receive regulatory approval before they can be marketed. Human therapeutic products are subject to rigorous preclinical and clinical testing and other pre-market approval procedures administered by the FDA and similar authorities in foreign countries. In accordance with the federal Food, Drug and Cosmetics Act, the FDA exercises regulatory authority over

the development, testing, formulation, manufacture, labeling, storage, record keeping, reporting, quality control, advertising, promotion, export and sale of our potential products. Similar requirements are imposed by foreign regulatory agencies. In some cases, state regulation may also apply.

Gene therapy is a relatively new technology that has not been extensively tested or shown to be effective in humans. The FDA reviews all product candidates for safety at each stage of clinical testing. Safety standards must be met before the FDA permits clinical testing to proceed to the next stage. Also, efficacy must be demonstrated before the FDA grants product approval. Obtaining approval from the FDA and other regulatory authorities for a new therapeutic product candidate, if approval is ever obtained, is likely to take several years. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or prevent the marketing of our product candidates. In addition, the regulatory requirements governing gene therapy product candidates and commercialized products are subject to change. The approval process, and ongoing compliance with applicable regulations after approval, involves substantial expenditures of financial and other resources.

Preclinical studies generally require studies in the laboratory or in animals to assess the potential product's safety and effectiveness. Preclinical studies include laboratory evaluation of toxicity, pharmacokinetics, or how the body processes and reacts to the drug, and pharmacodynamics, or whether the drug is actually having the expected effect on the body. Preclinical studies must be conducted in accordance with the FDA's Good Laboratory Practice regulations and, before any proposed clinical testing in humans can begin, the FDA must review the results of these preclinical studies as part of an Investigational New Drug application.

If preclinical studies of a product candidate, including animal studies, demonstrate safety, and laboratory test results are acceptable, then the potential product will undergo clinical trials to test the therapeutic agent in humans. Human clinical trials are subject to numerous governmental regulations that provide detailed procedural and administrative requirements designed to protect the trial participants. Each institution that conducts human clinical trials has an Institutional Review Board or Ethics Committee charged with evaluating each trial and any trial amendments to ensure that the trial is ethical, patients are protected and the trial meets the institutional requirements. These evaluations include reviews of how the institution will communicate the risks inherent in the clinical trial to potential participants, so that the patients may give their informed consent. Clinical trials must be conducted in accordance with the FDA's Good Clinical Practices regulations and the protocols the company establishes to govern the trial objectives, the parameters to be used for monitoring safety, the criteria for evaluating the efficacy of the potential product and the rights of each trial participant with respect to safety. FDA regulations require us to submit these protocols as part of the application. A FDA review or approval of the protocols, however, does not necessarily mean that the trial will successfully demonstrate safety and/or efficacy of the potential product.

Institutions that receive NIH funding for gene therapy clinical trials must also comply with the NIH Recombinant DNA Guidelines, and the clinical trials are subject to a review by the NIH's Office of Biotechnology Activities Recombinant DNA Advisory Committee, or RAC. The outcome of this review can be either an approval to initiate the trial without a public review or a requirement that the proposed trial be reviewed at a quarterly committee meeting. A clinical trial will be publicly reviewed when at least three of the committee members or the Director of the Office of Biotechnology Activities recommends a public review. Should the RAC require a public hearing, the start of the trial must be delayed until after the hearing date. Although the NIH guidelines do not have regulatory status, the RAC review process can impede the initiation of the trial, even if the FDA has reviewed the trial and approved its initiation. Additionally, before any clinical trial can be initiated at an NIH-funded site, the Institutional Biosafety Committee of that site must perform a review of the proposed clinical trial and ensure there are no safety issues associated with the trial.

Clinical trials are typically conducted in three phases often involving multiple clinical trials in each phase. In Phase I, clinical trials generally involve a small number of patients, who may or may not be afflicted with the target disease, to determine the preliminary safety profile. In Phase II, clinical trials are conducted with larger groups of patients afflicted with the target disease in order to establish

preliminary effectiveness and optimal dosages and to obtain additional evidence of safety. In Phase III, large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with the target disease in order to provide enough data for the statistical proof of efficacy and safety required by the FDA and other regulatory agencies for market approval. We report our progress in each phase of clinical testing to the FDA, which may require modification, suspension or termination of the clinical trial if it deems patient risk too high. The length of the clinical trial period, the number of trials conducted and the number of enrolled patients per trial vary, depending on our results and FDA requirements for the particular clinical trial. Although we and other companies in our industry have made progress in the field of gene therapy, we cannot predict what the FDA will require in any of these areas to establish to its satisfaction the safety and effectiveness of the product candidate.

If we successfully complete clinical trials for a product candidate, we must obtain FDA approval or similar approval required by foreign regulatory agencies, as well as the approval of several other governmental and nongovernmental agencies, before we can market the product in the United States or in foreign countries. Current FDA regulations relating to biologic therapeutics require us to submit an acceptable Biologics License Application, or BLA, to the FDA and receive approval before the FDA will permit commercial marketing. The BLA includes a description of our product development activities, the results of preclinical studies and clinical trials and detailed manufacturing information. Unless the FDA gives expedited review status, this stage of the review process generally takes at least one year. Should the FDA have concerns with respect to the potential product's safety and efficacy, it may request additional data, which could delay product review or approval. The FDA may ultimately decide that the BLA does not satisfy its criteria for approval and might require us to do any or all of the following:

- modify the scope of our desired product claims;
- add warnings or other safety-related information; and/or
- perform additional testing.

Because the FDA has not yet approved any gene therapy products, it is not clear what, if any, unforeseen issues may arise during the approval process. While we expect this regulatory structure to continue, we also expect the FDA's regulatory approach to product approval, and its requirements with respect to product testing, to become more predictable as its scientific knowledge and experience in the field of gene therapy increase. Adverse events in the field of gene therapy or other biotechnology-related fields, however, could result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approval of gene therapy products.

Once approved by the FDA, marketed products are subject to continual FDA review. Later discovery of previously unknown problems or failure to comply with applicable regulatory requirements may result in restrictions on marketing a product or in its withdrawal from the market, as well as potential criminal penalties or sanctions. In addition, the FDA requires that manufacturers of a product comply with current Good Manufacturing Practices requirements, both as a condition to product approval and on a continuing basis. In complying with these requirements, we expend significant amounts of time, money and effort in production, record keeping and quality control. Our manufacturing facilities are subject to periodic inspections by the FDA. If major problems are identified during these inspections that could impact patient safety, the FDA could subject us to possible action, such as the suspension of product manufacturing, product seizure, withdrawal of approval or other regulatory sanctions. The FDA could also require us to recall a product.

We are also subject to regulation under the Occupational Safety and Health Act, the Environmental Protection Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and other federal, state and local regulations. For example, our controlled use of hazardous materials in our research and development activities must comply with standards prescribed by state and federal law.

Employees

As of December 31, 2004, we had approximately 90 full-time-equivalent employees, which includes approximately 65 that are involved in our research and development activities, including manufacturing, quality assurance, quality control, process development, regulatory affairs and clinical affairs. Eleven of these employees have Ph.D. or M.D. degrees and a significant number of our management and professional employees have prior experience with other biotechnology or pharmaceutical companies. We also rely on a number of temporary staff positions and third party consultants. None of our employees are covered by a collective bargaining agreement.

Available Information

We were incorporated in the state of Washington in 1989. Our executive offices are located at 1100 Olive Way, Suite 100, Seattle, Washington 98101, and our telephone number is (206) 623-7612. We file annual, quarterly and current reports, proxy statements and other information with the SEC. We make available in the investor relations portion of our website, free of charge, copies of our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to these reports after filing these reports to the SEC. Our website is located at www.targetedgenetics.com. You may also inspect and copy the documents that we have filed with the SEC, at prescribed rates, at the SEC's Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. You may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains a Web site that contains reports, proxy and information statements and other information regarding issuers that file with the SEC at http://www.sec.gov.

Item 2. ***Properties.***

We have leased approximately 51,000 square feet of laboratory, manufacturing and office space in two buildings in Seattle, Washington. The lease on our primary laboratory, manufacturing and office space expires in April 2009 and has one option to renew for a five-year period. The lease on our administrative office space expires in March 2009 and includes two options to extend the lease for a total of five additional years. We have an option to cancel the lease on our administrative offices at any time between April 2006 and March 2009 with certain early termination penalties. We believe that our Seattle facilities are sufficient to support our research, manufacturing and administrative needs under our current operating plan.

In July 2000, we leased approximately 76,000 square feet of space in Bothell, Washington, intended for future large-scale manufacturing of our products. The lease on this facility expires in September 2015 and includes an option for us to extend its term for one additional five-year period. While preliminary design activities have been completed, we have never occupied this facility and do not currently plan to commence the construction of this facility unless and until product demands warrant resumption of construction activities. As a result, we are trying to sublease all or part of the facility, but may need to use a significant portion of the facility in the event that a decision is made to use this facility for our manufacturing needs. Any decision to resume use of the facility will be based on a number of factors, including the progress of our product candidates in clinical development, the estimated duration of facility design and construction, the estimated timing of product manufacturing requirements, the ability of our current manufacturing capabilities to meet demand, and the availability of resources.

We also leased a 30,000 square foot laboratory and office facility in Sharon Hill, Pennsylvania which we assumed following our acquisition of Genovo, Inc. in 2000. In November 2004, we entered into a termination agreement with respect to this lease and as a result have no further obligations under the lease.

Item 3. ***Legal Proceedings.***

We are not a party to any material legal proceedings.

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

No matters were submitted to a vote of our security holders during the fourth quarter of 2004.

PART II

Item 5. ***Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities.***

Market Information. Our common stock trades on the NASDAQ SmallCap Market under the symbol TGEN. From May 20, 1994 until January 8, 2003, our common stock was traded on the NASDAQ National Market, under the symbol TGEN.

The following table lists, for each calendar quarter indicated, the high and low bid quotations for our common stock, as quoted on the NASDAQ SmallCap Market or National Market as applicable. These quotes reflect inter-dealer prices, without retail mark-up or commission, and may not necessarily represent actual transactions.

	High	Low
2004:		
4th Quarter	$1.98	$1.13
3rd Quarter	1.62	0.94
2nd Quarter	2.22	1.24
1st Quarter	3.29	1.80
2003:		
4th Quarter	$3.00	$1.98
3rd Quarter	3.20	1.59
2nd Quarter	4.43	0.41
1st Quarter	0.70	0.25

The last reported bid quotation for our common stock, as quoted on the NASDAQ SmallCap Market on March 1, 2005 was $1.32 per share.

Holders. As of March 1, 2005, we had 371 shareholders of record and approximately 24,000 beneficial holders of our common stock.

Dividends. We have never paid cash dividends and do not anticipate paying them in the foreseeable future. In addition, our loan agreement with Biogen restricts the amount of cash dividends we could pay.

Item 6. *Selected Financial Data.*

	Year Ended December 31,				
	2004(4)(5)	2003(4)	2002(3)(4)	2001	2000(1)(2)
Statement of Operations Data					
Revenue	$ 9,652,000	$ 14,073,000	$ 19,333,000	$ 18,880,000	$ 11,403,000
Operating expenses	24,822,000	27,877,000	42,074,000	47,484,000	57,208,000
Loss from operations	(15,170,000)	(13,804,000)	(22,741,000)	(28,604,000)	(45,805,000)
Loss before cumulative effect of change in accounting principle	(14,257,000)	(14,833,000)	(23,767,000)	(27,170,000)	(43,973,000)
Cumulative effect of change in accounting principle	—	—	—	—	(3,682,000)
Net loss	$(14,257,000)	$(14,833,000)	$(23,767,000)	$(27,170,000)	$(47,655,000)
Basic and diluted net loss per share:					
Loss before cumulative effect of change in accounting principle	$ (0.18)	$ (0.26)	$ (0.52)	$ (0.62)	$ (1.16)
Cumulative effect of change in accounting principle	—	—	—	—	(0.10)
Net loss per basic and diluted common share	$ (0.18)	$ (0.26)	$ (0.52)	$ (0.62)	$ (1.26)
Shares used in computing basic and diluted net loss per common share	79,451,000	57,486,000	45,767,000	43,928,000	37,752,000

	December 31,				
	2004	2003	2002	2001	2000
Balance Sheet Data					
Cash and cash equivalents	$ 34,096,000	$ 21,057,000	$ 12,606,000	$ 25,186,000	$ 38,630,000
Total assets	69,965,000	57,672,000	52,713,000	71,038,000	87,974,000
Long-term obligations	10,182,000	11,227,000	20,494,000	16,403,000	2,447,000
Preferred stock(6)	—	12,015,000	12,015,000	12,015,000	12,015,000
Total shareholders' equity	49,762,000	33,479,000	5,896,000	25,386,000	51,417,000

(1) Effective January 1, 2000, we changed our method of accounting for nonrefundable up-front license fees.

(2) In 2000, operating expenses include a charge for acquired in-process research and development of $28.0 million recorded in connection with our acquisition of Genovo.

(3) Effective January 1, 2002, we changed our method of accounting for goodwill and other intangible assets. See Note 1 of the Notes to our Consolidated Financial Statements.

(4) Operating expenses include restructure charges of $2.3 million in 2002, $5.2 million in 2003 and $884,000 in 2004. See Note 3 of the Notes to our Consolidated Financial Statements.

(5) Reflects a $1.0 million gain on the sale of a majority-owned subsidiary. See Note 5 of the Notes to our Consolidated Financial Statements.

(6) As a result of the expiration of an exchange right of the holder in April 2003, we reclassified the Series B preferred stock from mezzanine equity to shareholders' equity. The Series B preferred stock was converted by the holder into common stock in March 2004.

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

Overview

We develop gene therapy products and technologies to treat both acquired and inherited diseases on our own and through various research and development collaborations with others. We have financed our product development activities and general corporate functions primarily through proceeds from public and private sales of our equity securities, through cash payments received from our collaborative partners and proceeds from the issuance of debt. To a lesser degree, we have also financed our operations through interest earned on cash and short-term investments, loan funding under equipment leasing agreements and research grants. These financing sources have historically allowed us to maintain adequate levels of cash and investments. A significant portion of our operating expenses has been funded through collaborations with third parties which are summarized below.

Ongoing collaborations:

- a collaboration with IAVI to develop an AIDS vaccine, which will conclude in December 2006, unless extended;
- a development collaboration with the CF Foundation established in April 2003 that provides funding to support our current Phase II clinical trial for our product candidate for treating cystic fibrosis. Under this collaboration, the CF Foundation is providing funding directly to the sites conducting this study to cover their direct costs of the trial;
- a development collaboration with Celladon established in December 2004 focused on the development of AAV-based drugs for the treatment of congestive heart failure. In connection with the formation of this collaboration, certain of Celladon's investors purchased $6 millions worth of our common stock. We have agreed to use $2 million of the proceeds from this stock issuance to support development activities under the Celladon collaboration; and
- a development collaboration with Sirna established in January 2005 focused on the development of AAV-delivered RNAi for the treatment of Huntington's Disease. We have agreed to share the costs of development and any revenues that may be generated under the collaboration with Sirna.

Collaborations that ended in 2003 and 2002:

- a multiple-product collaboration with Biogen which concluded in September 2003;
- a collaboration with Wyeth to develop treatments for hemophilia, which was terminated in February 2003;
- a collaboration with Celltech to develop our product candidate for the treatment of cystic fibrosis, which was terminated in November 2002;
- a research and development joint venture with Elan, called Emerald, to develop enhanced gene delivery technologies, which concluded in August 2002; and
- a collaboration with Genzyme to develop treatments for lysosomal storage diseases, which concluded in August 2002.

Our development collaborations have typically provided us with funding, including purchases of our equity securities, loans, payments for reimbursement of research and development costs and milestone fees and payments. We and our partners typically agree on a target disease and create a development plan for the product candidate, which often extends for multiple years and subject to termination or extension. The product candidate's progress is periodically reviewed with the partner. We generally maintain manufacturing and royalty-based interests in successfully developed product candidates.

Our most advanced product candidate is tgAAVCF for treating cystic fibrosis. tgAAVCF is being evaluated in a second Phase II clinical trial that was initiated in July 2003. We designed this trial to enroll up to 100 patients and are conducting it in collaboration with the CF Foundation. We expect to

present data from the trial in mid to late March of 2005. Review of the primary endpoint, safety and secondary endpoints in the trial will be become the basis for determining how, or if, to continue development of tgAAVCF.

We have two product candidates in Phase I clinical trials. The first is tgAAC09 which is an AAV-based prophylactic vaccine intended for use in high-risk populations in developing nations to protect against the progression of HIV infection to AIDS. This product candidate is being developed in a collaboration with the International AIDS Vaccine Initiative, or IAVI, a non-profit organization, and The Columbus Children's Research Institute at Children's Hospital in Columbus, Ohio, or CCRI. In December 2003, IAVI initiated a Phase I dose-escalation safety trial of tgAAC09 in Europe. This trial was designed to enroll up to 50 healthy volunteers who are uninfected with HIV. Preliminary results from this study were announced in February 2005 and suggest that tgAAC09 was safe and well-tolerated in this trial. Results also showed that at the doses evaluated in this initial trial, a single administration of tgAAC09 did not elicit a significant immune response. These results support further development of tgAAC09, including clinical evaluation at higher dose levels. The current Phase I clinical trial of tgAAC09 is the initial step in a comprehensive development strategy of this vaccine program. IAVI recently expanded the single-dose Phase I trial to include sites in India. While these clinical trials are underway, we continue to pursue the development of additional vaccine candidates, including vaccines based on different serotypes, or strains, of AAV believed to be more efficient delivery systems for gene-based vaccines to muscle. We also plan to pursue multivalent vaccines that contain genetic material for multiple proteins from HIV, which may have the most potential to inhibit HIV entry or replication and thus protect against AIDS progression.

Our second product candidate in a Phase I clinical trial is an AAV-based product candidate for the treatment of inflammatory arthritis. In March 2004, we initiated a Phase I human clinical trial in patients with rheumatoid arthritis. Patients will be monitored primarily for safety and we expect to collect data on any improvements in arthritis signs and symptoms. We expect to complete patient accrual and dosing in this trial and to be able to present data from the trial in mid-2005.

