TARGETED GENETICS CORP /WA/
Form 10-K/A
August 14, 2002
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K/A
Amendment No. 1

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

For the fiscal year ended December 31, 2001

OR

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

For the transition period from to
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, $.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 x No ¨

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

Indicate the aggregate market value of voting stock held by nonaffiliates of the Registrant as of August 1, 2002: $39,942,000

Indicate the number of shares outstanding of each of the Registrant s classes of common stock as of August 1, 2002:

Title of Class	Number of shares
Common Stock, $0.01 par value	44,158,730

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 9, 2002. The definitive proxy statement will be filed with the Securities and Exchange Commission within 120 days after December 31, 2001, the end of the fiscal year to which this report relates.

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Explanatory Note

Targeted Genetics files this amendment to its Annual Report on Form 10-K/A for the year ended December 31, 2001 to reflect a restatement of its financial statements related to the classification of its Series B convertible exchangeable preferred stock outside of permanent equity and the elimination of dividends on such preferred stock in the computation of net loss per common share. Targeted Genetics filed the original Form 10-K for the year ended December 31, 2001 on March 21, 2002. Unless otherwise indicated, all information is as of December 31, 2001.

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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 believes, expects, anticipates, intends and other words of similar meaning 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.

Overview

Targeted Genetics Corporation was incorporated in the State of Washington in 1989 and 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 inserting genes into target cells and activating the inserted gene 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 genes into cells, processes to manufacture gene delivery product candidates and other proprietary technologies and processes. In addition, we have established expertise and development capabilities focused in the areas of preclinical research and biology, 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 insert genetic material into target cells. Our proprietary vector technologies include both viral vector technologies and synthetic vector technologies. Our viral vector development activities, which use modified viruses to deliver genes into cells, focus primarily on adeno-associated virus, or AAV, a common human 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 of our potential gene therapy products. Our synthetic vectors deliver genes using lipids, which are fatty, water-insoluble organic substances that can be absorbed through cell membranes. We believe that synthetic vectors may provide a number of gene delivery advantages for repeated, efficient delivery of therapeutic genes into rapidly dividing cells, such as certain types of tumor cells. We believe that using both viral and synthetic approaches provides advantages in our corporate partnering efforts and increases the probability of our potential products reaching the market.

We have two lead product candidates under development, one for treating cystic fibrosis and another for treating cancer. We also have a pipeline of product candidates focused on treating hemophilia, arthritis and cancer, as well as lysosomal storage disorders, which are a class of genetic diseases in which missing enzymes cause a buildup of metabolic byproducts in tissue. We are also developing a vaccine candidate for the prevention of AIDS. We have entered into six partnering relationships with pharmaceutical and biotechnology companies and a public health organization to develop these product candidates. In each of our partnerships, we have retained a substantial financial interest in the sales of any commercial products that result from our work. Through our partnership activities and other internally funded efforts, we have successfully advanced our product candidates into clinical development, including Phase II clinical trials for our lead cystic fibrosis and cancer product candidates. In

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addition, we have developed processes to manufacture our potential products at a scale amenable to clinical development and expandable to large-scale production for commercialization, pending successful completion of clinical trials and regulatory approval. We believe that these successes in assembling a broad platform of proprietary intellectual property for developing and manufacturing potential products and in establishing collaborative relationships and advancing our potential products to clinical evaluation serve to demonstrate the value of our intellectual property and our potential to develop gene therapy product candidates to treat a range of diseases.

Our business strategy reflects the following five key elements:

Develop multiple gene delivery systems to maximize product opportunities. We believe 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. Accordingly, we are developing both viral and synthetic vector technologies. Our primary viral vector development activities focus on AAV vectors, which we and others have shown to be efficient in transferring genes to a wide variety of target cells. Because AAV vectors can deliver genes 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, hemophilia and arthritis, which require long-term expression of the gene that is delivered to the cell. Additionally, the long-term expression profile of AAV vectors may support the development of vaccines capable of conferring long-term protection against a number of infectious diseases. Our synthetic vectors deliver genes 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 we are the only company that has advanced product candidates using both viral and synthetic vectors into Phase II clinical trials. We believe that using both types of vectors gives us one of the broadest 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 for two other viruses, retroviruses and adenoviruses, that can be used to deliver genes into cells.

Build a strong product development infrastructure. Although a great deal of research has been focused on gene discovery, much less research has been focused on gene delivery techniques and on creating the product development infrastructure that is necessary to convert gene discovery into products that can be evaluated in clinical trials and applied to patient care. We have therefore focused significant efforts on establishing product development expertise in the areas of preclinical research and biology, manufacturing process development and scale-up, quality control, quality assurance, regulatory affairs and clinical trials. We believe that our product development focus provides advantages in our corporate partnering efforts and increases our probability of reaching the market with products having a higher likelihood of becoming commercially successful.

Demonstrate clinical proof of concept. We believe that by providing strong evidence of the clinical benefit of our products, we can significantly enhance shareholder value. We have two lead product candidates that we believe could potentially demonstrate clinical proof of concept in the near term: tgAAVCF for treating cystic fibrosis and tgDCC-E1A for treating cancer. Both of these products entered Phase II clinical trials in late 2000 and we expect to have data available to us in 2002. We believe that clinical proof of concept data in our cystic fibrosis and cancer programs would demonstrate both the value of these two lead product candidates and the broader value of our AAV and synthetic gene delivery technologies.