We have established broad delivery capabilities and a development infrastructure that can be leveraged into several potential new areas in addition to our three programs in clinical development. We believe that this may enable us to establish new strategic or collaborative relationships with others, such as the collaboration that was initiated in December 2004 with Celladon Corporation, Celladon, to pursue the development of AAV delivered products for the treatment of congestive heart failure and with Sirna Therapeutics, Inc. in January 2005 to pursue the development of AAV delivered products for Huntington's disease. We have developed processes to manufacture our potential products using methods and at a scale amenable to clinical development and expandable to large-scale production for advancing our potential products to commercialization. These methods are similar to the methods used to manufacture other biologics. As a result, we can pursue opportunities to utilize excess capacity, when such capacity exits, to manufacture biologics for other companies. For example, in March 2003, we entered into a manufacturing services agreement with GenVec, Inc., or GenVec, to manufacture clinical supply of GenVec's cancer product candidate, an adenoviral-based gene therapy product. This project was completed in 2004.

Although we believe that our technology appears promising, we do not know whether any commercially viable products will result from our research and development efforts or those of our collaborators. We anticipate that we will not generate revenue from the sale of commercial products for at least the next several years. Unless and until we successfully commercialize one or more product candidates, we expect to generate revenue primarily through research funding from our current collaborators, and research funding, milestone payments and licensing fees from potential future corporate collaborators. The timing and amount of our future revenue will be subject to significant fluctuations, based in part on the success of our research activities, the receipt of necessary regulatory approvals, the timing of achievement of milestones and the extent to which associated costs are reimbursed under our collaborative arrangements. Each of our product candidates combines different licensed technology from several licensors. We will have an obligation to our licensors to pay royalties on products that utilize their technologies. Because each product may require a different set of technologies, third-party royalties will be determined and paid on a product-by-product basis. Royalty

payment rates may also vary between products depending on the extent of licensed technology or because some technology licenses provide for lower royalties when the licensed technologies are combined with other royalty-bearing technologies. The royalty payment rates that we owe to our licensors will significantly influence the price and viability of our potential products.

Our research and development expenses fluctuate due to the timing of expenditures for the varying stages of our research, product development and clinical development programs and the availability of capital resources. Because a significant portion of our revenue and expense is directly tied to our research and development activities, our revenue will fluctuate with the level of future research and development activities. We expect that our revenue and expense will continue to fluctuate as we proceed with our current development collaborations, enter into potential new development collaborations and licensing agreements, and potentially earn milestone payments.

As of December 31, 2004, our accumulated deficit totaled approximately $230.8 million. We expect to generate substantial additional losses for the foreseeable future, primarily due to the costs associated with our preclinical and clinical development programs, developing our manufacturing capabilities and preparing our products under development for commercialization. Our expenses are driven by the size and scope of our development programs, our staffing levels, outside costs for supplies and materials and clinical trial activities. We may be unable to achieve profitability on a sustained basis, if at all. Further, successful development of our product candidates will require that we access significantly higher amounts of capital than we currently have. We may be unable to obtain required funding when needed or on acceptable terms, obtain or maintain corporate partnerships or complete acquisition transactions necessary or desirable to complete the development of our product candidates.

Critical Accounting Policies, Estimates and Assumptions

Our discussion and analysis of our financial condition and results of operations is based upon financial statements that we have prepared in accordance with accounting principles generally accepted in the United States. As we prepare our financial statements we are required to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures. On an on-going basis, we evaluate these estimates, including those related to revenue, accrued restructure charges, goodwill and fixed assets. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions. Note 1 of the Notes to our Consolidated Financial Statements, *"Description of Business and Summary of Significant Accounting Policies,"* summarizes our significant accounting policies that we believe are critical to the presentation of our consolidated financial statements. Our most critical accounting policies, estimates and assumptions are:

Revenue Recognition Policy

We generate revenue from technology licenses, collaborative research arrangements and cost reimbursement agreements. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable, up-front license fees, collaborative research funding, technology access fees and various other payments. Revenue from nonrefundable, up-front license fees and technology access payments is recognized systematically over the related service period, which is often the development period, in the collaborative agreement. Revenue associated with performance milestones is recognized as earned, based upon the achievement of the milestones defined in the applicable agreements. Revenue under research and development cost-reimbursement contracts is recognized as the related costs are incurred. Advance payments received in excess of amounts earned are classified as deferred revenue.

Estimated Restructuring Charges Associated with the Reorganization of our Operations

We have adopted the provisions of Statement of Financial Accounting Standards No. 146, or SFAS No. 146, *"Accounting for Costs Associated with Exit or Disposal Activities,"* as it relates to our facility in Bothell, Washington and our former facility in Sharon Hill, Pennsylvania and we have recorded restructure charges on the related operating leases. Accrued restructuring charges, and in particular, those charges associated with exiting a facility, are subject to many assumptions and estimates. Under SFAS No. 146, an accrued liability for lease termination costs is initially measured at fair value, based on the remaining lease payments due under the lease and other costs, reduced by sublease rental income that could be reasonably obtained from the property, and discounted using a credit-adjusted risk-free interest rate. The assumptions as to estimated sublease rental income and the period of time and concessions necessary to enter into a sublease significantly impact the accrual and may differ from what actually occurs. We review these estimates and adjust the accrual if necessary. These changes can be material. For example, we recognized charges of $371,000 in 2004, $4.7 million in 2003, and $1.6 million in 2002 due to changes in our sublease assumptions and initial adoption of SFAS No. 146.

If we proceed with further development and commercialization of any of our product candidates, we may need to resume use of the Bothell facility to fulfill our manufacturing requirements. If we decide to resume use of this facility, any remaining accrued restructure charges related to the facility will be reversed. This reversal would be reflected as a one-time credit to restructuring expenses and reflected in the period in which use is resumed. We will continue to evaluate any additional information that may become available with respect to the estimates and assumptions as they relate to these facilities, which may result in further significant charges to our results of operations. We are unable to determine the likelihood of any future adjustments to our accrued restructuring charges.

Valuation of Our Goodwill and Intangible Assets

In 2000, we acquired Genovo, Inc., a development-stage biotechnology company, for a purchase price of $66.4 million. We allocated the excess of the acquisition cost over the fair value of the identifiable net assets acquired to goodwill totaling $38.2 million and to other purchased intangibles totaling $605,000. From 2000 through 2001, we recorded amortization expenses of $7.1 million of Genovo goodwill and purchased intangibles. We test goodwill for impairment at least annually, and more frequently when events or circumstances indicate the carrying value may be impaired, by comparing its carrying value to the market value of our shares outstanding. Events or circumstances which could trigger an impairment review include a significant adverse change in our business climate, significant changes in our use of acquired technology, and changes to our overall business strategy. In the event that our valuation tests show an impairment in the recorded value of our goodwill, we may record a significant non-cash charge to expense. We have performed annual impairment tests as of October 1 each year since the implementation of SFAS No. 142 and concluded that no impairment in the value of our goodwill had occurred.

Application of Assumptions and Estimates in Accounting for the CellExSys Merger Consideration

On July 27, 2004, Chromos, an early-stage life sciences company, acquired all of the outstanding shares of CellExSys through a merger between CellExSys and Chromos Inc., a wholly owned subsidiary of Chromos. Under the terms of the merger agreement, Chromos issued to CellExSys shareholders 1,500,000 shares of Chromos common stock and a secured convertible debenture totaling $3.4 million Canadian (approximately $2.5 million). The debenture bears annual interest of 2% and is payable in two annual installments on the first and second anniversary of the closing. We owned approximately 79% of CellExSys at the time of the merger and recorded the estimated fair value of our share of the merger consideration as a non-current asset. The consideration is comprised of shares of Chromos common stock received by us and our 79% share of the secured debenture issued by Chromos. Based on the market value and liquidity for Chromos stock and its general business condition, we valued our share of the sale proceeds at $453,000. We will continue to evaluate the merger consideration received from Chromos for value impairment and will record a reduction in the carrying value if we determine that there is an impairment in value that we deem to be other than

temporary. These ongoing impairment evaluations will be based on several factors including the market price and trading volume of Chromos common stock and the financial condition of Chromos. As of December 31, 2004, we do not believe that there is evidence of an impairment in value that warrants adjustment to our carrying value of the merger consideration.

Application of New Accounting Standards

In December 2004, the FASB released its final revised standard, SFAS No. 123R, *"Share-Based Payment."* SFAS No. 123R will require us to expense the fair value of stock options granted over the vesting period. Currently, we account for stock options under Accounting Principles Board No. 25, *"Accounting for Stock Issued to Employees,"* which uses the intrinsic value method and generally recognizes no compensation cost for employee stock option grants. Adoption of SFAS No. 123R is required for fiscal periods beginning after June 15, 2005. We are evaluating SFAS No. 123R and believe it will have a material effect on our Consolidated Financial Statements.

The summary of significant accounting policies should be read in conjunction with our consolidated financial statements and related notes and the following discussion of our results of operations and liquidity and capital resources.

Results of Operations

Revenue

Total revenue in 2004 was $9.7 million, compared to $14.1 million in 2003. Revenue in 2004 consists primarily of amounts earned under our AIDS vaccine collaboration with IAVI which increased to $8.3 million in 2004 from $4.4 million in 2003. This revenue reflects manufacturing activities and development activities towards expanded vaccine candidates. Other revenue in 2004 includes contract manufacturing revenue and other service and collaboration revenues earned. The decrease in total revenue for 2004 compared to 2003 is the result of revenues earned in 2003 under our former development collaboration with Biogen and Wyeth. Total revenue in 2003 was $14.1 million compared to $19.3 million in 2002. This decrease reflects the completion of activities in 2002 under our former collaborations with Wyeth, Celltech, and Emerald, partially offset by higher revenue under our collaboration with Biogen, which ended in September 2003. Revenue in 2003 includes $3.9 million of revenue related to the termination of our collaboration with Wyeth and $2.6 million in revenue recognized in connection with the completion of our collaboration with Biogen. The decrease in revenue during 2003 also reflects lower revenue earned under our AIDS vaccine collaboration with IAVI, which resulted from the completion of certain development activities as the program progressed toward the initiation of human clinical trials that began in December 2003. As of December 31, 2004, we recognized the remaining balance of deferred revenue.

	Year Ended December 31,		
	2004	2003	2002
Revenue from collaborative agreements:			
IAVI	$8,340,000	$ 4,409,000	$ 5,662,000
Biogen	—	5,112,000	2,871,000
Wyeth	—	3,894,000	7,543,000
Celltech	—	—	1,280,000
Emerald	—	—	1,971,000
Other	1,312,000	658,000	6,000
Total revenue	$9,652,000	$14,073,000	$19,333,000

We expect that substantially all of our 2005 revenue will consist of research and development revenue from our collaboration with IAVI. We expect these revenues will be lower in 2005 than in 2004 relating to the level of planned development activities under the collaboration. Our revenue for

the next several years will be dependent on the continuation of our current IAVI collaboration and whether we enter into any new collaborations.

Operating Expenses

Research and Development. Research and development expenses totaled $17.3 million in 2004, compared to $17.2 million in 2003. While total research and development expenses in 2004 were comparable to 2003, the costs associated with our programs in clinical development increased from $1.5 million in 2003 to $12.0 million in 2004 reflecting the initiation of clinical trials for our AIDS vaccine program in December 2003 and our inflammatory arthritis program in March 2004. Research and development expenses decreased to $17.2 million in 2003 from $29.4 million in 2002. This decrease represents the planned reductions in expenses that we implemented in 2002 and early 2003 and our focus on our cystic fibrosis, AIDS vaccine and inflammatory arthritis development programs. These reductions included suspension of our hemophilia and cancer programs and reduced investments in our technology development activities.

We expect our research and development expenses to increase in 2005 as the result of expanded development and manufacturing activities for our inflammatory arthritis product candidate and planned manufacturing activities for our cystic fibrosis product candidate, pending review of data from our ongoing Phase II clinical trial. We also expect moderate increases in our development infrastructure to support our new development collaborations and to support our efforts to add new collaborative agreements.

The following is an allocation of our total research and development expenses between our programs in clinical development and those that are in research or preclinical stages of development:

	Year Ended December 31,		
	2004	2003	2002
Programs in clinical development:			
Cystic fibrosis	$ 823,000	$ 566,000	$ 1,096,000
Cancer products	—	14,000	1,714,000
AIDS vaccine (initiated Phase I clinical trial in December 2003)	3,704,000	19,000	—
Inflammatory arthritis (initiated Phase I clinical trial in March 2004)	1,771,000	—	—
Indirect costs	5,660,000	888,000	2,957,000
Total programs in clinical development	11,958,000	1,487,000	5,767,000
Programs in research and preclinical development	5,330,000	15,710,000	23,622,000
Total research and development expense	$17,288,000	$17,197,000	$29,389,000

Research and development costs attributable to programs in clinical development include costs of salaries, benefits, clinical trial sites, outside services, materials and supplies incurred to support the clinical programs. Indirect costs allocated to clinical programs include facility and occupancy costs, research and development administrative costs, and license and royalty payments. These costs are further allocated between clinical and pre-clinical programs based on relative levels of program activity. IAVI separately manages and funds the clinical trial costs of our AIDS vaccine program and the CF Foundation has separately funded the external costs of our current Phase II clinical trial of tgAAVCF. As a result, we do not include those costs in our research and development expenses.

Costs attributed to programs in research and preclinical devlopment represent our earlier-stage development activities including costs incurred on programs prior to their transition into clinical trials. Because we conduct multiple research projects and utilize resources across several programs, the majority of our research and preclinical development costs are not directly assigned to individual programs, but are instead allocated among multiple programs. For purposes of reimbursement from

our collaboration partners, we capture the level of effort expended on a program through our project management system, which is based primarily on human resource time allocated to each program, supplemented by an allocation of indirect costs and other specifically identifiable costs, if any. As a result, the costs allocated to a program do not necessarily reflect the actual costs of the program.

We initiated clinical testing of our AIDS vaccine product candidate in December 2003 and our inflammatory arthritis product candidate in March 2004. As a result, all related development activities associated with our cystic fibrosis, inflammatory arthritis and AIDS vaccine programs are reflected as costs associated with programs in clinical development as of the date of initiation of clinical testing. Therefore, during 2004 our research and development expenses associated with programs under clinical development increased reflecting the transition of these programs into clinical testing. Costs associated with our clinical development programs decreased in 2003 compared to 2002 reflecting completion of Phase II clinical trial in 2002 of tgAAVCF as well as our decision in mid-2002 to suspend further development of our cancer product candidates. Costs associated with our preclinical program activities decreased to $15.7 million in 2003 compared to $23.6 million 2002 primarily due to decreased activity in our AIDS vaccine program as we prepared to initiate human clinical trials in December 2003 and cost reduction measures implemented in late 2002 and early 2003.

General and Administrative. We incurred general and administrative expenses of $6.7 million in 2004 compared to $5.5 million in 2003. This increase primarily reflects increased patent and intellectual property costs, personnel costs and administrative compliance costs. We incurred general and administrative expenses of $5.5 million in 2003 compared to $8.1 million in 2002. This decrease primarily reflects lower administrative support for our collaborative partnerships, reduced patent costs due to the consolidation of our patent portfolio and the implementation of cost reduction measures in late 2002 and early 2003.

Restructure Charges. We apply the provisions of SFAS No. 146 *"Accounting for the Costs Associates with Exit or Disposal Activities"* as it relates to the operating leases on our facility in Bothell and our former facility in Sharon Hill. SFAS No. 146 also applies to the restructuring of our operations in 2002 and early 2003. Accrued restructuring charges represent our best estimate of the fair value of the liability as determined under SFAS No. 146 and are computed as the fair value of the difference between the remaining lease payments due on these leases and estimated sub-lease costs and rentals. These assumptions are periodically reviewed and adjustment is made to the accrued restructure charge when necessary. We record accretion expense based upon changes in the accrued restructure liability that results from the passage of time and the assumed discount rate of 10% that we use to determine the accrued liability. In 2002, we reclassified the deferred rent liability of $1.5 million, related to the Bothell facility, to accrued restructure costs.

Restructuring charges consist of the following:

	Year Ended December 31,		
	2004	2003	2002
Accretion expense	$513,000	$ 435,000	$ —
Changes in estimates	371,000	4,718,000	1,602,000
Employee termination and other	—	37,000	725,000
Total restructuring charges	$884,000	$5,190,000	$2,327,000

As of December 31, 2004, our accrued restructure liability balance was $6.3 million related to our Bothell facility. If we proceed with further development and commercialization of any of our product candidates, we may need to resume use of the Bothell facility to fulfill our manufacturing requirements. If we decide to resume use of this facility, any remaining restructuring accrual related to the facility will be reversed. This will be reflected as a one-time credit to restructuring charges, reflected in the period in which use is resumed. Any decision to resume use of the facility will be based on a number of factors including the progress of our product candidates in clinical development, the estimated duration of design and construction, the estimated timing of manufacturing requirements, the ability of our current manufacturing capabilities to meet demand and the

availability of resources. Unless a decision is made to resume use of this facility, we will continue to evaluate any additional information that may become available with respect to the estimates and assumptions, which may result in further significant charges to our results of operations.

Equity in Net Loss of Unconsolidated, Majority-Owned Research and Development Joint Venture. Our net loss in Emerald decreased to zero in 2004 and 2003, compared to a loss of $1.9 million in 2002. Losses reflect our 80.1% equity share in the losses generated by Emerald. Emerald has had no significant operations since 2002 and has been dissolved.

Amortization of Acquisition-Related Intangibles. Amortization expense decreased to zero in 2004 and 2003, compared to $365,000 in 2002 as our intangible assets that were subject to amortization were fully amortized as of September 30, 2002. As a result of our adoption of SFAS No. 142, *"Goodwill and Other Intangible Assets,"* as of January 1, 2002, we no longer record amortization expense as it relates to our goodwill. Instead, we periodically evaluate the carrying value of our goodwill, if there is evidence of a impairment in value, we reduce the carrying value of the asset. As of December 31, 2004, we have concluded that there is no impairment in the carrying value of our goodwill.

Investment Income. Investment income was $383,000 in 2004 compared to $183,000 in 2003. This increase is primarily the result of a higher level of invested funds resulting from our common stock placement in February 2004 which resulted in net proceeds of $23.7 million, and to a lesser degree from higher yields on our investments. In 2002, investment income was $398,000 as compared to $183,000 in 2003 due to lower investment returns during the year.

Interest Expense. Interest expense relates to interest on outstanding loans from our collaborative partners, notes and obligations under equipment financing arrangements and installment loans we use to finance purchases of laboratory and computer equipment, furniture and leasehold improvements. Interest expense decreased to $476,000 in 2004 from $1.2 million in 2003 and $1.4 million in 2002. These decreases resulted from lower debt balances due to the conversion of $9.4 million owed to Elan into equity in September 2003.

Gain on sale of majority-owned subsidiary. In July 2004, Chromos Molecular Systems, Inc., or Chromos, acquired all of the outstanding shares of our majority-owned subsidiary, CellExSys, through a merger between CellExSys and Chromos Inc., a wholly-owned subsidiary of Chromos. Under the terms of the merger agreement, Chromos has issued to CellExSys shareholders 1,500,000 shares of Chromos common stock and a secured convertible debenture totaling approximately $3.4 million Canadian (approximately $2.5 million at the time of close), subject to certain purchase price adjustments. As a result of the merger, we recorded a gain of $1.0 million representing the deposits received from Chromos to fund pre-closing operating costs, the fair value of our share of the stock and debenture, and the net liabilities assumed by Chromos.

Net Loss per Common Share. Net loss per common share decreased in 2004, primarily as a result of the increase in the number of shares outstanding due to the sale of common stock for cash in February 2004 and the conversion of the Series B preferred stock in March 2004. The decrease in net loss per common share in 2003 is the result of lower losses in 2003 compared to 2002 and an increase in the number of shares outstanding due to the sales of common shares for cash in February 2003 and the conversion of debt owned to Elan into common stock in September 2003.

Liquidity and Capital Resources

Our cash and cash equivalents increased to $34.1 million at December 31, 2004, compared to $21.1 million at December 31, 2003 and our shareholders' equity increased to $49.8 million at December 31, 2004, compared to $33.5 million at December 31, 2003. These increases reflect net proceeds of $29.8 million from sales of our common stock, offset by our net loss for the year of $14.3 million and the resulting cash used in operations of $15.5 million.

We have financed our product development activities and general corporate functions primarily through proceeds from public and private sales of our equity securities, through cash payments received from our collaborative partners and proceeds from the issuance of debt. To a lesser degree,

we have also financed our operations through interest earned on cash and short-term investments, loan funding under equipment leasing agreements and research grants. These financing sources have historically allowed us to maintain adequate levels of cash and investments.

Our cystic fibrosis product candidate is in a confirmatory Phase II clinical trial, and our AIDS vaccine and inflammatory arthritis product candidates are in Phase I clinical trials. We expect to continue incurring significant expense in advancing our product candidates toward commercialization. As a result, we do not expect to generate sustained positive cash flow from our operations for at least the next several years and only then if we can successfully develop and commercialize our product candidates. We will require substantial additional financial resources to fund the development and commercialization of our product candidates and expand research and development of our product candidates for treating additional diseases.

Over the past several years, we have scaled our development activities to the level of available cash resources and financial support from collaboration partners. Research and development and general and administrative expenses decreased by approximately 40% in 2003, compared to 2002 and reflected our focus on our lead development programs and cost reduction measures that we implemented. Research and development and general and administrative expenses increased by approximately 6% in 2004, compared to 2003 and are expected to increase by approximately 20% to support the advancement of our clinical development programs. Assuming that our product development programs progress at the rates currently planned, we believe that our cash requirements during 2005 will range from $22 million to $24 million. This amount is subject to change as the result of the outcome of our product development and other efforts. We offset a portion of our expenses with revenue from collaborative agreements which totaled $9.7 million in 2004, $14.1 million in 2003 and $19.3 million in 2002.

We expect to continue to receive financial support for specific programs to offset some of the costs of development, including our ongoing collaboration with IAVI and Children's Research Institute to develop an AIDS vaccine. The term of this collaboration has been extended through December 2006. Assuming that we complete all of the planned development activities, we expect to receive up to approximately $5.6 million in funding from IAVI to cover the costs of this program in 2005. We had expected to receive funding of up to $10.7 million from IAVI to support development activities for our AIDS vaccine program in 2004. We did not conduct all of these activities in 2004, some of which we now expect to occur in 2005 and others have been removed from the work plan. As a result our revenues from IAVI in 2004 were $8.3 million.

We expect that our cash and cash equivalents at December 31, 2004, plus the funding expected from IAVI to fund 2005 work activities under our AIDS vaccine collaboration will be sufficient to fund our operations into 2006. We believe that this will be sufficient time to complete each of our current clinical trials, evaluate the results, and assuming satisfactory results, to plan or initiate further clinical testing. In 2001, we borrowed $10 million from Biogen to fund our general operations. In August 2006, this note becomes due, which will require that we raise additional capital to repay the note or seek an alternative arrangement to repay the note. We also have an interest-free $650,000 loan from Biogen (recorded at an imputed 5.6% discount rate) that becomes due in September 2005. Although our development collaboration with IAVI has been extended through the end of 2006, the development plan and budget under the collaboration is established on an annual basis. While we expect this program to continue through at least the duration of the collaboration term, we and IAVI have not established the work plan and budget for 2006 and therefore we have not yet made an assumption as to the level of funding that we may receive from IAVI in 2006.

We expect the level of our future operating expenses to be driven by the needs of our product development programs offset by the availability of funds through partner-funded collaborations, equity offerings or other financing activities. The size, scope and pace of our development activities depend on the availability of these resources. Our future cash requirements will depend on many factors, including:

- the rate and extent of scientific progress in our research and development programs;

- the timing, costs and scope of, and our success in clinical trials, obtaining regulatory approvals and filing, prosecuting and enforcing patents;
- competing technological and market developments;
- the timing and costs of, and our success in any product commercialization activities and facility expansions, if and as required; and
- the expense and outcome of any litigation or administrative proceedings involving our intellectual property, or access to third party intellectual property through licensing agreements.

IAVI has the right to terminate our collaboration and its obligation to provide research funding at any time for any reason with 90 days notice. If we were to lose the collaborative funding expected from IAVI and were unable to obtain alternative sources of funding for the AIDS vaccine product candidate, we may be unable to continue our research and development program for that product candidate.

We are seeking partners for our hemophilia and cancer programs and evaluating other opportunities to obtain additional capital to fund our future operations. Additional sources of financing could involve one or more of the following:

- entering into additional product development and funding collaborations or other strategic transactions, or extending or expanding our current collaborations;
- selling or licensing our technology or product candidates;
- issuing equity in the public or private markets; or
- issuing debt.

Additional funding may not be available to us on reasonable terms, if at all. Depending on our ability to successfully access additional funding, we may be forced to implement significant cost reduction measures. These adjustments may include scaling back, delaying or terminating one or more research and development programs, curtailing capital expenditures or reducing other operating activities. We may also be required to relinquish some rights to our technology or product candidates or grant licenses on unfavorable terms, either of which would reduce the ultimate value to us of the technology or product candidates.

Off-Balance Sheet Arrangements

Although we do not have any joint ventures or other similar off-balance sheet items, in the ordinary course of business we enter into agreements that require us to indemnify counterparties against third-party claims. These may include: agreements with vendors and suppliers, under which we may indemnify them against claims arising from our use of their products or services; agreements with clinical investigators, under which we may indemnify them against claims arising from their use of our product candidates; real estate and equipment leases, under which we may indemnify lessors against third-party claims relating to use of their property; agreements with licensees or licensors, under which we may indemnify the licensee or licensor against claims arising from their use of our intellectual property or our use of their intellectual property; and agreements with initial purchasers and underwriters of our securities, under which we may indemnify them against claims relating to their participation in the transactions.

The nature and terms of these indemnifications vary from contract to contract, and generally a maximum obligation is not stated. Because we are unable to estimate our potential obligation, and because management does not expect these indemnifications to have a material adverse effect on our consolidated financial position, results of operations or cash flows, no related liabilities are recorded at December 31, 2004 or 2003. We hold insurance policies that mitigate potential losses arising from certain indemnifications and, historically, we have not incurred significant costs related to performance under these obligations.

Tabular Disclosure of Contractual Obligations

We have significant lease commitments and long-term obligations which draw on our cash resources. The following are our contractual commitments associated with our debt and lease obligations:

	Payments Due through Year Ended December 31:						
Contractual Obligations	2005	2006	2007	2008	2009	Thereafter	Total
Long-term debt obligations	$ 718,000	$10,000,000	$ —	$ —	$ —	$ —	$10,718,000
Equipment financing obligations	498,000	155,000	26,000	1,000	—	—	680,000
Operating lease obligations	2,138,000	2,336,000	2,364,000	2,392,000	1,622,000	9,200,000	20,052,000
Purchase obligations	162,000	—	—	—	—	—	162,000
Other long-term obligations	53,000	—	—	—	—	—	53,000
Total	$3,569,000	$12,491,000	$2,390,000	$2,393,000	$1,622,000	$9,200,000	$31,665,000

We will need to raise additional capital in order to repay the $10.0 million of note payable to Biogen that is due in August 2006.

Impact of New Accounting Pronouncements

In December 2004, the FASB issued SFAS No. 123R *"Share Based Payment."* This statement is a revision to SFAS No. 123, supersedes APB No. 25, *"Accounting for Stock Issued to Employees,"* and amends SFAS No. 95, *"Statement of Cash Flows."* This statement will require us to expense the cost of employee services received in exchange for an award of equity instruments. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements, and is effective for the first interim reporting period that begins after June 15, 2005.

SFAS No. 123R permits public companies to choose between the following two adoption methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date, or

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

As permitted by SFAS No. 123, we currently account for share-based payments to employees using the APB No. 25 intrinsic value method and recognize no compensation cost for employee stock options. The impact of the adoption of SFAS No. 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, valuation of employee stock options under SFAS No. 123R is similar to SFAS No. 123, with minor exceptions. For information about what our reported results of operations and earnings per share would have been had we adopted SFAS No. 123, please see the discussion under the heading "Stock Compensation" in Note 1 of the Notes to our Consolidated Financial Statements. The adoption of SFAS No. 123R's fair value method will have a significant impact on our results of operations, although it will have no impact on our overall financial position. Due to timing of the release of SFAS No. 123R, we have not yet completed the analysis of the ultimate impact that this new pronouncement will have on the results of operations, nor the method of adoption for this new standard.

In December 2004, the FASB issued SFAS No. 153, *Exchanges of Nonmonetary Assets, an amendment of* APB No. 29, *Accounting for Nonmonetary Transactions.* SFAS No. 153 requires

exchanges of productive assets to be accounted for at fair value, rather than at carryover basis, unless (1) neither the asset received nor the asset surrendered has a fair value that is determinable within reasonable limits or (2) the transactions lack commercial substance. SFAS No. 153 is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. We do not expect the adoption of this standard to have a material effect on our financial position, results of operations or cash flows.

In March 2004, FASB issued Emerging Issues Task Force, or EITF, Issue No. 03-1, *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments."* EITF Issue 03-1 provides new guidance for determining the meaning of other-than-temporary impairment for investments accounted for under the cost method or the equity method. EITF Issue 03-1 also provides guidance for evaluating and recording impairment losses. The disclosure requirements of EITF Issue No. 03-1 are effective for annual financial statements for fiscal years ending after December 15, 2003. Our adoption on January 1, 2004 of EITF Issue No. 03-1 did not have any material effect on our financial position, results of operations, or cash flows.

Factors Affecting Our Operating Results, Our Business and Our Stock Price

In addition to the other information contained in this annual report, you should carefully read and consider the following risk factors. If any of these risks actually occur, our business, operating results or financial condition could be harmed. This could cause the trading price of our stock to decline, and you could lose all or part of your investment.

Risks Related to Our Business

We expect to continue to operate at a loss and may never become profitable.

Substantially all of our revenue has been derived under collaborative research and development agreements relating to the development of our potential product candidates. We have incurred, and will continue to incur for the foreseeable future, significant expense to develop our research and development programs, conduct preclinical studies and clinical trials, seek regulatory approval for our product candidates and provide general and administrative support for these activities. As a result, we have incurred significant net losses since inception, and we expect to continue to incur substantial additional losses in the future. As of December 31, 2004, we had an accumulated deficit of approximately $230.8 million. We may never generate profits and, if we do become profitable, we may be unable to sustain or increase profitability.

All of our product candidates are in early-stage clinical trials or preclinical development, and if we are unable to successfully develop and commercialize our product candidates we will be unable to generate sufficient capital to maintain our business.

In July 2003, we initiated a confirmatory Phase II clinical trial for our cystic fibrosis product candidate in the United States. In December 2003, we initiated a Phase I trial for our AIDS vaccine product candidate in Europe. In March 2004, we initiated a Phase I trial for our inflammatory arthritis product candidate in the United States and Canada. Our product candidates for cancer have been evaluated in Phase I and Phase II clinical trials. We will not generate any product revenue for at least several years and then only if we can successfully develop and commercialize our product candidates. Commercializing our potential products depends on successful completion of additional research and development and testing, in both preclinical development and clinical trials. Clinical trials may take several years or more to complete. The commencement, cost and rate of completion of our clinical trials may vary or be delayed for many reasons, including the risks discussed elsewhere in this section. If we are unable to successfully complete preclinical and clinical development of some or all of our product candidates in a timely manner, we may be unable to generate sufficient product revenue to maintain our business.

Even if our potential products succeed in clinical trials and are approved for marketing, these products may never achieve market acceptance. If we are unsuccessful in commercializing our product

candidates for any reason, including greater effectiveness or economic feasibility of competing products or treatments, the failure of the medical community or the public to accept or use any products based on gene delivery, inadequate marketing and distribution capabilities or other reasons discussed elsewhere in this section, we will be unable to generate sufficient product revenue to maintain our business.

The results we expect to receive in March 2005 from our confirmatory Phase II clinical trial for our cystic fibrosis product candidate may not support the further development of our cystic fibrosis product, therefore eliminating the potential to develop, or generate any revenue which would affect negatively our business both operationally and financially.

In July 2003, we initiated, in collaboration with CF Foundation Therapeutics, a confirmatory Phase II clinical trial for our cystic fibrosis product candidate, tgAAVCF, in the United States. We expect to unblind the study and begin to analyze the data from this Phase II trial in mid to late March of 2005. We will review and evaluate the trial data, and following our analysis, we expect to announce our conclusions. The cystic fibrosis Phase II trial is a double-blind placebo controlled study and the trial data remain blinded to us, study investigators and participants. Currently, we do not have any information on any of the results of the Phase II clinical trial for our cystic fibrosis product candidate, and we will not have any information on the Phase II clinical trial results until the study is unblinded and the preliminary statistical results are tabulated by an independent contract research organization.

If the data from our confirmatory Phase II clinical trial for our cystic fibrosis product candidate is negative or inconclusive, we may discontinue development, therefore eliminating the potential to develop, or generate any revenue from, a cystic fibrosis product. We may be unable to develop or obtain other drug candidates that could lead to collaborations that could help us to maintain our business both operationally and financially. Even if the trial results are positive and show statistically significant improvements in lung function, our review of other factors, including other trial end points, competing products or treatments, the failure of the medical community or the public to accept or use any products based on gene delivery, inadequate marketing and distribution capabilities, the greater relative cost or development difficulty of our cystic fibrosis product as compared to other product candidates or other reasons discussed elsewhere in this section, may lead us to the conclusion to discontinue development of tgAAVCF.

If we are unable to raise additional capital when needed, we will be unable to conduct our operations and develop our potential products.

Because internally generated cash flow will not fund development and commercialization of our product candidates, we will require substantial additional financial resources. Our future capital requirements will depend on many factors, including:

- the rate and extent of scientific progress in our research and development programs;
- the timing, costs and scope of, and our success in, conducting clinical trials, obtaining regulatory approvals and pursuing patent prosecutions;
- competing technological and market developments;
- the timing and costs of, and our success in, any commercialization activities and facility expansions, if and as required; and
- the existence and/or outcome of any litigation or administrative proceedings involving intellectual property.

As of December 31, 2004, we had approximately $34.1 million in cash and cash equivalents. We expect that our cash resources at December 31, 2004 and the funding expected from IAVI to fund 2005 work under our AIDS vaccine collaboration will be sufficient to fund our operations into 2006. We expect to receive up to $5.6 million of research and development funding from IAVI in 2005. While we expect this program to continue through at least the duration of the current collaboration term, we have not established the work plan and budget for 2006 with IAVI and have therefore not yet

made an assumption as to the level of funding that we may receive from IAVI in that year. We are evaluating opportunities to obtain additional capital to fund our operations beyond that time. Additional sources of financing could involve one or more of the following:

- extending or expanding our current collaborations;
- entering into additional product development collaborations;
- selling or licensing our technology or product candidates;
- borrowing under loan or equipment leasing arrangements;
- issuing equity in the public or private markets; or
- issuing debt.

Additional funding may not be available to us on reasonable terms, if at all.

The funding that we expect to receive from IAVI depends on continued scientific progress under the collaboration and IAVI's ability and willingness to continue or extend the collaboration. If we are unable to successfully access additional capital, we may need to scale back, delay or terminate one or more of our development programs, curtail capital expenditures or reduce other operating activities. We may also be required to relinquish some rights to our technology or product candidates or grant or take licenses on unfavorable terms, either of which would reduce the ultimate value to us of our technology or product candidates.

The regulatory approval process for our product candidates is costly, time-consuming and subject to unpredictable changes and delays, and our product candidates may never receive regulatory approval.

No gene therapy products have received regulatory approval for marketing from the U.S. Food and Drug Administration, or FDA. Because our product candidates involve new and unproven technologies, we believe that the regulatory approval process may proceed more slowly compared to clinical trials involving traditional drugs. The FDA and applicable state and foreign regulators must conclude at each stage of clinical testing that our clinical data suggest acceptable levels of safety in order for us to proceed to the next stage of clinical trials. In addition, gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or NIH, are subject to review by the NIH's Office of Biotechnology Activities Recombinant DNA Advisory Committee, or RAC. Although NIH guidelines do not have regulatory status, the RAC review process can impede the initiation of the trial, even if the FDA has reviewed the trial and approved its initiation. Moreover, before a clinical trial can begin at an NIH-funded institution, that institution's Institutional Biosafety Committee must review the proposed clinical trial to assess the safety of the trial.