Build a strong pipeline of product candidates with significant market potential. We believe that there is significant long-term potential for using our gene delivery systems to treat additional diseases. The infrastructure we have built to support the development of our tgAAVCF and tgDCC-E1A product candidates is available to support the development of new products based on our viral and synthetic gene delivery systems. We believe that we may derive significant future value by applying this infrastructure and the knowledge and expertise we gain in developing our two initial product candidates to our additional product candidates under development. Currently, we have ongoing preclinical product development activities in the areas of cancer, arthritis, hemophilia, lysosomal storage disorders and AIDS prophylaxis.

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Establish product development partnerships that allow for long-term value retention. We believe that our products under development have significant long-term potential. We now have collaborative programs underway with six large pharmaceutical and biotechnology companies and a public health organization. In all of these partnerships, we have retained a substantial financial interest in the sales of any commercial products that may result from our work. For products based on our AAV delivery system, we have retained manufacturing rights to any product candidates we develop. We have retained worldwide commercial rights to our tgDCC-E1A product candidate and plan to develop the product internally or through a collaborative relationship that will allow us to achieve substantial long-term participation in tgDCC-E1A s potential downstream commercial revenue.

The following table summarizes our product development programs:

Program/Product	Research	Preclinical	Phase I	Phase II	Phase III	Collaborator
AAV Vectors:						
Cystic Fibrosis						Celltech Group
Arthritis						
Hemophilia A						Wyeth/Genetics Institute
Lysosomal Storage Disorders						Genzyme
AIDS Prophylaxis						IAVI
Hyperlipidemia						
Synthetic Vectors:						
Head and Neck Cancer						
Ovarian Cancer						
Metastatic Cancer						
Adenoviral Vectors:						
Glioma						Biogen

Clinical Product Development Programs

tgAAVCF for Cystic Fibrosis

Cystic fibrosis is one of the most common single-gene deficiencies affecting the Caucasian population, afflicting approximately 30,000 people in the United States and 60,000 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, loss of lung function and early death. Current treatments for cystic fibrosis relieve only the symptoms of the disease, and cannot cure the disease or stop its progression.

Our cystic fibrosis product candidate, designated tgAAVCF, is comprised of a complete functional CFTR human gene delivered in an AAV vector. The objective of this gene therapy is to deliver a functional copy of the CFTR gene that 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-based approaches for treating cystic fibrosis, because the drug appears to have a good safety profile and an ability to deliver the CFTR gene to the appropriate cells in the lung and support production of the missing protein over an extended period. In preclinical studies, we have observed delivery of the CFTR gene in up to 50% of the targeted airway cells and expression of the CFTR gene in the lung for periods of up to six months with no side effects.

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Our early clinical trials involved the administration of tgAAVCF to the lung, nose or sinus of over 60 patients. The results of the trials indicated that the product was safe and well-tolerated with no significant inflammatory response or other side effects, even after repeat delivery. Additionally, in a clinical trial involving administration of the product to the maxillary sinus, we observed:

- dose-dependent gene transfer;
- persistence of the gene for up to 70 days after treatment;
- improvements in lung function measurements of chloride transport in biopsied cells after treatment; and
- reduction of sinus inflammation, as assessed by changes in levels of certain cytokines and immunoregulatory substances secreted by cells of the immune system.

In 1998, we entered into a license and collaboration agreement related to tgAAVCF with Medeva Pharmaceuticals, Inc., now a wholly owned subsidiary of Celltech Group plc. Under these agreements, Celltech owns exclusive worldwide marketing rights to tgAAVCF and provides significant funding to us. The section below entitled Research and Development Collaborations provides a detailed description of this relationship.

In 2000, we completed a Phase I clinical trial to test the safety of aerosol delivery of tgAAVCF to the lungs of cystic fibrosis patients. We treated 12 cystic fibrosis patients with a single dose of tgAAVCF in a dose escalation study. Data from this trial suggest that tgAAVCF delivered via a nebulizer was well tolerated and had a good safety profile at all doses evaluated. Additionally, we observed delivery of the CFTR gene to target cells in all patients at the highest dose and indications that tgAAVCF was well distributed throughout the upper airways of the patients. We also observed vector gene transfer in some patients 90 days after the single administration of aerosolized tgAAVCF. tgAAVCF has been granted orphan drug status by the United States Food and Drug Administration, or FDA, which provides for seven years of market exclusivity.

In November 2000, we began a Phase II clinical trial to explore the safety and clinical impact of repeated doses of aerosolized tgAAVCF delivered to the lungs of adult and adolescent cystic fibrosis patients. This double-blind, placebo-controlled trial will also evaluate the impact of tgAAVCF on lung function, lung inflammatory proteins and lung bacteria in patients with cystic fibrosis. We are conducting this trial in connection with the Cystic Fibrosis Foundation, the largest cystic fibrosis patient advocacy organization in the world. During 2001, an independent data and safety monitoring board that periodically reviews the safety profile of tgAAVCF for this trial allowed us to reduce the entry age criteria for patients that may be enrolled into this trial from 18 years of age to 15 years of age, and then subsequently reduce the entry age to 12 years of age. Because cystic fibrosis is a progressive disease, reducing the age criteria for patients in this trial will allow us to treat patients at an earlier stage of the disease, which we believe may better enable us to halt or significantly slow the development of lung damage. We plan to complete enrollment of patients into this trial and evaluate the trial results during 2002.

tgDCC-E1A for Cancer

Cancer is the second leading cause of death in the United States, with over one million new cases diagnosed each year. Cancer arises from the disruption of normal cell growth and division, which are regulated by cellular proteins and genes. Cancer can result from the structural alteration or abnormal expression of these genes or from mutation, or deletion, of tumor inhibitor genes.