The regulatory process for our product candidates is costly, time-consuming and subject to unpredictable delays. The clinical trial requirements of the FDA, NIH and other agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use of the potential products. In addition, regulatory requirements governing gene and cell therapy products have changed frequently and may change in the future. Accordingly, we cannot predict how long it will take or how much it will cost to obtain regulatory approvals for clinical trials or for manufacturing or marketing our potential products. Some or all of our product candidates may never receive regulatory approval. A product candidate that appears promising at an early stage of research or development may not result in a commercially successful product. Our clinical trials may fail to demonstrate the safety and efficacy of a product candidate or a product candidate may generate unacceptable side affects or other problems during or after clinical trials. Should this occur, we may have to delay or discontinue development of the product candidate, and the corporate partner that supports development of that product candidate may terminate its support. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

If we are unable to obtain or maintain licenses for necessary third-party technology on acceptable terms or to develop alternative technology, we may be unable to develop and commercialize our product candidates.

We have entered into exclusive and nonexclusive license agreements that give us and our partners rights to use technologies owned or licensed by commercial and academic organizations in the research, development and commercialization of our potential products. For example, we have a gene transfer technology license agreement with Amgen Inc., or Amgen, as the successor to Immunex Corporation, or Immunex, under which we have license rights to certain Immunex proprietary technology specifically applicable to gene therapy applications. In a February 2004 letter, Amgen took the position that we are not licensed, either exclusively or non-exclusively, to use Immunex intellectual property covering TNFR:Fc or therapeutic uses for TNFR:Fc. We have responded with a letter confirming our confidence that the gene transfer technology license agreement provides us with an exclusive worldwide license to use the gene construct coding for TNFR:Fc for gene therapy applications. We have had and continue to have further communications with Amgen regarding our differences. Notwithstanding our confidence, it is possible that a resolution of those differences, through litigation or otherwise, could cause delay or discontinuation of our development of tgAAC94 or our inability to commercialize any resulting product.

We believe that we will need to obtain additional licenses to use patents and unpatented technology owned or licensed by others for use, compositions, methods, processes to manufacture compositions, processes to manufacture and purify gene delivery product candidates and other technologies and processes for our present and potential product candidates. If we are unable to maintain our current licenses for third-party technology or obtain additional licenses on acceptable terms, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates. In addition, the license agreements for technology for which we hold exclusive licenses typically contain provisions that require us to meet minimum development milestones in order to maintain the license on an exclusive basis for some or all fields of the license. We also have license agreements for some of our technologies, which may require us to sublicense certain of our rights. If we do not meet these requirements, our licensor may convert all or a portion of the license to a nonexclusive license or, in some cases, terminate the license.

In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Failure to recruit patients could delay or prevent clinical trials of our potential products, which could delay or prevent the development of potential products.

Identifying and qualifying patients to participate in clinical trials of our potential products is critically important to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. We have experienced delays in some of our clinical trials, and we may experience similar delays in the future. If patients are unwilling to participate in our gene therapy trials because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products will be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

Litigation involving intellectual property, product liability or other claims and product recalls could strain our resources, subject us to significant liability, damage our reputation or result in the invalidation of our proprietary rights.

As our product development efforts progress, especially in potentially significant markets such as AIDS or rheumatoid arthritis therapies, the risk increases that others may claim that our processes and potential products infringe on their intellectual property rights. In addition, administrative proceedings, litigation or both may be necessary to enforce our intellectual property rights or determine the rights of others. Defending or pursuing these claims, regardless of their merit, would be costly and would likely divert management's attention and resources away from our operations. If there were to be an adverse outcome in litigation or an interference proceeding, we could face potential liability for significant damages or be required to obtain a license to the patented process or technology at issue, or both. If we are unable to obtain a license on acceptable terms, or to develop or obtain alternative technology or processes, we may be unable to manufacture or market any product or potential product that uses the affected process or technology.

Clinical trials and the marketing of any potential products may expose us to liability claims resulting from the testing or use of our products. Gene therapy treatments are new and unproven, and potential known and unknown side effects of gene therapy may be serious and potentially life-threatening. Product liability claims may be made by clinical trial participants, consumers, healthcare providers or other sellers or users of our products. Although we currently maintain liability insurance, the costs of product liability and other claims against us may exceed our insurance coverage. In addition, we may require increased liability coverage as additional product candidates are used in clinical trials and commercialized. Liability insurance is expensive and may not continue to be available on acceptable terms. A product liability or other claim or product recall not covered by or exceeding our insurance coverage could significantly harm our financial condition. In addition, adverse publicity resulting from a product recall or a liability claim against us, one of our partners or another gene therapy company could significantly harm our reputation and make it more difficult to obtain the funding and collaborative partnerships necessary to maintain our business.

If we lose IAVI as a partner, we may be unable to develop our AIDS vaccine product candidate.

We have a collaborative development agreement with IAVI, which expires in December 2006, that we expect to provide us with funding to reimburse research and development and manufacturing expenses we incur in connection with the collaboration. In addition, our collaboration with IAVI provides funding for the Phase I clinical trial for our AIDS vaccine product candidate. A significant portion of our operating and clinical trial expenses are funded through our collaborative agreements with IAVI.

IAVI has the right to terminate the collaboration or its obligation to provide funding at any time for any reason with 90 days notice, which would significantly affect our operating activities. The loss of significant amounts of collaborative or clinical trial funding could cause the delay, reduction or termination of the related research and development programs, and a reduction in capital expenditures

and other operating activities necessary to support general operations. Such a reduction could further impede our ability to develop our product candidates.

If we do not attract and retain qualified personnel, we may be unable to develop and commercialize some of our potential products.

Our future success depends in large part on our ability to attract and retain key technical and management personnel. All of our employees, including our executive officers, can terminate their employment with us at any time. We have programs in place designed to retain personnel, including competitive compensation packages and programs to create a positive work environment. Other companies, research and academic institutions and other organizations in our field compete intensely for employees, however, and we may be unable to retain our existing personnel or attract additional qualified employees and consultants. If we experience significant turnover or difficulty in recruiting new personnel, our research and development of product candidates could be delayed and we could experience difficulty in generating sufficient revenue to maintain our business.

If our partners or scientific consultants terminate, reduce or delay our relationships with them, we may be unable to develop our potential products.

Our partners provide funding, manage regulatory filings, aid and augment our internal research and development efforts and provide access to important intellectual property and know-how. Their activities include, for example, support in processing the regulatory filings of our product candidates and funding clinical trials. Our outside scientific consultants and contractors perform research, develop technology and processes to advance and augment our internal efforts and provide access to important intellectual property and know-how. Their activities include, for example, clinical evaluation of our product candidates, product development activities performed under our research collaborations, research under sponsored research agreements and contract manufacturing services. Collaborations with established pharmaceutical and biotechnology companies and academic, research and public health organizations often provide a measure of validation of our product development efforts in the eyes of securities analysts, investors and the medical community. The development of certain of our potential products, and therefore the success of our business, depends on the performance of our partners, consultants and contractors. If they do not dedicate sufficient time, regulatory or other technical resources to the research and development programs for our product candidates or if they do not perform their obligations as expected, we may experience delays in, and may be unable to continue, the preclinical or clinical development of those product candidates. Each of our collaborations and scientific consulting relationships concludes at the end of the term specified in the applicable agreement unless we and our partners agree to extend the relationship. Any of our partners may decline to extend the collaboration, or may be willing to extend the collaboration only with a significantly reduced scope, for a number of scientific or business reasons. Competition for scientific consultants and partners in gene therapy is intense. We may be unable to successfully maintain our existing relationships or establish additional relationships necessary for the development of our product candidates on acceptable terms, if at all. If we are unable to do so, our research and development programs may be delayed or we may lose access to important intellectual property or know-how.

The success of our clinical trials and preclinical studies may not be indicative of results in a large number of patients of either safety or efficacy.

The successful results of our technology in preclinical studies using animal models may not be predictive of the results that we will see in our clinical trials. In addition, results in early-stage clinical trials are based on limited numbers of patients and generally test for drug safety rather than efficacy. Our reported progress and results from our early phases of clinical testing of our product candidates may not be indicative of progress or results that will be achieved from larger populations, which could be less favorable. Moreover, we do not know if the favorable results we have achieved in clinical trials will have a lasting effect. If a larger group of patients does not experience positive results, or if any favorable results do not demonstrate a beneficial effect, our product candidate for cystic fibrosis, or

any other potential products that we advance to clinical trials, may not receive approval from the FDA for further clinical trials or commercialization.

We may be unable to adequately protect our proprietary rights domestically or overseas, which may limit our ability to successfully market any product candidates.

Our success depends substantially on our ability to protect our proprietary rights and operate without infringing on the proprietary rights of others. We own or license patents and patent applications, and will need to license additional patents, for genes, processes, practices and techniques critical to our present and potential product candidates. If we fail to obtain and maintain patent or other intellectual property protection for this technology, our competitors could market competing products using those genes, processes, practices and techniques. The patent process takes several years and involves considerable expense. In addition, patent applications and patent positions in the field of biotechnology are highly uncertain and involve complex legal, scientific and factual questions. Our patent applications may not result in issued patents and the scope of any patent may be reduced both before and after the patent is issued. Even if we secure a patent, the patent may not provide significant protection and may be circumvented or invalidated.

We also rely on unpatented proprietary technology and technology that we have licensed on a nonexclusive basis. While we take precautions to protect our proprietary unpatented technology, we may be unable to meaningfully protect this technology from unauthorized use or misappropriation by a third party. Our competitors could also obtain rights to our nonexclusively licensed proprietary technology. In any event, other companies may independently develop equivalent proprietary information and techniques. If our competitors develop and market competing products using our unpatented or nonexclusively licensed proprietary technology or substantially similar technology, our products, if successfully developed, could suffer a reduction in sales or be forced out of the market.

If we do not develop adequate development, manufacturing, sales, marketing and distribution capabilities, either alone or with our business partners, we will be unable to generate sufficient product revenue to maintain our business.

Our potential products require significant development of new processes and design for the advancement of the product candidate through manufacture, preclinical and clinical testing. We may be unable to continue development or meet critical milestones with our partners due to technical or scientific issues related to manufacturing or development. We currently do not have the physical capacity to manufacture large-scale quantities of our potential products. This could limit our ability to conduct large clinical trials of a product candidate and to commercially launch a successful product candidate. In order to manufacture product at such scale, we will need to expand or improve our current facilities and staff or supplement them through the use of contract providers. If we are unable to obtain and maintain the necessary manufacturing capabilities, either alone or through third parties, we will be unable to manufacture our potential products in quantities sufficient to sustain our business. Moreover, we are unlikely to become profitable if we, or our contract providers, are unable to manufacture our potential products in a cost-effective manner.

In addition, we have no experience in sales, marketing and distribution. To successfully commercialize any products that may result from our development programs, we will need to develop these capabilities, either on our own or with others. We intend to enter into collaborations with other entities to utilize their mature marketing and distribution capabilities, but we may be unable to enter into marketing and distribution agreements on favorable terms, if at all. If our current or future collaborative partners do not commit sufficient resources to timely marketing and distributing our future products, if any, and we are unable to develop the necessary marketing and distribution capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business.

Post-approval manufacturing or product problems or failure to satisfy applicable regulatory requirements could prevent or limit our ability to market our products.

Commercialization of any products will require continued compliance with FDA and other federal, state and local regulations. For example, our current manufacturing facility, which is designed for manufacturing our AAV vectors for clinical and development purposes, is subject to the Good Manufacturing Practices requirements and other regulations of the FDA, as well as to other federal, state and local regulations such as the Occupational Health and Safety Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act and the Environmental Protection Act. Any future manufacturing facilities that we may construct for large-scale commercial production will also be subject to regulation. We may be unable to obtain regulatory approval for or maintain in operation this or any other manufacturing facility. In addition, we may be unable to attain or maintain compliance with current or future regulations relating to manufacture, safety, handling, storage, record keeping or marketing of potential products. If we fail to comply with applicable regulatory requirements or discover previously unknown manufacturing, contamination, product side effects or other problems after we receive regulatory approval for a potential product, we may suffer restrictions on our ability to market the product or be required to withdraw the product from the market.

Risks Related to Our Industry

Adverse events in the field of gene therapy could damage public perception of our potential products and negatively affect governmental approval and regulation.

Public perception of our product candidates could be harmed by negative events in the field of gene therapy. For example, in 2002, ten patients in a French academic clinical trial being treated for x-linked severe combined immunodeficiency in a gene therapy trial using a retroviral vector showed correction, however, two patients in the trial developed leukemia. Serious adverse events, including patient deaths have occurred in clinical trials. Adverse events and the resulting publicity, as well as any other adverse events in the field of gene therapy that may occur in the future, could result in a decrease in demand for any products that we may develop. The commercial success of our product candidates will depend in part on public acceptance of the use of gene therapy for preventing or treating human diseases. If public perception is influenced by claims that gene therapy is unsafe, our product candidates may not be accepted by the general public or the medical community. The public and the medical community may conclude that our technology is unsafe.

Future adverse events in gene therapy or the biotechnology industry could also result in greater governmental regulation, unfavorable public perception, stricter labeling requirements and potential regulatory delays in the testing or approval of our potential products. Any increased scrutiny could delay or increase the costs of our product development efforts or clinical trials.

Our use of hazardous materials exposes us to liability risks and regulatory limitations on their use, either of which could reduce our ability to generate product revenue.

Our research and development activities involve the controlled use of hazardous materials, including chemicals, biological materials and radioactive compounds. Our safety procedures for handling, storing and disposing of these materials must comply with federal, state and local laws and regulations, including, among others, those relating to solid and hazardous waste management, biohazard material handling, radiation and air pollution control. We may be required to incur significant costs in the future to comply with environmental or other applicable laws and regulations. In addition, we cannot eliminate the risk of accidental contamination or injury from hazardous materials. If a hazardous material accident were to occur, we could be held liable for any resulting damages, and this liability could exceed our financial resources. Accidents unrelated to our operations could cause federal, state or local regulatory agencies to restrict our access to hazardous materials needed in our research and development efforts, which could result in delays in our research and development programs. Paying damages or experiencing delays caused by restricted access could reduce our ability to generate revenue and make it more difficult to fund our operations.

The intense competition and rapid technological change in our market may result in pricing pressures and failure of our potential products to achieve market acceptance.

We face increasingly intense competition from a number of commercial entities and institutions that are developing gene therapy and cell therapy technologies. Our competitors include early-stage and more established gene delivery companies, other biotechnology companies, pharmaceutical companies, universities, research institutions and government agencies developing gene therapy products or other biotechnology-based therapies designed to treat the diseases on which we focus. We also face competition from companies using more traditional approaches to treating human diseases, such as surgery, medical devices and pharmaceutical products. As our product candidates become commercial gene therapy products that may affect commercial markets of the analogous protein or traditional pharmaceutical therapy, disputes including lawsuits, demands, threats or patent challenges may arise in an effort to slow our development. In addition, we compete with other companies to acquire products or technology from research institutions or universities. Many of our competitors have substantially more financial and infrastructure resources and larger research and development staffs than we do. Many of our competitors also have greater experience and capabilities than we do in:

- research and development;
- clinical trials;
- obtaining FDA and other regulatory approvals;
- manufacturing; and
- marketing and distribution.

In addition, the competitive positions of other companies, institutions and organizations, including smaller competitors, may be strengthened through collaborative relationships. Consequently, our competitors may be able to develop, obtain patent protection for, obtain regulatory approval for, or commercialize new products more rapidly than we do, or manufacture and market competitive products more successfully than we do. This could limit the prices we could charge for the products that we are able to market or result in our products failing to achieve market acceptance.

Gene therapy is a rapidly evolving field and is expected to continue to undergo significant and rapid technological change and competition. Rapid technological development by our competitors, including development of technologies, products or processes that are more effective or more economically feasible than those we have developed, could result in our actual and proposed technologies, products or processes losing market share or becoming obsolete.

Healthcare reform measures and the unwillingness of third-party payors to provide adequate reimbursement for the cost of our products could impair our ability to successfully commercialize our potential products and become profitable.

Sales of medical products and treatments depends substantially, both domestically and abroad, on the availability of reimbursement to the consumer from third-party payors. Our potential products may not be considered cost-effective by third-party payors, who may not provide coverage at the price set for our products, if at all. If purchasers or users of our products are unable to obtain adequate reimbursement, they may forego or reduce their use of our products. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

Increasing efforts by governmental and third-party payors, such as Medicare, private insurance plans and managed care organizations, to cap or reduce healthcare costs will affect our ability to commercialize our product candidates and become profitable. We believe that third-party payors will attempt to reduce healthcare costs by limiting both coverage and level of reimbursement for new products approved by the FDA. There have been and will continue to be a number of federal and state proposals to implement government controls on pricing, the adoption of which could affect our ability to successfully commercialize our product candidates. Even if the government does not adopt any such proposals or reforms, their announcement could impair our ability to raise capital.

Risks Related to Our Common Stock

Concentration of ownership of our common stock may give certain shareholders significant influence over our business.

A small number of investors own a significant number of shares of our common stock. As of December 31, 2004, Biogen and Elan (together with its affiliates) each held approximately 12.1 million shares of our common stock, or approximately 28.3% of our common shares outstanding as of December 31, 2004. This concentration of stock ownership may allow these shareholders to exercise significant control over our strategic decisions and block, delay or substantially influence all matters requiring shareholder approval, such as:

- election of directors;
- amendment of our charter documents; or
- approval of significant corporate transactions, such as a change of control of Targeted Genetics.

The interests of these shareholders may conflict with the interests of other holders of our common stock with regard to such matters. Furthermore, this concentration of ownership of our common stock could allow these shareholders to delay, deter or prevent a third party from acquiring control of Targeted Genetics at a premium over the then-current market price of our common stock, which could result in a decrease in our stock price.

Market fluctuations or volatility could cause the market price of our common stock to decline and limit our ability to raise capital.

The stock market in general and the market for biotechnology-related companies in particular have experienced extreme price and volume fluctuations, often unrelated to the operating performance of the affected companies. The market price of the securities of biotechnology companies, particularly companies such as ours without earnings and product revenue, has been highly volatile and is likely to remain so in the future. Any report of clinical trial results that are below the expectations of financial analysts or investors could result in a decline in our stock price. We believe that in the past, similar levels of volatility have contributed to the decline in the market price of our common stock, and may do so again in the future. Trading volumes of our common stock can increase dramatically, resulting in a volatile market price for our common stock. In addition, the trading price of our common stock could decline significantly as a result of sales of a substantial number of shares of our common stock, or the perception that significant sales could occur.

For example, at December 31, 2004, Elan held 12.1 million shares of our common stock. Between December 31, 2004 and January 5, 2005, Elan reported the sale of 395,000 shares of our common stock. In accordance with the termination agreement that we entered into in Elan with in March 2004, Elan is permitted to sell quantities of stock our equal to 175% of the volume limitation set forth in Rule 144(e)(1) promulgated under the Securities Act of 1933, as amended. The sale of significant quantities of stock by Elan, or other holders of significant shares of our stock, could adversely impact the price of our common stock.

In the past, securities class action litigation has been brought against companies that experience volatility in the market price of their securities. Market fluctuations in the price of our common stock could also adversely affect our collaborative opportunities and our future ability to sell equity securities at a price we deem appropriate. As a result, you could lose all or part of your investment.

Item 7A. *Quantitative and Qualitative Disclosures About Market Risk*

Short-term investments: Because of the short-term nature of our investments, we believe that our exposure to market rate fluctuations on those investments is minimal. Currently, we do not use any derivative or other financial instruments or derivative commodity instruments to hedge any market risks and do not plan to employ these instruments in the future. At December 31, 2004, we held $34.1 million in cash and cash equivalents, which are primarily invested in money market funds and

a limited-term bond fund denominated in U.S. dollars that invest in securities that, on the average, mature in less than 12 months. An analysis of the impact on these securities of a hypothetical 10% change in short-term interest rates from those in effect at December 31, 2004, indicates that such a change in interest rates would not have a significant impact on our financial position or on our expected results of operations in 2005.

Notes payable: Our results of operations are affected by changes in short-term interest rates as a result of a loan from Biogen that contains a variable interest rate. Interest payments on this loan are determined by the LIBOR plus a margin of 1%. The carrying amount of the note payable approximates fair value because the interest rate on this instrument changes with, or approximates, market rates. The following table provides information as of December 31, 2004, about our obligations that are sensitive to changes in interest rate fluctuations:

	Expected Maturity Date					
	2005	2006	2007	2008	2009	Total
Maturities of long-term obligations:						
Variable rate note	$ —	$10,000,000	$ —	$ —	$ —	$10,000,000
Fixed rate notes	771,000	—	—	—	—	771,000
Fixed rate equipment financing	498,000	155,000	26,000	1,000	—	680,000
Total	$ 1,269,000	$10,155,000	$ 26,000	$ 1,000	$ —	$11,451,000

Item 8. ***Financial Statements and Supplementary Data.***

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of Targeted Genetics Corporation

We have audited the accompanying consolidated balance sheets of Targeted Genetics Corporation as of December 31, 2004 and 2003, and the related consolidated statements of operations, preferred stock and shareholders' equity, and cash flows for each of the three years in the period ended December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Targeted Genetics Corporation at December 31, 2004 and 2003, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Targeted Genetics Corporation's internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 3, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Seattle, Washington
March 3, 2005

TARGETED GENETICS CORPORATION

CONSOLIDATED BALANCE SHEETS

	December 31, 2004	December 31, 2003
ASSETS		
Current assets:		
Cash and cash equivalents	$ 34,096,000	$ 21,057,000
Accounts receivable	404,000	166,000
Prepaid expenses and other	653,000	409,000
Total current assets	35,153,000	21,632,000
Property and equipment, net	2,495,000	3,423,000
Goodwill, net	31,649,000	31,649,000
Other assets	668,000	968,000
Total assets	$ 69,965,000	$ 57,672,000
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	$ 1,289,000	$ 1,271,000
Accrued employee expenses	1,030,000	1,564,000
Accrued restructure charges	407,000	1,404,000
Deferred revenue	—	1,180,000
Current portion of long-term obligations	1,269,000	1,290,000
Total current liabilities	3,995,000	6,709,000
Accrued restructure charges and deferred rent	6,026,000	5,507,000
Long-term obligations	10,182,000	11,227,000
Commitments (Note 9)		
Minority interest in preferred stock of subsidiary	—	750,000
Shareholders' equity:		
Preferred stock, $0.01 par value, 6,000,000 shares authorized:		
Series A preferred stock, 800,000 shares designated, none issued and outstanding	—	—
Series B preferred stock, no shares issued or outstanding at December 31, 2004 and 12,015 shares designated, issued and outstanding at December 31, 2003	—	—
Common stock, $0.01 par value, 120,000,000 shares authorized, 85,626,326 shares issued and outstanding at December 31, 2004 and 66,206,230 shares issued and outstanding at December 31, 2003	856,000	662,000
Additional paid-in capital	279,745,000	249,399,000
Accumulated deficit	(230,839,000)	(216,582,000)
Total shareholders' equity	49,762,000	33,479,000
Total liabilities and shareholders' equity	$ 69,965,000	$ 57,672,000

See accompanying notes to consolidated financial statements

TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2004	2003	2002
Revenue:			
Collaborative agreements	$ 9,652,000	$ 14,073,000	$ 17,362,000
Collaborative agreement with unconsolidated, majority-owned research and development joint venture	—	—	1,971,000
Total revenue	9,652,000	14,073,000	19,333,000
Operating expenses:			
Research and development	17,288,000	17,197,000	29,389,000
General and administrative	6,650,000	5,490,000	8,067,000
Restructure charges	884,000	5,190,000	2,327,000
Equity in net loss of unconsolidated, majority-owned research and development joint venture	—	—	1,926,000
Amortization of acquisition-related intangibles	—	—	365,000
Total operating expenses	24,822,000	27,877,000	42,074,000
Loss from operations	(15,170,000)	(13,804,000)	(22,741,000)
Investment income	383,000	183,000	398,000
Interest expense	(476,000)	(1,212,000)	(1,424,000)
Gain on sale of majority-owned subsidiary	1,006,000	—	—
Net loss	$(14,257,000)	$(14,833,000)	$(23,767,000)
Net loss per common share (basic and diluted)	$ (0.18)	$ (0.26)	$ (0.52)
Shares used in computation of basic and diluted net loss per common share	79,451,000	57,486,000	45,767,000

See accompanying notes to consolidated financial statements

TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF PREFERRED STOCK AND SHAREHOLDERS' EQUITY

	Series B Preferred Stock		Common Stock		Additional Paid-In-Capital	Accumulated Deficit	Total Shareholders' Equity
	Shares	Amount	Shares	Amount			
Balance at December 31, 2001	12,015	$ 12,015,000	44,125,677	$441,000	$202,927,000	$(177,982,000)	$ 25,386,000
Net loss and comprehensive loss — 2002	—	—	—	—	—	(23,767,000)	(23,767,000)
Cancellation of shares held in escrow related to Genovo acquisition	—	—	(1,549)	—	(20,000)	—	(20,000)
Exercise of stock options	—	—	35,053	1,000	37,000	—	38,000
Issuance of shares to Biogen for cash, net of issue costs of $23,000	—	—	5,804,673	58,000	3,919,000	—	3,977,000
Issuance of shares related to Genovo acquisition	—	—	602,494	6,000	276,000	—	282,000
Balance at December 31, 2002	12,015	12,015,000	50,566,348	506,000	207,139,000	(201,749,000)	5,896,000
Net loss and comprehensive loss — 2003	—	—	—	—	—	(14,833,000)	(14,833,000)
Reclassification of Series B convertible preferred stock	—	(12,015,000)	—	—	12,015,000	—	12,015,000
Issuance of shares for cash, net of issue costs of $1,387,000	—	—	7,777,778	78,000	16,037,000	—	16,115,000
Issuance of shares to Biogen for cash, net of issue costs of $2,000	—	—	2,515,843	25,000	4,768,000	—	4,793,000
Issuance of shares to Elan for debt conversion	—	—	5,203,244	52,000	9,315,000	—	9,367,000
Exercise of stock options	—	—	143,017	1,000	125,000	—	126,000
Balance at December 31, 2003	12,015	—	66,206,230	662,000	249,399,000	(216,582,000)	33,479,000
Net loss and comprehensive loss — 2004	—	—	—	—	—	(14,257,000)	(14,257,000)
Conversion of Series B convertible preferred stock	(12,015)	—	4,330,000	43,000	(43,000)	—	—
Issuance of shares for cash, net of issue costs of $1,742,000	—	—	10,854,257	109,000	23,657,000	—	23,766,000
Issuance of shares for cash, net of issue costs of $28,000	—	—	3,954,132	39,000	5,933,000	—	5,972,000
Issuance of shares to acquire minority interest in majority-owned subsidiary	—	—	158,764	2,000	748,000	—	750,000
Exercise of stock options	—	—	122,943	1,000	51,000	—	52,000
Balance at December 31, 2004	—	$ —	85,626,326	$856,000	$279,745,000	$(230,839,000)	$ 49,762,000

See accompanying notes to consolidated financial statements

TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2004	2003	2002
Operating activities:			
Net loss	$(14,257,000)	$(14,833,000)	$(23,767,000)
Adjustments to reconcile net loss to net cash used in operating activities:			
Gain on sale of majority-owned subsidiary	(1,006,000)	—	—
Depreciation and amortization	1,289,000	2,420,000	3,252,000
Non cash interest expense	63,000	822,000	825,000
Equity in net loss of unconsolidated, majority-owned research and development joint venture	—	—	1,926,000
Amortization of acquisition-related intangibles	—	—	365,000
Loss (gain) on sale of fixed assets	(51,000)	—	99,000
Changes in assets and liabilities:			
Decrease (increase) in accounts receivable	(155,000)	1,004,000	77,000
Decrease in prepaid expenses and other	104,000	43,000	482,000
Decrease in other assets	341,000	348,000	174,000
Increase (decrease) in current liabilities	(193,000)	394,000	(1,609,000)
Decrease in deferred revenue	(1,180,000)	(4,861,000)	(3,555,000)
Increase (decrease) in accrued restructure expenses and deferred rent	(478,000)	3,433,000	1,635,000
Net cash used in operating activities	(15,523,000)	(11,230,000)	(20,096,000)
Investing activities:			
Purchases of property and equipment	(408,000)	(316,000)	(563,000)
Investment in unconsolidated, majority-owned research and development joint venture	—	—	(1,926,000)
Net cash used in investing activities	(408,000)	(316,000)	(2,489,000)
Financing activities:			
Net proceeds from sales of capital stock	29,790,000	21,028,000	4,014,000
Proceeds from leasehold improvements and equipment financing arrangements	46,000	229,000	607,000
Payments under leasehold improvements and equipment financing arrangements	(866,000)	(1,260,000)	(1,316,000)
Loan proceeds from collaborative partners	—	—	5,950,000
Minority interest contribution	—	—	750,000
Net cash provided by financing activities	28,970,000	19,997,000	10,005,000
Net increase (decrease) in cash and cash equivalents	13,039,000	8,451,000	(12,580,000)
Cash and cash equivalents, beginning of year	21,057,000	12,606,000	25,186,000
Cash and cash equivalents, end of year	$ 34,096,000	$ 21,057,000	$ 12,606,000
Supplemental information:			
Cash paid for interest	$ 413,000	$ 459,000	$ 439,000

See accompanying notes to consolidated financial statements

1. Description of Business and Summary of Significant Accounting Policies

Description of Business

Targeted Genetics was incorporated in the state of Washington in March 1989. We conduct research and development of gene therapy products and technologies for treating both acquired and inherited diseases. We develop these programs on our own and under various collaborative agreements with others.

Basis of Presentation

Our consolidated financial statements include the accounts of Targeted Genetics, our wholly owned subsidiaries Genovo, Inc. *(inactive)* and TGCF Manufacturing Corporation *(inactive),* and until its sale in July 2004, our majority-owned subsidiary, CellExSys, Inc., or CellExSys. The consolidated balance sheet as of December 31, 2003, and our results of operations for the years ended December 31, 2002 and 2003, do not include the accounts of Emerald Gene Systems, Ltd., or Emerald, our then majority-owned research and development joint venture with Elan International Services Ltd., or Elan, because we did not have operating control of Emerald during those periods. In connection with a termination agreement with Elan effective March 31, 2004, we acquired all of Elan's equity interest in Emerald. As a result, Emerald became a wholly-owned subsidiary as of March 31, 2004, and is consolidated into our financial statements as of that date. The operations of Emerald terminated during 2002 and it has been dissolved; therefore, the impact of consolidating the accounts of Emerald into our financial results is not significant. All significant intercompany transactions have been eliminated in consolidation.

Cash Equivalents

Cash equivalents include short-term investments that have a maturity at the time of purchase of three months or less, are readily convertible into cash and we believe have an insignificant level of valuation risk attributable to potential changes in interest rates. Our cash equivalents are recorded at cost, which approximates fair market value, and consist primarily of money market accounts and shares in a limited-term bond fund.

Fair Value of Financial Instruments

We believe that the carrying amounts of financial instruments such as cash and cash equivalents, accounts receivable and accounts payable approximate fair value because of the short-term nature of these items. We believe that the carrying amounts of the notes payable and equipment financing obligations approximate fair value because the interest rates on these instruments change with, or approximate, market interest rates.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation. We compute depreciation of property and equipment using the straight-line method over the asset's estimated useful life, which ranges from three to ten years. Leasehold improvements are amortized over the asset's estimated useful life or the lease term, whichever is shorter. Depreciation and amortization expense was $1.3 million in 2004, $2.4 million in 2003 and $3.3 million in 2002.

Goodwill and Purchased Intangibles

In 2000, we acquired Genovo, Inc., a development-stage biotechnology company, for a purchase price of $66.4 million. We allocated the excess of the acquisition cost over the fair value of the identifiable net assets acquired to goodwill totaling $38.2 million and to other purchased intangibles totaling $605,000. From 2000 through 2001, we recorded amortization expenses of $7.1 million of goodwill and purchased intangibles. We test goodwill for impairment at least annually, and more frequently when events or circumstances indicate the carrying value may be impaired, by comparing its carrying value to the market value of our shares outstanding. Events or circumstances which could trigger an impairment review include a significant adverse change in our business climate, significant changes in our use of acquired technology, and changes to our overall business strategy. In the event that our valuation tests show an impairment in the recorded value of our goodwill, we may record a significant non-cash charge to expense. We have performed annual impairment tests as of October 1 each year since our January 1, 2002 implementation of SFAS No. 142 *"Goodwill and Other Intangible Assets"* and concluded that no impairment in the value of our goodwill had occurred.

Other Assets

Other assets consists primarily of the estimated fair value of the consideration we received from the sale of CellExSys in July 2004. We periodically evaluate this merger consideration for value impairment and will record a reduction in the carrying value if we determine that there is an impairment in value that is deemed to be other than temporary. We assess impairment based on factors outlined by the Financial Accounting Standards Board, or FASB, in Emerging Issues Task Force, or EITF, Issue No. 03-1 *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments"*, which include the investee's financial condition, business prospects, industry conditions operating cash, stock price, trading volume and liquidity.

Long-Lived Assets

In accordance with SFAS No. 144, *"Accounting for the Impairment or Disposal of Long-Lived Assets,"* we review the carrying value and fair value of long-lived assets whenever events or changes in circumstances indicate that there may be impairment in value. Conditions that would necessitate an impairment assessment include a significant decline in the observable market value of an asset, a significant change in the extent or manner in which an asset is used, or a significant adverse change that would indicate that the carrying amount of an asset or group of assets is not recoverable.

Accrued Restructure Charges

We apply the provisions of SFAS No. 146, *"Accounting for Costs Associated with Exit or Disposal Activities,"* as it relates to our facilities in Bothell, Washington and our former facility in Sharon Hill, Pennsylvania. As a result, we have recorded restructuring charges on the operating leases for these facilities. Accrued restructuring charges, and in particular, those charges associated with exiting a facility, are subject to many assumptions and estimates. Under SFAS No. 146, an accrued liability for lease termination costs is initially measured at fair value, based on the remaining lease payments due under the lease and other costs, reduced by sublease rental income that could be reasonably obtained from the property, and discounted using a credit-adjusted risk-free interest rate. We use a risk-free annual interest rate of 10%. The assumptions as to estimated sublease rental income, the period of time to execute a sublease and the costs and concessions necessary to enter into a sublease significantly impact the accrual and may differ from what actually occurs. We review these estimates periodically and adjust the accrual if necessary.

Series B Convertible Preferred Stock

In July 1999, we issued shares of our Series B convertible exchangeable preferred stock, valued at $12 million, to Elan in exchange for our 80.1% interest in Emerald. The Series B preferred stock and accrued dividends were convertible at Elan's option into shares of our common stock, at a conversion price of $3.32 per share. Compounding dividends accrued semi-annually at 7% per year on the $1,000 per share face value of the preferred stock. Dividends were not paid in cash, but rather resulted in an increase to the number of shares of common stock issued upon conversion.

Elan was entitled to exchange the Series B preferred stock for all shares of preferred stock that we held in Emerald until this exchange right expired in April 2003. Prior to the expiration of the exchange right, the carrying value of the Series B preferred stock was reflected as mezzanine equity in our financial statements. Upon expiration of the exchange right, we reclassified the Series B preferred stock from mezzanine equity to shareholders' equity. Elan converted the Series B preferred stock into 4,330,000 shares of common stock in March 2004.

Stock Compensation

As permitted by the provisions of SFAS No. 123, *"Accounting for Stock-Based Compensation,"* we have elected to follow Accounting Principles Board, APB, No. 25, *"Accounting for Stock Issued to Employees,"* which uses the intrinsic value method and generally recognizes no compensation cost for employee stock option grants. We do not recognize any compensation expense for options granted to employees because we grant all options at fair market value on the date of grant. The adoption of SFAS No. 123R in 2005 will require us to expense stock option grants.