In 1996, we acquired the rights to the E1A gene, which is derived from a common virus. E1A regulates the expression of viral and cellular genes within cells infected by the virus. 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 and radiation. To deliver the E1A gene into human cells, we have combined E1A with two of our proprietary lipid-based vectors, DCC-Cholesterol and LPD (lipids, which are fats, polycations, which are compounds with multiple positive charges and DNA) to create two potential delivery systems for the E1A gene. We believe these delivery systems may have the necessary characteristics for repeated and efficient delivery of the E1A gene into rapidly dividing cells, such as tumor cells.

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Our product candidate for treating cancer is based on the E1A gene. We have exclusive worldwide rights to issued patents covering the use of the E1A gene in cancer therapy. Research data indicate that E1A can function as an inhibitor of the HER-2/neu oncogene, which is known to be over-expressed in many cancers. Research also indicates that E1A has anti-tumor effects unrelated to the inhibition of HER-2/neu expression. For example, our preclinical studies of our tgDCC-E1A product candidate in mice with tumors indicate that tgDCC-E1A inhibits expression of the HER-2/neu oncogene, inhibits growth and metastasis of the tumor cells and increases significantly the long-term survival of the mice. Other preclinical studies indicate that tgDCC-E1A sensitizes tumor cells to certain chemotherapeutic agents or radiation used to destroy the tumor cell.

We completed a series of Phase I and Phase II clinical trials of our tgDCC-E1A product candidate as a single agent in several different cancers before testing the product candidate in combination with chemotherapy and radiation treatments. In these trials, we delivered tgDCC-E1A into the peritoneal cavity of ovarian cancer patients and into the pleural cavity of breast cancer patients. The results indicated that clinicians could safely administer the drug in biologically active amounts and that the E1A gene was present and active in tumor cells. Additionally, in some patients, we observed decreased levels of HER-2/neu expression and decreased numbers of tumor cells.

In Phase I and Phase II clinical trials in head and neck cancer patients who had failed to respond to previous chemotherapy and radiation treatments, we delivered tgDCC-E1A as a single agent by direct injection into their tumors. The results of these trials also indicated that clinicians could safely administer the drug in biologically active amounts and that the E1A gene was present and active in tumor cells.

In late 1999, we began the first clinical trial of tgDCC-E1A administered in combination with chemotherapeutic drugs. In this Phase I clinical trial, we are treating advanced-stage ovarian cancer patients with a combination of tgDCC-E1A and two chemotherapy products, Taxol® and Cisplatin, at increasing dosage levels. tgDCC-E1A and Cisplatin are administered directly to the peritoneal cavity and Taxol® is administered intravenously. This trial is designed to evaluate drug safety and to assess maximum tolerable dose levels, as well as measure the biologic activity of E1A. We anticipate presenting preliminary data from this clinical trial in mid-2002.

In late 2000, we began a multi-center Phase II clinical trial of tgDCC-E1A administered together with radiation therapy to patients with recurrent or inoperable head and neck cancer. We are treating patients with twice-weekly injections of tgDCC-E1A throughout six to seven weeks of radiation therapy. Primary endpoints of this trial include tumor response, as measured by CT scan 12 weeks following completion of therapy, and safety and tolerability of tgDCC-E1A in combination with radiation. Other endpoints include time-to-progression of treated tumors, length of relapse-free periods, overall survival rates and comparison of responses of tumor sites treated with both tgDCC-E1A and radiation to tumors treated with radiation alone. We plan to perform an interim data analysis for this trial upon completing treatment of several patients in this trial.

For a description of research and development expenses related to our clinical development programs, see the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations Results of Operations in Part II, Item 7 of this annual report.

Preclinical Product Development Programs

Rheumatoid 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 20 and 45. Direct and indirect costs associated with RA cost the U.S. economy nearly $65 billion per year. 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 TNFa plays a pivotal role in this disease process and have validated anti-TNFa therapies as a valuable strategy to treat RA. RA is currently treated with protein therapies such as Immunex Corporation s Enbrel®, a variety of systemic treatments, including steroid and nonsteroid anti-inflammatory drugs, and other drugs such as methotrexate, cyclosporine, and other monoclonal antibody therapies such as Remicade®.

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We believe that local administration of DNA sequence encoding anti-TNFa proteins may be a potentially useful alternative to systemic administration of anti-TNFa proteins for treating RA and other inflammatory diseases. The characteristics of AAV vectors make them well suited for delivery of genes to joints and other local environments. We are developing an AAV-based product as a potential alternative or supplement to systemic protein therapy in patients with RA symptoms limited to one or several joints, or in situations where systemic delivery of the protein therapy may not be possible.

We have administered AAV-ratTNFR:Fc, a vector carrying the DNA sequence that expresses a soluble form of protein that binds TNFa, to the muscle or the joint of rats with experimentally induced RA. Data from these studies show that a single administration of AAV-ratTNFR:Fc to one ankle joint suppressed joint inflammation, pannus formation (inflammatory cells) and cartilage and bone damage in the treated ankle.