As allowed by SFAS No. 123, we do not recognize compensation expense on stock options granted to employees and directors. If we had elected to recognize compensation expense based on the fair market value at the grant dates for the stock options granted, the pro forma net loss and net loss per common share would have been as follows:

	Year Ended December 31,		
	2004	2003	2002
Net loss:			
as reported	$(14,257,000)	$(14,833,000)	$(23,767,000)
stock-based compensation under SFAS 123	(1,564,000)	(780,000)	(2,532,000)
pro forma	$(15,821,000)	$(15,613,000)	$(26,299,000)
Basic net loss per share:			
as reported	$ (0.18)	$ (0.26)	$ (0.52)
pro forma	(0.20)	(0.27)	(0.57)

Revenue Recognition under Collaborative Agreements

We generate revenue from technology licenses, collaborative research arrangements and cost reimbursement contracts. Revenue under technology licenses and collaborative agreements typically consists of nonrefundable, up-front license fees, collaborative research funding, technology access fees and various other payments.

Revenue from nonrefundable, up-front license fees and technology access payments is initially deferred and then recognized systematically over the service period of the collaborative agreement, which is often the development period. Revenue associated with performance milestones is recognized as earned, based upon the achievement of the milestones defined in the applicable agreements. Revenue under research and development cost reimbursement contracts is recognized as the related costs are incurred. Payments received in excess of amounts earned are classified as deferred revenue in the accompanying Consolidated Balance Sheets.

Significant Revenue Relationships and Concentration of Risk

Revenues under our collaboration with the International AIDS Vaccine Initiative, or IAVI, and under our former collaborations with Biogen, Celltech and Wyeth accounted for substantially all of the revenue we recorded from collaborative agreements in 2004, 2003 and 2002. Revenue in 2002 from the collaborative agreement with unconsolidated, majority-owned research and development joint venture is from Emerald. Our collaborations with Biogen, Celltech, Wyeth and Emerald have concluded and these sources of revenue have ended leaving IAVI as our primary source of revenue for 2005. A significant change in the level of work or timing of work activities and the funding received from IAVI could disrupt our business and adversely affect our cash flow and results of operations.

Research and Development Costs

Research and development costs include salaries, costs of outside collaborators and outside services, clinical trial expenses, royalty and license costs and allocated facility, occupancy and utility expenses. We expense research and development costs as incurred. Costs and expenses related to programs conducted under collaborative agreements that result in collaborative revenue totaled approximately $7.1 million in 2004 and in 2003 and $14.7 million in 2002.

Net Loss per Common Share

Net loss per common share is based on net loss divided by the weighted average number of common shares outstanding during the period. Our diluted net loss per share is the same as our basic net loss per share because all stock options, warrants and other potentially dilutive securities are antidilutive and therefore excluded from the calculation of diluted net loss per share. The total number of shares that we excluded from the calculations of net loss per share were 8,093,058 shares in 2004, 10,867,013 shares in 2003 and 17,284,151 shares in 2002.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Our actual results may differ from those estimates.

Recently Issued Accounting Standards

In December 2004, the FASB issued SFAS No. 123R *"Share Based Payment."* This statement is a revision to SFAS No. 123, supersedes APB No. 25, *"Accounting for Stock Issued to Employees,"* and amends SFAS No. 95, *"Statement of Cash Flows."* This statement will require us to expense the cost of employee services received in exchange for an award of equity instruments. This statement also provides guidance on valuing and expensing these awards, as well as disclosure requirements, and is effective for the first interim reporting period that begins after June 15, 2005.

SFAS No. 123R permits public companies to choose between the following two adoption methods:

1. A "modified prospective" method in which compensation cost is recognized beginning with the effective date (a) based on the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) based on the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date, or

2. A "modified retrospective" method which includes the requirements of the modified prospective method described above, but also permits entities to restate based on the amounts previously recognized under SFAS No. 123 for purposes of pro forma disclosures either (a) all prior periods presented or (b) prior interim periods of the year of adoption.

As permitted by SFAS No. 123, we currently account for share-based payments to employees using the APB No. 25 intrinsic value method and recognize no compensation cost for employee stock options. The impact of the adoption of SFAS No. 123R cannot be predicted at this time because it will depend on levels of share-based payments granted in the future. However, valuation of employee stock options under SFAS No. 123R is similar to SFAS No. 123, with minor exceptions. For information about what our reported results of operations and earnings per share would have been had we adopted SFAS No. 123, see the discussion under the heading "Stock Compensation" in this note. The adoption of SFAS No. 123R's fair value method will have a significant impact on our results of operations, although it will have no impact on our overall financial position. Due to timing of the release of SFAS No. 123R, we have not yet completed the analysis of the ultimate impact that this new pronouncement will have on the results of operations, nor the method of adoption for this new standard.

In December 2004, the FASB issued SFAS No. 153, *Exchanges of Nonmonetary Assets, an amendment of* APB No. 29, *Accounting for Nonmonetary Transactions.* SFAS No. 153 requires exchanges of productive assets to be accounted for at fair value, rather than at carryover basis, unless (1) neither the asset received nor the asset surrendered has a fair value that is determinable within reasonable limits or (2) the transactions lack commercial substance. SFAS No. 153 is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. We do not expect the adoption of this standard to have a material effect on our financial position, results of operations or cash flows.

In March 2004, FASB issued EITF Issue No. 03-1, *"The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments,"* which provides new guidance for determining the meaning of other-than-temporary impairment for investments accounted for under the cost method or the equity method and guidance for evaluating and recording impairment losses. Our adoption on January 1, 2004 of EITF Issue No. 03-1 did not have any material effect on our financial position, results of operations, or cash flows.

Reclassifications

Certain reclassifications have been made to conform prior year results to the current year presentation.

2. Property and Equipment

Property and equipment consisted of the following:

	December 31,	
	2004	2003
Furniture and equipment	$ 6,410,000	$ 7,270,000
Leasehold improvements	9,739,000	9,635,000
	16,149,000	16,905,000
Less accumulated depreciation and amortization	(13,654,000)	(13,482,000)
	$ 2,495,000	$ 3,423,000

We finance a portion of our equipment through equipment financing arrangements, which include extension and purchase options, and require us to pledge the equipment as security for the financing. The cost of equipment that has been pledged under financing arrangements totaled $2.6 million at December 31, 2004 and $3.6 million at December 31, 2003.

3. Accrued Restructure Charges

In December 2002, we began to pursue options to sublease, or terminate, our lease on the Bothell facility and in February 2003, we closed our facility in Sharon Hill. We record accrued restructure charges as they relate to the leases on these facilities. Accrued restructure charges represent our best estimate of the fair value of the liability remaining under the lease and are computed as the present value of the difference between the remaining lease payments due less the net of sublease income and expense. These assumptions are periodically reviewed and adjustments are made to the accrued restructure charge when necessary. We record accretion expense based upon changes in the accrued restructure liability that results from the passage of time and the assumed discount rate of 10%. Accretion expense is recorded on an ongoing basis through the end of the lease term in September 2015 and is reflected as a charge in the accompanying statements of operations as a restructuring charge.

The tables below present our total estimated restructure charges and a reconciliation of the associated liability:

	Employee Termination Benefits	Contract Termination Costs	Other Associated Costs	Total
Incurred in 2002	$725,000	$ 1,602,000	$ —	$ 2,327,000
Incurred in 2003	5,000	5,153,000	32,000	5,190,000
Incurred in 2004	—	884,000	—	884,000
Cumulative incurred to date	730,000	7,639,000	32,000	8,401,000
Estimated future charges	—	2,532,000	—	2,532,000
Total expected to be incurred	$730,000	$10,171,000	$32,000	$10,933,000

	Contract Termination Costs
December 31, 2003 accrued liability	$ 6,870,000
Charges incurred in 2004	513,000
Adjustments to the liability, net	371,000
Amount paid in 2004	(1,406,000)
December 31, 2004 accrued liability	$ 6,348,000

Charges incurred in 2004 represent accretion expense of $513,000 and adjustments represent additional net charges of $94,000 due to changes in estimates and termination of the lease related to the Sharon Hill facility and $277,000 related to additional time that we believe it may require to identify a sublease tenant for the portion of our Bothell facility that we intend to sublease. In November 2004, we entered into an agreement to terminate our lease on the Sharon Hill facility. Amounts paid in 2004 include a lease termination payment of $125,000 and application of $335,000 of deposits retained by the landlord toward settlement of the Sharon Hill lease. Estimated future charges represent our estimate of the accretion expense throughout the remainder of the Bothell lease term.

Further development or commercialization of any of our product candidates, may require the use of a portion of the Bothell facility to fulfill our manufacturing requirements. While the application of SFAS No. 146 includes an assumption for potential sublease income from the facility, we do not currently intend to sublease a portion of the Bothell facility. The assumed net sublease income as it relates to that portion of the facility is expensed ratably as research and development expense over the remaining term of the lease. If we decide to utilize this facility, any remaining accrued restructure charges related to the manufacturing facility will be reversed and recorded as a one-time credit to restructure charges, reflected in the period in which use is resumed. Any decision to resume use of the facility will be based on a number of factors, including the progress of our product candidates in clinical development, the estimated duration of facility design and construction, the estimated timing of product manufacturing requirements, the ability of our current manufacturing capabilities to meet demand, and the availability of resources. However, unless we resume use of the Bothell facility, we will continue to account for the lease in accordance with SFAS No. 146 and will periodically evaluate the assumptions and record additional restructure charges if necessary. Because the restructure charge is an estimate based upon assumptions regarding the timing and amounts of future events, significant adjustments to the accrual may be necessary in the future based on the actual outcome of events and as we become aware of new facts and circumstances.

4. Long-Term Obligations

Long-term obligations consisted of the following:

	December 31, 2004	December 31, 2003
Loan payable to Biogen, due August 2006	$10,000,000	$10,000,000
Loan payable to Biogen, due September 2005	624,000	590,000
Equipment financing obligations	680,000	1,501,000
Other long-term obligations	147,000	426,000
	11,451,000	12,517,000
Less current portion	(1,269,000)	(1,290,000)
	$10,182,000	$11,227,000

Future aggregate principal payments related to long-term obligations are $1,269,000 in 2005, $10,155,000 in 2006, $26,000 in 2007, $1,000 in 2008 and zero in 2009.

During 2001, we borrowed $10.0 million from Biogen to fund our general operations under the terms of an unsecured loan agreement. Outstanding borrowings under this unsecured loan agreement bear interest at the one-year LIBOR rate plus 1%, which is reset quarterly. At December 31, 2004, the interest rate was 4.1%. The loan agreement contains financial covenants establishing limits on our ability to declare or pay cash dividends. In connection with our acquisition of Genovo in 2000, we also assumed a promissory note payable to Biogen. This promissory note has an outstanding principal amount of $650,000 and bears no interest. Upon our assumption of this note, we discounted the note to reflect market interest rates, using an imputed interest rate of 5.6%.

Equipment financing obligations relate to secured financing for the purchase of capital equipment and leasehold improvements. These obligations bear interest at rates ranging from 8.15% to 13.64% and mature from May 2005 to February 2008.

5. Sale of Majority-Owned Subsidiary

On July 27, 2004, Chromos acquired all of the outstanding shares of our majority-owned subsidiary, CellExSys, through a merger between CellExSys and Chromos Inc., a wholly owned subsidiary of Chromos. Under the terms of the merger agreement, Chromos has issued to CellExSys shareholders 1,500,000 shares of Chromos common stock and a secured convertible debenture totaling approximately $3.4 million Canadian (approximately $2.5 million at the time of the closing). The debenture bears annual interest of 2% and is payable in two annual installments on the first and second anniversary of the closing.

Each shareholder of CellExSys received a pro rata distribution of Chromos common stock issued at the time of the merger, and will receive a pro-rata distribution of principal and interest payments received on the debenture. Each shareholder's pro-rata distribution is based on their equity interest in CellExSys as of July 27, 2004, the date of closing. We owned approximately 79% of CellExSys at the time of the merger. The debenture is repayable by Chromos at its option in either cash or by the issuance of shares of Chromos common stock, assuming certain limited conditions are met by Chromos. In combination with the shares of Chromos common stock issued at closing, if the debenture is fully paid in shares of Chromos common stock, the shareholders of CellExSys would receive up to a total of 3.5 million shares of Chromos common stock. If the debenture is fully repaid in common stock by Chromos, our ownership in Chromos could be as high as 12%.

As a result of the sale of our share of CellExSys, we recorded a gain in 2004 which is comprised of the following:

Deposits received from Chromos to fund pre-closing operating costs	$ 502,000
Estimated fair value of consideration received	453,000
Net liabilities assumed by Chromos	51,000
	$1,006,000

Chromos funded $502,000 of CellExSys' operating costs through the closing of the merger and assumed CellExSys' net liabilities as of the merger date of $51,000 consisting primarily of trade and employee payables partially offset by an employee note receivable. We estimated the fair value of the stock and debenture we received based on several factors including the market price and trading volume of Chromos common stock and Chromos' financial and business condition. Based on our review as of December 31, 2004 we do not believe that there is evidence of an impairment in value that warrants adjustment to our carrying value of the merger consideration.

For a limited period of time, we have agreed to provide certain transition services and assistance to CellExSys, which Chromos pays for on a monthly basis and is reflected in revenue.

6. Shareholders' Equity

Purchase of Minority Interest in CellExSys

In February 2004, we issued 158,764 shares of our common stock to Itochu Corporation valued at $375,000 for Itochu's interest in the preferred stock of CellExSys. The carrying value of the minority interest prior to purchase was $750,000. The difference between the carrying value of the minority interest of the value of the common stock issued is reflected as additional paid-in-capital as of December 31, 2004.

Conversion of Series B Convertible Preferred Stock

On March 31, 2004 Elan converted the Series B convertible preferred stock into 4,330,000 shares of our common stock. The Series B preferred stock and accrued dividends were convertible into 4,765,500 shares of our common stock at December 31, 2003 and 4,448,645 shares at December 31, 2002. The conversion of the preferred stock was made in connection with a termination agreement that we entered into with Elan which included, among other things, the conversion of the preferred stock by Elan and us receiving Elan's 19.9% ownership interest in Emerald Gene Systems. We also provided our consent for Elan to sell shares of our common stock that it holds, within certain market volume-based limitations.

Stock Purchase Warrants

In 1999, in connection with a technology license agreement, we issued to Alkermes, Inc. a warrant to purchase 1,000,000 shares of our common stock at an exercise price of $2.50, expiring in June 2007, and a warrant to purchase 1,000,000 shares at an exercise price of $4.16 per share, expiring in June 2009. Both of these warrants were outstanding at December 31, 2004.

Shareholder Rights Plan

In 1996, our Board of Directors adopted a shareholder rights plan. Under our rights plan, each holder of a share of outstanding common stock is also entitled to one preferred stock purchase right. We adopted the rights plan to guard against partial tender offers and other abusive tactics that might be used in an attempt to gain control of Targeted Genetics without paying all shareholders a fair price for their shares. The rights plan will not prevent a change of control, but is designed to deter coercive

takeover tactics and to encourage anyone attempting to acquire us to first negotiate with our board. Generally, if any person or group becomes the beneficial owner of more than 15% of our outstanding common stock (an acquiring person), then each preferred stock purchase right not owned by the acquiring person or its affiliates would entitle its holder to purchase a share of our common stock at a 50% discount, which would result in a significant dilution of the acquiring person's interest in Targeted Genetics. If we or 50% or more of our assets or earnings are thereafter acquired, each right will entitle its holder to purchase a share of common stock of the acquiring entity for a 50% discount.

The shareholder rights plan expires in October 2006. Our board of directors will generally be entitled to redeem the rights for $0.01 per right at any time before a person or group acquires more than 15% of our common stock. In addition, at any time after an acquiring person crosses the 15% threshold but before it acquires us or 50% of our assets or earnings, the board may exchange all or part of the rights (other than those held by the acquiring person) for one share of common stock per right.

Stock Options

We have various stock option plans (Option Plans) that provide for the issuance of nonqualified and incentive stock options to acquire up to 12,979,444 shares of our common stock. These stock options may be granted by our Board of Directors to our employees, directors and officers and to consultants, agents, advisors and independent contractors who provide services to us, or our subsidiaries. The exercise price for incentive stock options shall not be less than the fair market value of the shares on the date of grant. Options granted under our Option Plans expire no later than ten years from the date of grant and generally vest and become exercisable over a four-year period following the date of grant. However in 2003, we granted options to purchase 655,000 shares of our common stock with vesting periods which range from twelve to eighteen months. Each non-employee member of our Board of Directors receives an annual stock option grant to purchase 20,000 shares, which vests over a 12 month period provided that they provide continued service to us.

The following table summarizes activity related to our Option Plans:

	Shares	Weighted Average Exercise Price	Options Exercisable
Balance, January 1, 2002	3,883,833	$4.55	1,861,093
Granted	1,347,500	1.72	
Exercised	(35,053)	1.06	
Forfeited	(756,873)	4.12	
Balance, December 31, 2002	4,439,407	3.80	2,389,393
Granted	1,060,250	0.54	
Exercised	(143,017)	0.88	
Expired	(4,400)	0.55	
Forfeited	(1,254,553)	3.78	
Balance, December 31, 2003	4,097,687	3.07	2,706,127
Granted	2,517,950	1.35	
Exercised	(122,943)	0.43	
Expired	(97,666)	4.81	
Forfeited	(301,970)	3.52	
Balance, December 31, 2004	6,093,058	2.36	3,416,598

The following table summarizes information regarding our outstanding and exercisable options at December 31, 2004:

	Outstanding			Exercisable	
Range of Exercise Prices	Number of Option Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (Years)	Number of Option Shares	Weighted Average Exercise Price
$ 0.29-$ 1.22	1,216,271	$ 0.63	7.72	893,745	$ 0.56
1.26- 1.31	2,165,417	1.31	9.39	252,580	1.31
1.32- 2.25	1,114,349	1.88	5.47	871,050	1.94
2.41- 6.66	1,315,779	4.57	5.59	1,117,981	4.82
8.56- 14.88	278,042	9.38	5.29	278,042	9.38
21.38- 21.38	3,200	21.38	5.16	3,200	21.38

We estimated the fair value of each option on the date of grant using the Black-Scholes pricing model with the following weighted average assumptions:

	2004	2003	2002
Expected dividend rate	Nil	Nil	Nil
Expected stock price volatility range	1.12-1.47	1.47-1.51	1.48
Risk-free interest rate range	2.71-4.47%	1.62-4.19%	2.46-4.80%
Expected life of options	4 years	4 years	4 years
Weighted average fair value (per share) of options granted	$1.27	$0.49	$1.58

Reserved Shares

As of December 31, 2004, we had reserved shares of our common stock for future issuance as follows:

Stock options granted	6,093,058
Available for future stock option grants under Option Plans	4,096,772
Stock purchase warrants	2,000,000
Total shares reserved	12,189,830

7. Collaborative and Other Agreements

We have entered into various relationships with pharmaceutical and biotechnology companies and a non-profit organization to develop our product candidates. Under these partnerships, we typically receive reimbursement for research and development activities performed by us under the

collaboration as well as milestone and upfront payments. Revenues earned under our research and development collaborations are as follows.

	Year Ended December 31,		
	2004	2003	2002
IAVI	$8,340,000	$ 4,409,000	$ 5,662,000
Former collaborations:			
Biogen	—	5,112,000	2,871,000
Wyeth	—	3,894,000	7,543,000
Celltech	—	—	1,280,000
Other	1,312,000	658,000	6,000
	$9,652,000	$14,073,000	$17,362,000

International AIDS Vaccine Initiative Agreement

In February 2000, we entered into a three-year development collaboration with IAVI and Columbus Children's Research Institute at Children's Hospital in Columbus, Ohio to develop a vaccine to protect against the progression of HIV infection to AIDS. This collaboration has been extended through December 2006. Under the terms of the collaboration, IAVI provides funding to us to support development, preclinical studies and manufacturing of product for clinical trials on a cost reimbursement basis. IAVI independently monitors and funds clinical development costs under the collaboration.

Under the terms of the IAVI agreement, we have retained exclusive rights to commercialize any product that results from the collaboration in developed countries and have agreed to manufacture vaccines that result from the collaboration for IAVI to distribute in developing countries. If we decline, or are unable, to produce the vaccine for developing countries in reasonable quantity and at a reasonable price, IAVI has the right to contract with other manufacturers to make the vaccine for use in those countries.

Cystic Fibrosis Foundation Agreement

In July 2003, we established a collaboration with the CF Foundation related to our current Phase II clinical trial for our product candidate for treating cystic fibrosis called tgAAVCF. Under this collaboration, the CF Foundation is providing funding of up to $1.7 million directly to the sites conducting the study to cover their direct trial costs. If tgAAVCF is commercialized, the CF Foundation is entitled to a return on its investment in this clinical trial to be paid out over five years from the date of product commercialization.

Celladon Collaboration

In December 2004, we established a collaboration with Celladon Corporation focused on the development of AAV-based drugs for the treatment of congestive heart failure. In connection with the formation of this collaboration, certain of Celladon's investors purchased 3,954,132 shares of our common stock at $1.52 per share for net proceeds of $6.0 million. The proceeds were recorded in equity at the fair value of the common stock which approximated market value. We have agreed to contribute up to $2 million to support development activities under the Celladon collaboration, which will consist primarily of internal development and manufacturing efforts. We are entitled to receive milestone payments during the development of product candidates under the collaboration as well as royalties and manufacturing profits from the commercialization of product candidates developed under the collaboration.

Former Biogen Collaboration

In September 2000, we established a three-year multiple-product development and commercialization collaboration with Biogen. Upon initiation of the collaboration in 2000, Biogen paid us $8.0 million, which included an upfront technology license of $5.0 million and up-front prepaid research and development funding of $3.0 million. Under this agreement, Biogen provided $3.0 million of additional research and development funding, paid at a minimum rate of $1.0 million per year. We amortized the $8.0 million upfront fee paid by Biogen over the initial research and development collaboration period which ended on September 30, 2003. We recognized revenue on the $1.0 million minimum annual project funding as we performed specified research and development.

As part of this collaboration, Biogen also agreed to provide us with loans of up to $10.0 million and committed to purchase, at our discretion, up to $10.0 million of our common stock. In 2001, we borrowed $10.0 million under the loan commitment. In September 2002, we issued 5,804,673 shares of our common stock to Biogen at a price of approximately $0.69 per share and received proceeds of $4.0 million and in August 2003, we issued 2,515,843 shares of our common stock to Biogen at a price of $1.91 per share and received proceeds of $4.8 million. As of December 31, 2004, Biogen owned approximately 12.1 million shares of our common stock or approximately 14.2% of our total common shares outstanding.

Former Wyeth Collaboration

In November 2000, we entered into a collaboration to develop gene therapy products for treating hemophilia with Wyeth. Under the terms of a research and development funding agreement, Wyeth paid us upfront payments of $5.6 million and ongoing payments for research and development activities performed under the collaboration. In November 2002, Wyeth elected to terminate this collaboration and related agreements. Under the terms of our agreements with Wyeth, all rights that we granted or otherwise extended to Wyeth related to the hemophilia technology have returned to us. In February 2003, we entered into a termination agreement with Wyeth that provided for a $3.2 million cash payment from Wyeth, in payment of an account receivable of $637,000 recorded in 2002 for services performed prior to Wyeth's termination and as a termination settlement of approximately $2.6 million to be recognized as revenue. We also recognized $1.3 million in previously received up front cash payments as revenue upon termination of the Wyeth agreement.

8. Former Emerald Gene Systems Joint Venture

In July 1999, we formed Emerald Gene Systems, Ltd., or Emerald, our joint venture with Elan International Services, Ltd., a wholly-owned subsidiary of Elan Corporation plc, or Elan. We and Elan formed Emerald to develop enhanced gene delivery systems, based on a combination of our gene delivery technologies and Elan's drug delivery technologies. The initial development period for Emerald ended in August 2002 and since then, there have been no operating activities within the joint venture. On March 31, 2004, we entered into a termination agreement with Elan and have dissolved Emerald.

The termination agreement provided for, among other things, our acquisition of Elan's equity interest in Emerald, the termination of technology license agreements between Emerald and both Targeted Genetics and Elan in accordance with the original terms of those license agreements, the full conversion of the Series B preferred stock held by Elan into shares of our common stock, and certain restrictions under which Elan could sell its holdings in our common stock. Elan also waived its right to nominate a director to our Board of Directors. In accordance with the termination agreement the Series B preferred stock was converted into 4.33 million shares of our common stock. As of December 31, 2004 Elan held approximately 12.1 million shares of our common stock or approximately 14.1% of our total common shares outstanding.

Prior to the termination agreement with Elan, we owned 80.1% of Emerald's common and preferred stock and Elan owned the remaining 19.9% of Emerald's common and preferred stock. The common stock of Emerald held by Elan was similar in all respects to the common stock held by us, except that the common shares held by Elan did not have voting rights, but could have been converted into voting common shares at Elan's election. Although we held 100% of the voting stock, Elan and its subsidiaries retained significant minority investor rights that were considered participating rights under EITF Bulletin 96-16, *Investors' Accounting for an Investee When the Investor Has a Majority of the Voting Interest but the Minority Shareholder Has Certain Approval or Veto Rights*. Because Elan's participating rights prevented us from exercising control over Emerald, we did not consolidate the financial statements of Emerald until we became the 100% owner, but instead accounted for our investment in Emerald under the equity method of accounting.

We acquired our 80.1% interest and Elan acquired its 19.9% interest in Emerald in exchange for capital contributions receivable of $12.0 million and $3.0 million, respectively. Both Elan and we licensed intellectual property to Emerald. Emerald valued the technology licensed by Elan to Emerald at $15.0 million, which represented the consideration to be paid under the license agreement. Simultaneous with the formation of the joint venture, we issued to Elan shares of our Series B convertible exchangeable preferred stock valued at $12.0 million. These shares were issued in exchange for Elan's assumption of our capital contribution to Emerald.

We and Elan funded the expenses of Emerald in proportion to our respective ownership interests. Since formation we provided Emerald cash funding totaling $7.5 million which included zero in 2004 and 2003, and $1.9 million in 2002. We and Elan conducted research and development for Emerald and Emerald reimbursed each company for the costs of research and development and related expenses plus a profit percentage. We recorded reimbursements that we received from Emerald as revenue from collaborative agreement with unconsolidated, majority-owned joint venture in the Consolidated Statements of Operations and we recorded the related expenses in research and development expense. Under a convertible note facility provided to us from Elan, we borrowed a total of $8.0 million against this facility to fund our share of Emerald's expenses. During 2003, we converted these loans and $1.4 million of accrued interest payable to Elan into 5,203,244 shares of our common stock in accordance with the original terms of the debt agreement.

9. Commitments

We lease our research and office facilities in Seattle, Washington under two non-cancelable operating leases. The lease on our primary laboratory, manufacturing and office space expires in April 2009 and contains an option to renew the lease for a five-year period. The lease on our administrative office space expires in March 2009, includes two options to extend the lease for a total of five additional years and includes an option to cancel the lease at any time between April 2006 and March 2009 with certain early termination penalties. We lease a facility in Bothell, Washington under a non-cancelable operating lease that expires in September 2015, which was intended to accommodate future manufacturing of our product candidates. We have adopted SFAS No. 146 as it relates to our Bothell facility lease and have recorded accrued restructuring costs of $6.3 million as of December 31, 2004. This accrual represents the present value of future lease payments, net of assumed sublease payments. Future lease payments on our facility in Bothell will reduce the amount

of the accrued restructure charges and are included in future minimum lease payments under non-cancelable operating leases which are as follows:

Year Ending December 31,	
2005	$ 2,138,000
2006	2,336,000
2007	2,364,000
2008	2,392,000
2009	1,622,000
Thereafter	9,200,000
Total minimum lease payments	$20,052,000

Rent expense under operating leases was $1.6 million in 2004, $1.7 million in 2003 and $3.3 million in 2002.

10. Employee Retirement Plan

We sponsor an employee retirement plan under Section 401(k) of the Internal Revenue Code. All of our employees and those of our subsidiaries who meet the minimum eligibility requirements are eligible to participate in the plan. Our matching contributions to the 401(k) plan are made at the discretion of our Board of Directors and were $133,000 in 2004, zero in 2003, and $181,000 in 2002.

11. Income Taxes

At December 31, 2004, we had net operating loss carry-forwards of approximately $150.7 million and research tax credit carry-forwards of $7.0 million. The carry-forwards will begin to expire in 2007 if not utilized, and may be further subject to the application of Section 382 of the Internal Revenue Code of 1986, as amended, as discussed further below. We have provided a valuation allowance to offset the deferred tax assets, due to the uncertainty of realizing the benefits of the net deferred tax asset.

Significant components of our deferred tax assets and liabilities were as follows:

	December 31, 2004	December 31, 2003
Deferred tax assets		
Net operating loss carry-forwards	$ 51,230,000	$ 48,560,000
Capital loss carry-forwards	2,080,000	—
Research and orphan drug credit carry-forwards	7,000,000	6,130,000
Depreciation and amortization	3,270,000	3,380,000
Restructure and other	2,430,000	2,540,000
Gross deferred tax assets	66,010,000	60,610,000
Valuation allowance for deferred tax assets	(66,010,000)	(60,610,000)
Net deferred tax asset	$ —	$ —

The change in the valuation allowance was $5.4 million for 2004 and $8.1 million for 2003. As a result of the sale of CellExSys, which we describe in Note 5 of the Notes to the Consolidated Financial Statements, our deferred tax asset attributable to net operating loss carry-forwards decreased

by $2.3 million compared to the balance as of December 31, 2003 and the tax loss on the sale of CellExSys shares resulted in a capital loss. As we have incurred losses in prior years, this capital loss may only be carried forward to offset future capital gains and will expire after 2009 if not utilized. Our valuation allowance as of December 31, 2004 includes an allowance for this capital loss carry-forward.

Our past sales and issuances of stock have likely resulted in ownership changes as defined by Section 382 of the Internal Revenue Code of 1986, as amended. As a result, the utilization of our net operating losses and tax credits will be limited and a portion of the carry-forwards may expire unused.

12. Condensed Quarterly Financial Information (unaudited)

The following tables present our unaudited quarterly results for 2004 and 2003. The loss in the third quarter of 2004 reflects a $1.0 million gain on the sale of a majority-owned subsidiary. The loss in the first quarter of 2003 reflects a $2.6 million termination settlement payment from Wyeth. The losses in the third quarter of 2003 reflect $2.6 million of revenue from previously deferred payments received from Biogen. We believe that the following information reflects all normal recurring adjustments for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Quarter Ended			
	March 31, 2004	June 30, 2004	September 30, 2004	December 31, 2004
Revenue	$ 1,320,000	$ 2,761,000	$ 2,388,000	$ 3,183,000
Restructure charges	195,000	221,000	381,000	87,000
Loss from operations	(4,862,000)	(4,354,000)	(3,737,000)	(2,217,000)
Net loss	(4,858,000)	(4,450,000)	(2,724,000)	(2,225,000)
Basic and diluted net loss per common share	(0.07)	(0.05)	(0.03)	(0.03)

	Quarter Ended			
	March 31, 2003	June 30, 2003	September 30, 2003	December 31, 2003
Revenue	$5,639,000	$ 2,053,000	$5,002,000	$ 1,379,000
Restructure charges	281,000	2,899,000	374,000	1,636,000
Loss from operations	(520,000)	(6,611,000)	(452,000)	(6,221,000)
Net loss	(830,000)	(6,915,000)	(780,000)	(6,308,000)
Basic and diluted net loss per common share	(0.02)	(0.13)	(0.01)	(0.10)

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.***

None.

Item 9A. ***Controls and Procedures.***

Evaluation of disclosure controls and procedures. Our management evaluated, with the participation of our Chief Executive Officer and our Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms.

Management's annual report on internal control over financial reporting. We are responsible for establishing and maintaining an adequate internal control structure and procedures our financial reporting. We have assessed the effectiveness of internal control over financial reporting as of December 31, 2004. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, Internal Control-Integrated Framework.

Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

(1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect our transactions and dispositions of the assets;

(2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and board of directors; and

(3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Based on using the COSO criteria, we believe our internal control over financial reporting as of December 31, 2004 was effective.

Our independent registered public accounting firm has audited the consolidated financial statements included in this Annual Report on Form 10-K and has issued a report on management's assessment of our internal control over financial reporting as well as on the effectiveness of our internal control over financial reporting, as stated in their report which is included elsewhere herein.

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

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Targeted Genetics Corporation

We have audited management's assessment, included in the accompanying management's annual report on internal control over financial reporting, that Targeted Genetics maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Targeted Genetics Corporation's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that Targeted Genetics Corporation maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Targeted Genetics Corporation maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Targeted Genetics Corporation as of December 31, 2004 and 2003, and the related consolidated statements of operations, preferred stock and shareholders' equity, and cash flows for each of the three years in the period ended December 31, 2004, and our report dated March 3, 2005 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Seattle, Washington
March 3, 2005

PART III

Item 10. *Directors and Executive Officers of Registrant*

The information required by this Item is incorporated by reference to the sections captioned "Proposal One — Election of Directors," "Executive Officers," and "Section 16(a) Beneficial Ownership Reporting Compliance" in the proxy statement for our annual meeting of shareholders to be held on May 26, 2005.

Code of Ethics

We have a Code of Conduct, which applies to all employees, officers and directors of Targeted Genetics. Our Code of Conduct meets the requirements of a "code of ethics" as defined by Item 406 of Regulation S-K, and applies to our Chief Executive Officer, Chief Financial Officer (who is both our principal financial and principal accounting officer), as well as all other employees. Our Code of Conduct also meets the requirements of a code of conduct under Marketplace Rule 4350(n) of the National Association of Securities Dealers, Inc. Our Code of Conduct is posted on our website at http://www.targetedgenetics.com/investor/corp-info.php under the heading "Corporate Governance".

Item 11. *Executive Compensation.*

The information required by this Item with respect to executive compensation is incorporated by reference to the section captioned "Executive Compensation" in the proxy statement for our annual meeting of shareholders to be held on May 26, 2005.

Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Shareholder Matters.*

The information required by this Item with respect to beneficial ownership is incorporated by reference to the section captioned "Principal Shareholders" and "Securities Authorized for Issuance Under Equity Compensation Plans" in the proxy statement for our annual meeting of shareholders to be held on May 26, 2005.

Securities Authorized for Issuance under Equity Compensation Plans. In March 2004, our board of directors approved an increase in the number of shares available for issuance under our 1999 Stock Option Plan from 6,000,000 shares to 9,500,000 shares. The following table lists our equity compensation plans, including individual compensation arrangements, under which equity securities are authorized for issuance as of December 31, 2004:

	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans
Equity compensation plans approved by security holders	6,093,058	$2.36	4,096,772
Equity compensation plans not subject to approval by security holders	2,000,000	3.33	—
Total	8,093,058	$2.60	4,096,772

In 1999, in connection with a technology license agreement, we issued to Alkermes, Inc. a warrant to purchase 1,000,000 shares of our common stock at an exercise price of $2.50 per share, expiring in June 2007, and a warrant to purchase 1,000,000 shares of our common stock at an exercise price of $4.16 per share, expiring in June 2009. These warrants are presented in the table above as "Equity compensation plans not subject to approval by security holders."

Item 13. ***Certain Relationships and Related Transactions.***

The information required by this Item with respect to certain relationships and related-party transactions is incorporated by reference to the sections captioned "Executive Compensation — Change of Control Arrangements" and "Executive Compensation — Arrangements with Management" in the proxy statement for our annual meeting of shareholders to be held on May 26, 2005.

Item 14. ***Principal Accountant Fees and Services.***

The information required by this Item with respect to principal accountant fees and services is incorporated by reference to the section captioned "Proposal Three — Ratification of Independent Auditors" in the proxy statement for our annual meeting of shareholders to be held on May 26, 2005.

PART IV

Item 15. ***Exhibits, Financial Statement Schedules and Reports on Form 8-K.***

1. ***Financial Statements***

The following consolidated financial statements are submitted in Part II, Item 8 of this annual report:

2. ***Financial Statement Schedules***

All financial statement schedules have been omitted because the required information is either included in the consolidated financial statements or the notes thereto or is not applicable.