Hemophilia A

Hemophilia A is a hereditary disorder caused by the absence or severe deficiency of Factor VIII, a blood protein that is essential for proper coagulation. According to the National Hemophilia Foundation, approximately 14,000 people in the United States suffer from hemophilia A. Hemophilia A patients face 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 Factor VIII protein. If slow, chronic bleeding is not treated, progressive, irreparable physical damage may result. Because both manufactured and naturally-derived Factor VIII proteins are expensive, protein therapy is generally limited to treating 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 believe that there is strong rationale for developing a gene therapy product that could be administered prophylactically to hemophilia A patients to prevent spontaneous bleeding incidents, for the following reasons:

- hemophilia A results from a single gene defect that is well understood, and replacement of the missing protein has been used as an effective therapy for the disease;
- overproduction of the Factor VIII protein has not been shown to be harmful, which reduces the need for precise regulation of gene expression;
- researchers believe that production of as little as 5% of normal levels of the Factor VIII protein could effectively prevent chronic bleeding incidents in hemophilia A patients;
- the high cost of protein therapy generally limits its use to treating bleeding incidents, which may provide a significant market opportunity for gene-based prophylactic products that address the underlying disease; and
- the current global market for Factor VIII protein products, which is estimated at $1.2 billion, not including hospitalization costs, represents a significant market opportunity.

We also believe that AAV vectors represent a promising means of delivering a gene to trigger production of the Factor VIII protein for treating hemophilia A. The characteristics of AAV vectors, including their good safety profile and ability to persist in cells and express genes for extended periods of time, should provide important advantages compared to other gene delivery methods. We have invested in significant infrastructure to support the development of tgAAVCF, our AAV-based product candidate for treating cystic fibrosis, and we believe this infrastructure can be efficiently adapted to developing an AAV-based gene therapy product for treating hemophilia A.

In November 2000, we entered into a collaboration with Wyeth/Genetics Institute, a unit of Wyeth Pharmaceuticals, to develop gene therapy products for treating hemophilia. Under the terms of the collaboration agreement Wyeth/Genetics Institute provides us with significant funding and owns exclusive worldwide marketing rights to any products resulting from the collaboration. The section below entitled Research and Development Collaborations provides a detailed description of this relationship.

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Lysosomal Storage Disorders

Lysosomal storage disorders are a family of diseases caused by the absence of enzymes that are essential for removing certain metabolic byproducts from cellular tissues. The buildup, or storage, of these substances causes a loss of function in many crucial areas of the body, which may result in mental and physical disability and, in most cases, shortened lifespan. While each of these diseases typically affects fewer than 5,000 to 20,000 people worldwide, according to the National Tay Sachs & Allied Diseases Association, there are more than 40 different lysosomal storage disorders, including Tay Sachs, Pompe, Gaucher, Fabry and Batten disease.

We began collaborating with Genzyme Corporation in the area of lysosomal storage disorders after completing our acquisition of Genovo, Inc. in September 2000. Genzyme and Genovo had initiated a research and development collaboration in this area in 1999. In November 2000, following our acquisition of Genovo, we amended the research and development agreement previously entered into between Genovo and Genzyme to define the scope and level of work that we would perform for Genzyme in developing products for treating lysosomal storage disorders. Under the terms of the amended agreement, we will work with Genzyme to develop potential gene therapies for lysosomal storage disorders and Genzyme will be responsible for clinical development and commercialization of any products resulting from the collaboration. The section below entitled Research and Development Collaborations provides a detailed description of this relationship.

HIV Vaccine

According to the International AIDS Vaccine Initiative, or IAVI, more than 40 million people worldwide suffer from AIDS or are infected with HIV, the virus that causes AIDS. An additional 14,000 men, women and children worldwide are infected daily. 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 prophylactic vaccine to protect against infection by HIV could have significant market potential. To date, no company has applied for regulatory approval of a prophylactic AIDS vaccine, although several vaccines are under development.

We are collaborating with IAVI and Children s Research Institute, or CRI, on the campus of Children s Hospital in Columbus, Ohio to develop a vaccine to protect against HIV infection. The vaccine will utilize our AAV vectors to deliver HIV genes that express viral proteins that can be detected by the immune system to elicit a protective immune response against HIV. We believe that a single dose of an AAV-based vaccine containing HIV genes could allow for a sustained and high level of gene expression of HIV proteins *in vivo*, thereby eliciting a robust and sustained immune response without exposing the patient to HIV. Data from studies in nonhuman primates suggest that AAV vector vaccines may hold significant promise. Monkeys immunized with AAV vectors carrying SIV genes, the primate equivalent of HIV, develop immune responses that are very similar to those induced by the human form of HIV. These data provide the basis for moving forward with further preclinical development that we believe will support Phase I clinical trials in humans. Under the terms of the public-private collaboration, IAVI will fund work at Targeted Genetics and at CRI focused on development and preclinical and Phase I studies of a vaccine candidate. We have the right to commercialize in industrialized countries any vaccine that may result from this development collaboration, and we have the option to manufacture the vaccine for nonindustrialized nations. The section below entitled Research and Development Collaborations provides a detailed description of this collaboration.

Metastatic Cancer

We believe that our clinical testing of tgDCC-E1A, our synthetic vector-based product candidate for treating cancer, has demonstrated the potential of E1A as a tumor inhibitor. We therefore believe that if we are able to deliver E1A systemically to reach tumor sites throughout the body, we could significantly expand the utility of E1A as a potential cancer treatment. We are therefore developing new formulations of E1A, which we believe have the potential to target cancer cells when administered systemically.

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One of these formulations, tgLPD-E1A is based on a non-viral gene delivery vehicle called LPD, which contains lipids, polycations and DNA, and results in the formation of small, stable DNA particles encapsulated in a lipid shell. We believe that this condensed DNA delivery platform provides the basis for developing a systemic delivery system for administering E1A or other genes to tumors. Several preclinical studies of tgLPD-E1A indicate promising results. In a mouse model of human breast cancer tumors, we administered tgLPD-E1A systemically to evaluate its ability to inhibit tumor growth. The results indicated that the impact of tgLPD-E1A on tumor growth was comparable to the impact observed when administrating Taxol®, a chemotherapeutic drug. Additionally, administering both Taxol® and tgLPD-E1A inhibited tumor growth in mice significantly better than administering either agent alone. Furthermore, additional studies at Targeted Genetics and Emerald Gene Systems, our joint venture with Elan Corporation, suggest that the LPD platform could be modified to provide an enhanced efficacy and safety profile. Consequently, we plan to perform evaluations of these alternate formulations before deciding which formulation, if any, will advance into a clinical development phase.