3. *Exhibits*

3.1	Amended and Restated Articles of Incorporation (Exhibit 3.1)	(S)
3.2	Amended and Restated Bylaws (Exhibit 3.2)	(D)
4.1	Rights Agreement, dated as of October 17, 1996, between Targeted Genetics and ChaseMellon Shareholder Services (Exhibit 2.1)	(C)
4.2	First Amendment of Rights Agreement, dated July 21, 1999, between Targeted Genetics and ChaseMellon Shareholder Services (Exhibit 1.9)	(J)
4.3	Second Amendment to Rights Agreement, dated September 25, 2002, between Targeted Genetics and Mellon Investor Services LLC (formerly known as ChaseMellon Investor Services L.L.C.) (Exhibit 10.1)	(T)
4.4	Third Amendment to Rights Agreement, dated January 23, 2003, between Targeted Genetics and Mellon Investor Services LLC (Exhibit 4.4)	(V)
4.5	Fourth Amendment to Rights Agreement, dated as of September 2, 2003, between Targeted Genetics and Mellon Investor Services LLC (Exhibit 4.1)	(Y)
10.1	Form of Indemnification Agreement between Targeted Genetics and its officers and directors (Exhibit 10.1)	(K)
10.2	Form of Senior Management Employment Agreement between the registrant and its executive officers (Exhibit 10.2)	(D)
10.3	Gene Transfer Technology License Agreement, dated as of February 18, 1992, between Immunex Corporation and Targeted Genetics* (Exhibit 10.3)	(K)
10.4	PHS Patent License Agreement — Non-Exclusive, dated as of July 13, 1993, between National Institutes of Health Centers for Disease Control and Targeted Genetics* (Exhibit 10.4)	(K)
10.5	Patent License Agreement, dated as of December 25, 1993, between The University of Florida Research Foundation, Inc. and Targeted Genetics* (Exhibit 10.5)	(K)
10.6	PHS Patent License Agreement — Exclusive, dated as of March 10, 1994, between National Institutes of Health Centers for Disease Control and Targeted Genetics* (Exhibit 10.10)	(E)
10.7	License Agreement, dated as of March 28, 1994, between Targeted Genetics and the University of Michigan* (Exhibit 10.13)	(E)
10.8	Patent and Technology License Agreement, effective as of March 1, 1994, between the Board of Regents of the University of Texas M.D. Anderson Cancer Center and RGene Therapeutics, Inc.* (Exhibit 10.29)	(A)
10.9	First Amended and Restated License Agreement, effective as of October 12, 1995, between The University of Tennessee Research Corporation and RGene Therapeutics, Inc.* (Exhibit 10.30)	(A)
10.10	Amendment to First Amended and Restated License Agreement, dated as of June 19, 1996, between The University of Tennessee Research Corporation and RGene Therapeutics, Inc.* (Exhibit 10.1)	(B)
10.11	Second Amendment to First Amended and Restated License Agreement, dated as of April 17, 1998, between The University of Tennessee Research Corporation and RGene Therapeutics, Inc.* (Exhibit 10.16)	(G)
10.12	License Agreement, dated as of March 15, 1997, between the Burnham Institute and Targeted Genetics* (Exhibit 10.23)	(E)
10.13	Exclusive Sublicense Agreement, dated June 9, 1999, between Targeted Genetics and Alkermes, Inc.* (Exhibit 10.36)	(I)
10.14	Amendment No. 2 to Exclusive Sublicense Agreement, dated as of May 29, 2003, between Targeted Genetics and Alkermes, Inc.* (Exhibit 10.1)	(X)
10.15	Master Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.1)	(H)
10.16	License and Collaboration Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.2)	(H)

10.17	Supply Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.3)	(H)
10.18	Credit Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva PLC (Exhibit 1.5)	(H)
10.19	Funding Agreement, dated as of July 21, 1999, among Targeted Genetics, Elan International Services, Ltd., and Elan Corporation, plc (Exhibit 1.3)	(J)
10.20	Subscription, Joint Development and Operating Agreement, dated as of July 21, 1999, among Elan Corporation, plc, Elan International Services, Ltd., Targeted Genetics and Targeted Genetics Newco, Ltd.* (Exhibit 1.4)	(J)
10.21	Convertible Promissory Note, dated July 21, 1999, issued by Targeted Genetics to Elan International Services, Ltd. (Exhibit 1.5)	(J)
10.22	License Agreement dated July 21, 1999, between Targeted Genetics Newco, Ltd. and Targeted Genetics* (Exhibit 1.6)	(J)
10.23	License Agreement, dated July 21, 1999, between Targeted Genetics Newco, Ltd. and Elan Pharmaceutical Technologies, a division of Elan Corporation, plc* (Exhibit 1.7)	(J)
10.24	Office Lease, dated as of October 7, 1996, between Benaroya Capital Company, LLC and Targeted Genetics (Exhibit 10.26)	(D)
10.25	First Lease Amendment, dated May 12, 1997, between Targeted Genetics and Benaroya Capital Company, LLC (Exhibit 10.1)	(R)
10.26	Second Lease Amendment, dated February 25, 2000, between Targeted Genetics and Benaroya Capital Company, LLC (Exhibit 10.2)	(R)
10.27	Third Lease Amendment, dated April 19, 2000, between Targeted Genetics and Benaroya Capital Company, LLC (Exhibit 10.3)	(R)
10.28	Fourth Lease Amendment, dated March 28, 2001, between Targeted Genetics and Benaroya Capital Company, LLC (Exhibit 10.4)	(R)
10.29	Fifth Lease Amendment, dated January 2, 2004, between Targeted Genetics and Benaroya Capital Company, LLC* (Exhibit 10.3)	(AA)
10.30	Canyon Park Building Lease, dated as of June 30, 2000, between Targeted Genetics and CarrAmerica Corporation (Exhibit 10.1)	(L)
10.31	Olive Way Building Lease, dated as of November 20, 1993, as amended, between Targeted Genetics and Ironwood Apartments, Inc. (successor in interest to Metropolitan Federal Savings and Loan Association) (Exhibit 10.29)	(K)
10.32	Fifth Amendment to Lease Agreement, dated as of June 20, 2003, between Targeted Genetics and Ironwood Apartments, Inc. (Exhibit 10.2)	(X)
10.33	Sixth Amendment to Lease Agreement, dated as of November 1, 2003, between Targeted Genetics and Ironwood Apartments, Inc.* (Exhibit 10.1)	(AA)
10.34	1992 Restated Stock Option Plan (Exhibit 99.1)	(F)
10.35	Stock Option Plan for Nonemployee Directors (Exhibit 10.34)	(E)
10.36	1999 Restated Stock Option Plan, as restated on January 23, 2001 (Exhibit 10.2)	(Q)
10.37	2000 Genovo Inc. Roll-Over Stock Option Plan (Exhibit 99.1)	(O)
10.38	Agreement and Plan of Merger dated as of August 8, 2000, among Targeted Genetics, Inc., Genovo, Inc., TGC Acquisition Corporation and Biogen, Inc.* (Exhibit 2.1)	(M)
10.39	Development and Marketing Agreement, dated as of August 8, 2000, between Targeted Genetics, Genovo, Inc. and Biogen, Inc. (Exhibit 10.1)	(N)
10.40	Funding Agreement dated as of August 8, 2000, between Targeted Genetics and Biogen, Inc. (Exhibit 10.2)	(N)
10.41	Amendment to Funding Agreement, dated as of July 14, 2003, between Targeted Genetics and Biogen, Inc. (Exhibit 10.3)	(X)
10.42	Product Development Agreement, dated as of November 9, 2000, between Targeted Genetics and Genetics Institute, Inc.* (Exhibit 10.1)	(P)
10.43	Supply Agreement, dated as of November 9, 2000, between Targeted Genetics and Genetics Institute, Inc.* (Exhibit 10.2)	(P)

10.44	Amendment No. 1 to Product, Development and Supply Agreement, dated February 24, 2003, between Genetics Institute LLC (formerly known as Genetics Institute, Inc.) and Targeted Genetics* (Exhibit 10.41)	(V)
10.45	Industrial Collaboration Agreement, dated as of February 1, 2000, between the International Aids Vaccine Initiative, Inc., Children's Research Institute and Targeted Genetics* (Exhibit 10.1)	(U)
10.46	Amendment No. 1 to Industrial Collaboration Agreement, dated as of March 14, 2003, among the International Aids Vaccine Initiative, Inc., Children's Research Institute and Targeted Genetics* (Exhibit 10.42)	(V)
10.47	Amendment No. 2 to Industrial Collaboration Agreement, dated August 1, 2003, among Targeted Genetics, International Aids Vaccine Initiative, Inc. and Children's Research Institute* (Exhibit 10.2)	(Z)
10.48	Amendment No. 3 to Industrial Collaboration Agreement, dated December 2, 2003, among Targeted Genetics, International Aids Vaccine Initiative, Inc. and Children's Research Institute* (Exhibit 10.2)	(AA)
10.49	Settlement and Termination Agreement, dated as of December 19, 2002, between Celltech Pharmaceuticals Inc., Medeva Limited and Targeted Genetics (Exhibit 10.40)	(V)
10.50	Biological Processing Services Agreement, dated as of March 28, 2003, between GenVec, Inc. and Targeted Genetics* (Exhibit 10.1)	(W)
10.51	Study Funding Agreement, dated as of April 23, 2003, between Targeted Genetics and Cystic Fibrosis Foundation Therapeutics, Inc.* (Exhibit 10.2)	(W)
10.52	Amendment Agreement to Exclusive Sublicense Agreement, dated as of March 12, 2002, between Targeted Genetics and Alkermes, Inc.*	
10.53	Common Stock and Warrants Issuance Agreement, dated June 9, 1999, by and between Targeted Genetics and Alkermes, Inc. (Exhibit 10.37)	(I)
10.54	Warrant Agreements, dated June 9, 1999, by and between Targeted Genetics and Alkermes, Inc. (Exhibit 10.38)	(I)
10.55	Registration Rights Agreement, dated as of July 21, 1999, by and among the Company and EIS.	(J)
10.56	Collaboration Agreement, dated December 31, 2004, between Targeted Genetics and Celladon Corporation.*	
10.57	Manufacturing Agreement, dated December 31, 2004, between Targeted Genetics and Celladon Corporation.*	
10.58	Common Stock Purchase Agreement, dated December 31, 2004, by and among Targeted Genetics, Enterprise Partners and Venrock Partners.	
21.1	Subsidiaries of Targeted Genetics	
23.1	Consent of Independent Registered Public Accounting Firm	
31.1	Section 302 Certification of Chief Executive Officer	
31.2	Section 302 Certification of Chief Financial Officer	
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002	

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* Portions of these exhibits have been omitted based on a grant of or application for confidential treatment from the SEC. The omitted portions of these exhibits have been filed separately with the SEC.

(A) Incorporated by reference to the designated exhibit included with Targeted Genetics' Registration Statement on Form S-1 (No. 333-03592) filed on April 16, 1996, as amended.

(B) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended June 30, 1996, filed on August 12, 1996.

(C) Incorporated by reference to Targeted Genetics' Registration Statement on Form 8-A filed on October 22, 1996.

(D) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K (No. 0-23930) for the year ended December 31, 1996, filed on March 17, 1997.

(E) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K (No. 0-23930) for the year ended December 31, 1997, filed on March 31, 1998.

(F) Incorporated by reference to the designated exhibit included with Targeted Genetics' Registration Statement on Form S-8 (No. 333-58907), filed on July 10, 1998.

(G) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K (No. 0-23930) for the year ended December 31, 1998, filed on March 10, 1999.

(H) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on January 6, 1999.

(I) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended June 30, 1999, filed on August 5, 1999.

(J) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on August 4, 1999.

(K) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K (No. 0-23930) for the year ended December 31, 1999, filed on March 23, 2000.

(L) Incorporated by reference to Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended June 30, 2000, filed on August 11, 2000.

(M) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on August 23, 2000.

(N) Incorporated by reference to the designated exhibit included with Targeted Genetics Current Report on Form 8-K (No. 0-23930) filed on September 13, 2000.

(O) Incorporated by reference to the designated exhibit included with Targeted Genetics' Registration Statement on Form S-8 (No. 333-48220), filed on October 19, 2000.

(P) Incorporated by reference to the designated exhibit included with Targeted Genetics Current Report on Form 8-K (No. 0-23930) filed on February 21, 2001.

(Q) Incorporated by reference to Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended March 31, 2001, filed on May 11, 2001.

(R) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended June 30, 2001, filed on August 14, 2001.

(S) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended June 30, 2002, filed on August 14, 2002.

(T) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on October 11, 2002.

(U) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended September 30, 2002, filed on October 14, 2002.

(V) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K (No. 0-23930) for the year ended December 31, 2002, filed on March 27, 2003.

(W) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended March 31, 2003, filed on May 15, 2003.

(X) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on July 22, 2003.

(Y) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on October 1, 2003.

(Z) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q (No. 0-23930) for the period ended September 30, 2003, filed on October 31, 2003.

(AA) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K (No. 0-23930) filed on January 13, 2004.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized in the city of Seattle, state of Washington, on March 1, 2005.

TARGETED GENETICS CORPORATION

By: /s/ H. STEWART PARKER
H. Stewart Parker
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints H. Stewart Parker and Todd E. Simpson, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file, any and all amendments to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ H. STEWART PARKER H. Stewart Parker	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2005
/s/ TODD E. SIMPSON Todd E. Simpson	Vice President, Finance and Administration and Chief Financial Officer, Secretary and Treasurer (Principal Financial and Accounting Officer)	March 1, 2005
/s/ JEREMY L. CURNOCK COOK Jeremy L. Curnock Cook	Chairman of the Board	March 1, 2005
/s/ JACK L. BOWMAN Jack L. Bowman	Director	March 1, 2005
/s/ JOSEPH M. DAVIE, PH.D., M.D. Joseph M. Davie, Ph.D., M.D.	Director	March 1, 2005
/s/ LOUIS P. LACASSE Louis P. Lacasse	Director	March 1, 2005
/s/ NELSON L. LEVY, PH.D., M.D. Nelson L. Levy, Ph.D., M.D.	Director	March 1, 2005
/s/ MARK H. RICHMOND, PH.D. Mark H. Richmond, Ph.D.	Director	March 1, 2005

Corporate Information

Board of Directors

Jeremy L. Curnock Cook
Chairman, Targeted Genetics
Executive Chairman
Bioscience Managers Limited

Jack L. Bowman
Former Group Chairman
Johnson & Johnson

Joseph M. Davie, Ph.D., M.D.
Former Senior Vice President,
Research
Biogen, Inc.

Louis P. Lacasse
President
GeneChem Management, Inc.

Nelson L. Levy, Ph.D., M.D.
Former President
Fujisawa Pharmaceutical Company

H. Stewart Parker
President and Chief Executive Officer
Targeted Genetics Corporation

Mark H. Richmond, Ph.D., D.Sc.
Former Director of Research
Glaxo plc

Management

H. Stewart Parker
President and Chief Executive Officer

Barrie J. Carter, Ph.D.
Executive Vice President
Chief Scientific Officer

Todd E. Simpson
Vice President, Finance & Administration
Chief Financial Officer

Pervin Anklesaria, Ph.D.
Vice President, Product Development

Richard W. Peluso, Ph.D.
Vice President, Process Sciences
and Manufacturing

B.G. Susan Robinson
Vice President, Business Development

Jonathan K. Wright, J.D.
General Counsel

Haim Burstein, Ph.D.
Senior Director, Product Discovery

Kim Wieties Clary, Ph.D.
Senior Director, Intellectual Property

David J. Poston
Senior Director, Finance

Stacie D. Byars
Director, Communications

Kenneth D. Hammer
Director, Operations

Alison E. Heald, M.D.
Director, Clinical Affairs

Ralph W. Paul, Ph.D.
Director, Technology Evaluation

Rae M. Saltzstein
Director, Quality and Regulatory Affairs

Ryan K. Takeya
Director, Manufacturing

Barbara A. Thorne, Ph.D.
Director, Process Development

Corporate Headquarters

Targeted Genetics Corporation
1100 Olive Way, Suite 100
Seattle, Washington 98101
Telephone 206.623.7612
www.targetedgenetics.com

Transfer Agent and Registrar

Mellon Investor Services
85 Challenger Road
Ridgefield Park, New Jersey 07660
Telephone 1.800.522.6645

Shareholder Inquiries

Inquiries regarding the company and its activities may be directed to the Communications Department at 206.521.7392 or info@targen.com. Inquiries concerning stock and transfer requirements, lost certificates and changes of address should be directed to the transfer agent.

Legal Counsel

Orrick, Herrington & Sutcliffe LLP
Seattle, Washington

Independent Auditors

Ernst & Young LLP
Seattle, Washington

Corporate Information

News releases, corporate governance documents and SEC filings are available on the Internet at www.targetedgenetics.com.

Stock Listing

Targeted Genetics' common stock is traded on the Nasdaq SmallCap Market under the symbol TGEN.

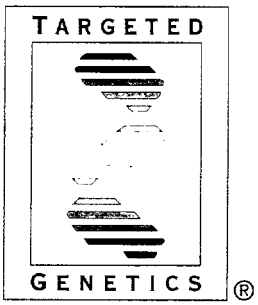
Common Stock

As of March 1, 2005, there are approximately 24,000 holders of Targeted Genetics' common stock. Targeted Genetics has never paid dividends and the company does not anticipate paying dividends in the foreseeable future.

Annual Meeting

The annual meeting of shareholders will be held at 9:00 a.m. on Thursday, May 26, 2005, at the Washington Athletic Club, 1325 Sixth Avenue, Seattle, Washington.

This Annual Report contains forward-looking statements. Forward-looking statements are based on the opinions and estimates of management at the time the statements are made and are subject to known and unknown risks and uncertainties and inaccurate assumptions that could cause actual results to differ materially from those expected or implied by the forward-looking statements. Our actual results could differ materially from those anticipated in the forward-looking statements for many reasons, including the risks described under "Factors Affecting Our Operating Results, Our Business and Our Stock Price" in our Annual Report on Form 10-K for the year ended December 31, 2004, and in the filings we make with the Securities and Exchange Commission from time to time. You should not place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report.



Targeted Genetics
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