Glioma

Glioma is a type of brain cancer that affects 17,000 people in the United States each year. Current treatment options for glioma include surgery, radiation therapy, chemotherapy or a combination of these treatments. Our collaboration with Biogen expanded upon a collaboration that Biogen had with Genovo prior to the acquisition. As part of this collaboration, 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. Localized, sustained production of interferon beta may result in superior anti-tumor efficacy with little or no systemic toxicity. We believe that preclinical studies in several animal cancer models validate this approach. Biogen owns worldwide rights to product candidates resulting from this research and has initiated a Phase I clinical trial for this product candidate. We are entitled to receive a royalty on any future sales resulting from this product candidate.

Hyperlipidemia

We are exploring gene therapies for cardiovascular disease by applying our AAV vector technology to treating hyperlipidemia, the elevation of lipids (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, we acquired a product development program aimed at assessing the delivery of genes to treat dyslipidemia, a condition of increased levels of vLDL-type cholesterol. We are conducting further research studies to assess the potential clinical utility of our AAV-VLDLR product candidate for treating hyperlipidemia. We have exclusive rights to certain intellectual property related to the use of AAV-based gene therapy for treating hypercholesterolemia.

For a description of research and development expenses related to our clinical development programs, see the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations Results of Operations in Part II, Item 7 of this annual report.

Core Technology Platform

We have assembled a broad base of core proprietary technologies that we believe will allow us to address a number of different diseases. We believe that different disease targets will require different methods of gene delivery. The best gene delivery method for a particular disease will depend on the targeted gene, the type of cell to be modified, the duration of effect desired and the need for *in vivo* or *ex vivo* delivery. Accordingly, our strategy has been to develop multiple gene delivery systems based on both AAV vector and synthetic vector technologies. We also have capabilities and intellectual property in two other types of viral vectors, adenoviruses and retroviruses. In addition, through our Emerald Gene Systems joint venture, we are working to create enhanced lipid-based delivery systems that would further extend the applicability of our technology base. We believe that our broad base of proprietary gene-delivery technologies will give us the flexibility to develop gene therapies for a wider range of diseases than we could develop using any single gene delivery system.

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Gene Therapy

Overview. Gene therapy is an approach to treating or preventing genetic and acquired diseases that involves inserting a functional gene 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 produce, 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 contains 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 genes are 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 function or an absence of specific genes causes proteins to be overproduced, underproduced, or produced incorrectly, any of which can cause disease. These diseases include cystic fibrosis, in which a defective protein is produced, and hemophilia, in which a protein is underproduced. Deficient or absent genes can also cause cells to incorrectly regulate gene expression which can cause diseases such as certain types of cancer. 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, thus 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 to date 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 genes into cells and, once inserted into 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. 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 genes, transfer the genes into a sufficient number of target cells and enable the delivered genes to persist in the host cell and produce proteins for long duration. We and others are using a variety of viral vectors, including AAV and retroviral vectors, for potential gene therapy applications requiring long-term gene expression.

Our 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 contain no viral genes that could produce unwanted cellular immune responses leading to side effects or reduced efficacy;

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AAV vectors can introduce genes into nondividing or slowly dividing cells;

AAV vectors can persist in the host cell to provide relatively long-term gene expression; and

Our AAV vectors can be manufactured using methods utilized in the manufacture of other biopharmaceutical products.

We are building our proprietary position in AAV-based technology through our development or acquisition of exclusive 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.

In addition to our tgAAVCF clinical development program for treating cystic fibrosis, we are conducting preclinical experiments to assess the potential for using AAV vectors to deliver genes to other target cells for treating other diseases. Currently, we are evaluating the use of AAV vectors to deliver genes to joints, muscles, the lung, the liver and the cardiovascular system (heart and blood vessels). Upon receiving additional financial and scientific resources, we intend to examine, both internally and through collaborators, the use of AAV vectors in additional cell types.

Our 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:

encapsulating genes into lipid carriers such as liposomes, which facilitate the entry of DNA into cells;

combining negatively charged DNA with positively charged cationic lipids;

injecting pure plasmid, or naked, DNA in an aqueous solution; and

directing DNA to receptors on target cells by combining the gene with molecules (ligands) that bind to the receptors.

We have exclusive rights to a significant body of synthetic gene delivery technology based on cationic lipids. These synthetic vectors, such as DCC-Cholesterol, are formulated by mixing negatively charged DNA with positively charged cationic lipids, which promotes uptake of genes 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 genes in rapidly dividing or non-dividing cells; and

ability to target to specific cell receptors.

We are working to expand our synthetic vector capabilities by developing enhancements to cationic lipid- based systems that will expand the potential uses of synthetic vectors. In one enhancement, which we call LPD, DNA is condensed and then combined with cationic lipids and polycations to generate stable particles of defined size that have significantly enhanced gene transfer efficiency and stability in the bloodstream. We believe that LPD-based formulations may be useful for delivering genes by intravenous administration.

Our Enhanced Vector Systems. Emerald Gene Systems, our joint venture with Elan, was formed to develop enhanced gene delivery systems that combine our AAV and synthetic gene delivery technologies with Elan s drug delivery technologies. Elan s licensed technologies include targeting ligands and polymers. We plan to develop enhanced gene delivery systems that can be systemically or orally administered to target the desired cells within the body.

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Cell Therapy

In November 2000, we established CellExSys, Inc., a majority-owned subsidiary, to further develop our *ex vivo* cell therapy capabilities. CellExSys portfolio of intellectual property includes 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. Through our ownership of CellExSys, we own or have rights to over 75 issued patents and patent applications in the area of cell therapy and other applications of T-cell technology.

Cell therapy involves transplanting living cells into a patient to treat disease, either in place of, or in combination with, other pharmaceuticals. One type of cell therapy involves the use of cytotoxic T lymphocytes, also known as CTLs, which are a type of immune system cell. The function of CTLs is to destroy foreign or diseased cells in the body. CellExSys is developing technology and expertise that enables the isolation of potent, disease-specific CTLs from small samples of patient blood, which can then be grown into a larger number of cells and used to treat disease. Key to this technology is a proprietary rapid expansion method, or REM. We have exclusive rights to a patent on REM that was issued to the Fred Hutchinson Cancer Research Center in October 1998. Using the REM process, CellExSys can grow billions of CTLs from small quantities of starting cells over several weeks, while preserving the cells specific disease-fighting capabilities. We believe that CellExSys technology and expertise could support development of a series of cell-based therapies to treat infectious diseases and cancer. In addition to the potential therapeutic uses of the REM technology, we believe that REM also has utility in new drug discovery and vaccine development.

The applications of the REM technology, an *ex vivo* therapeutic approach, are quite distinct from our *in vivo* gene delivery technologies and product development programs. As a result, we transferred our interests in our cell therapy and *ex vivo* therapy-related patents and patent applications to CellExSys. As a separate subsidiary focused on patient-specific cell therapy and other applications of REM technology, we believe that CellExSys is well-positioned to identify and take advantage of desirable product, partnership and financial opportunities that fall outside the field of *in vivo* gene therapy. CellExSys intends to fund further development of these cell therapy technologies by selling its equity securities to third party investors. Upon completion of these funding activities, we expect that we would no longer be the majority equity owner of CellExSys.

Research and Development Collaborations

Medeva Pharmaceuticals, Inc./Celltech Group plc

In 1998, we entered into a collaboration with Medeva Pharmaceuticals, Inc., now a wholly owned subsidiary of Celltech Group plc, to develop and commercialize tgAAVCF, our gene therapy product candidate for treating cystic fibrosis. Medeva committed to provide annual funding of up to $5 million for up to three years, to support our tgAAVCF research and development activities, including:

- scale-up and validation of manufacturing processes;
- development and validation of analytical methods;
- conduct of Phase I clinical trials; and
- other activities in support of product testing and commercialization.

In addition, Medeva agreed to pay the costs of Phase II and subsequent clinical trials of our tgAAVCF product candidate. Although we are currently managing a Phase II clinical trial in the United States, the agreements provide that Medeva will conduct all other trials and assume responsibility for securing worldwide registration of tgAAVCF.

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Under the terms of the Medeva/Celltech collaboration, we granted Medeva/Celltech an exclusive worldwide license to sell any tgAAVCF products resulting from the collaboration but retained rights for manufacturing and supplying bulk tgAAVCF product to support clinical trials and product commercialization. Our supply rights survive for the term of the patents covering tgAAVCF. Medeva loaned us $2 million to partially fund the construction of a pilot-scale tgAAVCF manufacturing facility and agreed to loan us, under specified conditions, up to an additional $10 million toward building a Good Manufacturing Practices compliant manufacturing facility for higher-volume production of tgAAVCF. To date, we have received approximately $28 million in funding from Celltech out of a potential $54 million in license fees, development funding, milestone payments, loans and equity investments connected with the Medeva/Celltech agreements. Assuming successful commercialization, we will also receive proceeds from sales of tgAAVCF products, based on a pricing formula intended to provide us with a significant percentage of Celltech s net revenue from tgAAVCF product sales.

In November 2000, we initiated a Phase II, double-blind, placebo-controlled clinical trial to evaluate our tgAAVCF product candidate. In the fourth quarter of 2001, we completed the initial three-year term of our tgAAVCF product research and development efforts with Medeva. Depending on the results of the current Phase II clinical trial, we will either:

- work with Celltech toward supporting the design and execution of one or more pivotal clinical trials required for product registration and approval;
- work with Celltech to design and execute additional clinical trials to further evaluate the therapeutic potential of tgAAVCF; or
- discontinue our work with Celltech and evaluate our strategic options for continuing the development of a gene therapy-based cystic fibrosis product.

Celltech may terminate the collaboration at will with 180 days notice. If Celltech exercises its termination right, all rights related to tgAAVCF that we have granted or otherwise extended to Celltech would return to us.

Emerald Gene Systems, Ltd.

In July 1999, we formed Emerald Gene Systems, Ltd., our joint venture with Elan International Services, Ltd., a wholly owned subsidiary of Elan Corporation plc. Emerald was formed to develop enhanced gene delivery systems, based on a combination of our gene delivery technologies and Elan s drug delivery technologies. These gene delivery systems could potentially be systemically or orally administered to deliver genes targeting the desired cells within the body.

We own 80.1% of Emerald s common stock and 80.1% of Emerald s preferred stock and Elan owns the remaining 19.9% of Emerald s common and preferred stock. The common stock of Emerald held by Elan is similar in all respects to the common stock held by us, except that those shares held by Elan do not have voting rights. The common shares held by Elan may be converted into voting common shares at Elan s election. Although we currently own 100% of the voting stock, Elan and its subsidiaries have 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 prevent us from exercising control over Emerald, we do not consolidate the financial statements of Emerald, but instead account for our investment in Emerald under the equity method of accounting.

We and Elan fund the expenses of Emerald in proportion to our respective ownership interests. A joint operating committee determines the nature and scope of activities to be performed by the joint venture on a periodic basis and at least annually. To date, we and Elan have jointly conducted Emerald s research and development activities. Emerald reimburses each company for the costs of research and development and related expenses, plus a profit percentage.

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

- Elan purchased $5 million of our common stock in 1999 at the closing of the joint venture agreements and purchased an additional $5 million of our common stock in 2000;
- In September 2001, we drew $2 million under a $12 million convertible note commitment by Elan to fund a portion of our investment in Emerald; and
- In 1999 at the closing of the joint venture agreements, Elan received $12 million of our Series B convertible exchangeable preferred stock in exchange for our 80.1% interest in Emerald.

At Elan s option, the Series B convertible exchangeable preferred stock can be converted into shares of our common stock. The Series B preferred stock will automatically convert into common stock upon the occurrence of specified transactions involving a change of control of Targeted Genetics. Alternatively, Elan can exchange its Series B preferred stock for the preferred shares we hold in Emerald, which would bring Elan s ownership in Emerald to 50%. If Elan exercises its exchange right, it must make a cash payment to us equal to 30.1% of the joint venture losses that we and Elan funded to Emerald after its formation.

Elan, as a holder of Series B preferred stock, is not entitled to vote together with the holders of our common stock, including with respect to the election of directors, or as a separate class, except as otherwise provided by the Washington Business Corporation Act.

We may borrow up to $12 million from Elan in the form of a convertible note, to fund our ongoing investment in Emerald. We can draw on this note on a quarterly basis until July 21, 2002 or through the end of the initial development period, which may be extended beyond July 21, 2002. Total draws cannot exceed our cumulative investment in Emerald. Borrowings under the loan facility are subject to the following terms:

- the outstanding principal balance bears interest at 12% per year, compounded semi-annually;
- interest is payable semi-annually in cash or can be capitalized and added to the principal amount outstanding; and
- principal and interest outstanding under the loan facility is due July 21, 2005, payable in cash or shares of our common stock.

Elan has the option to convert principal and interest outstanding under the loan facility, on a per-draw basis, into shares of our common stock. If Elan elects to convert outstanding amounts into our common stock, the conversion price will be 150% of the average closing price of our common stock for a specified period of time before the date of each applicable draw under the loan facility.

We have the option to prepay the principal and interest outstanding under the loan facility, in whole or on a per-draw basis, in either cash or shares of our common stock. If we elect to prepay amounts outstanding with our common stock, the conversion price will be the lower of 150% of the average closing price of our common stock for a specified period of time before the date of the applicable draw and the average closing price of our common stock for a specified period of time before the date of prepayment. If we elect to prepay outstanding amounts in cash, we will pay an amount equal to the higher of the amount of principal and interest outstanding under the applicable draw and the fair market value of our common stock into which the outstanding amount is convertible, based on a price per share equal to the average closing price of our common stock for a specified period of time before the date of prepayment.

As of December 31, 2001, we had provided $5.8 million of cash funding to the Emerald joint venture and we had borrowed $2 million against the loan facility.

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Biogen, Inc.

In September 2000, in connection with our acquisition of Genovo, we established a three-year, multiple-product development and commercialization collaboration with Biogen, Inc. Under the terms of a development agreement, Biogen has the option to collaborate with us to develop up to four new gene therapy product candidates. The specific genes to be delivered will be determined by Biogen and us over the initial three-year development period. Two of these genes have been identified, one for treating an infectious disease and the other for treating a genetic disorder. We are responsible for manufacturing and supplying bulk vector supplies to Biogen to support product development, clinical trials and product commercialization.

Upon initiation of the collaboration Biogen paid us $8 million in research funding and milestone payments. Under a related funding agreement, Biogen will provide us with a minimum of $1 million per year in research and development funding over the initial three-year development period. Minimum annual funding could be increased by mutual agreement between Biogen and us. Biogen also agreed to provide us with loans of up to $10 million and to purchase up to $10 million of our common stock, each at our discretion. During 2001, we borrowed $10 million from Biogen under this commitment. The loan is due in September 2006 and bears interest at market rates. We can elect to have Biogen purchase the common stock in one or more tranches through August 2003. The price per share for any share purchase will equal the average of the daily closing prices of a share of our common stock for a specified period of time before and after the applicable exercise date.

Assuming successful commercialization of products under the Biogen collaboration, we could receive an aggregate of up to $125 million in license fees, development funding, milestone payments, loans and equity investments connected to the Biogen agreements. We granted Biogen an exclusive worldwide license to sell any products developed in the collaboration. We will either receive royalties on sales of any products developed under the collaboration, or alternatively, we will sell products developed under the collaboration to Biogen at transfer prices that include sales-based and cost-based components, under a pricing formula specified in the developing and marketing agreement. The product manufacturing and supply provisions of the agreements are effective for the term of the patents covering our technology used to develop the product. Although Biogen may terminate the development and marketing agreement at any time after September 2001, its obligation under the related funding agreement to pay $1 million in annual research funding payments continues through September 2003.

Wyeth/Genetics Institute

In November 2000, we entered into a collaboration with Wyeth/Genetics Institute, a unit of Wyeth Pharmaceuticals, to develop AAV vector-based gene therapy products for treating hemophilia A and, potentially, hemophilia B.

Under the terms of the collaboration agreements, Wyeth/Genetics Institute agreed to pay us $5.6 million in up-front payments and up to $15 million over the initial three-year development period for developing a hemophilia A product candidate. We also granted Wyeth/Genetics Institute an option to collaborate on the development of a hemophilia B product candidate, which if exercised, could provide us with additional development and milestone payments. Assuming successful commercialization of both products under this collaboration, we could receive an aggregate of up to approximately $80 million in license fees, development funding and milestone payments. Wyeth/Genetics Institute will manage and fund the costs of clinical trials and related regulatory filings required for product approval and marketing and will have global marketing rights for any products resulting from the collaboration.

Wyeth/Genetics Institute also has agreed to loan us up to $10 million to finance manufacturing facility expansions if specified conditions are met. In addition, Wyeth/Genetics Institute has agreed to pay us to manufacture product for clinical trials and, upon approval, for commercial use, according to a sales-based formula.

The research and development funding agreement is effective until October 2003, with an option to extend the term if both parties agree. The supply agreement is effective for the term of the initial product development period and can be extended should regulatory agencies approve a product for commercial use. Wyeth/Genetics Institute has the right to terminate both agreements at will, with 180 days notice. If Wyeth/Genetics Institute exercises this right to terminate, all rights related to the hemophilia technology that we have granted or otherwise extended to Wyeth/Genetics Institute will return to us. If Wyeth/Genetics Institute exercises their right to terminate both agreements at will or if we exercise our right to terminate for cause, we would have an option to acquire a right and license to certain hemophilia patent rights controlled by Wyeth/Genetics Institute.

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Genzyme Corporation

In 1999, Genovo entered into a research and development collaboration with Genzyme Corporation to develop potential products for treating lysosomal storage disorders. Under the terms of the development agreement, Genovo was committed to perform, for up to three years and at its own cost, up to $2.9 million per year of research and development activities. A related option agreement gave Genzyme the option to purchase up to $11.4 million of Genovo equity during the three-year research and development period, of which $3.4 million had been purchased before our acquisition of Genovo in 2000. We assumed the Genzyme agreements when we acquired Genovo.

In 2000, we amended the 1999 development agreement to expand its technological scope and financial terms and establish a development plan for the second year of the three-year collaboration. Under the amended agreement, Genzyme will be required to pay milestone payments upon our achievement of specified regulatory milestones and to pay royalties on sales of any products developed under the collaboration. The development program under our agreement with Genzyme is effective through August 2002 and includes an option to extend the term if both parties agree. Genzyme has the right to terminate the development program at will, with 90 days notice. If Genzyme exercises this right to terminate the development program, or upon its expiration, all rights that we have granted or otherwise extended to Genzyme will return to us, except that Genzyme will retain an exclusive license to certain Genovo-related manufacturing technology for use in the field of lysosomal storage disorders.

After executing the amended agreement, Genzyme exercised its option to purchase 311,295 shares of our common stock (as successor company to Genovo) at a purchase price of $12.8495 per share, resulting in proceeds to us of $4 million. Genzyme has not exercised a second option to acquire up to an additional 311,295 shares of our common stock also at a price of $12.8495 per share. We are in negotiations with Genzyme to define the scope of ongoing development activities and the parameters around which Genzyme would make a further investment in us. If Genzyme elects not to make an additional investment or to provide less than the $4 million we would receive if Genzyme exercised the second stock purchase option, the former Genovo shareholders and option holders will receive up to 155,648 additional shares of our common stock.

International AIDS Vaccine Initiative

In February 2000, we entered into a three-year collaboration with the International AIDS Vaccine Initiative and Children s Research Institute to develop a vaccine to prevent AIDS. The vaccine, which will utilize our AAV vectors to deliver selected HIV genes as a vaccine, is designed to elicit a protective immune response against HIV. Under this collaboration, vaccine candidates will be constructed based on subtypes of the virus most prevalent in Southern and Eastern Africa, and are expected to be evaluated in those regions. Under the terms of this public-private collaboration, IAVI will fund development, preclinical studies and Phase I clinical trials performed by us and by CRI. IAVI has also agreed to invest up to $6 million in research funding during the initial three years of the collaboration.

Assuming successful development, we expect to manufacture the vaccine and will retain exclusive worldwide commercialization rights to any product that may stem from the collaboration. Under the terms of the collaboration, IAVI has retained rights to ensure that any successful vaccine will be distributed in developing countries at a reasonable price to be determined by IAVI. If we decline to produce the vaccine for developing countries in reasonable quantities and at a reasonable price, IAVI will have rights to obtain licenses from us that will allow IAVI to contract with other manufacturers to make the vaccine available at a reasonable price in those countries. In any event, however, we will retain exclusive rights to commercialize in industrialized countries any vaccine resulting from the collaboration.

The initial development periods of our collaborations with Genzyme and Elan will conclude in 2002 and the initial development periods of our other collaborations will conclude in 2003, unless we and our collaborators agree to extend the agreements. Substantially all of our revenue, and substantially all of our expected revenue for the next several years, is derived from our product development collaborations. If we were to lose the product development and other funding that our collaborative partners provide and are unable to obtain alternative funding, we may be unable to commercialize the product candidate covered by the affected collaborations. For a more detailed description of the risk, see the section entitled Factors Affecting Our Operating Results, Our Business and Our Stock Price If we lose significant collaborative funding or we are unable to raise additional capital when needed, we may be unable to develop our potential products and conduct our operations in Part II, Item 7 of this annual report.

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Alkermes, Inc.

In June 1999, we entered into a license agreement with Alkermes, Inc. in which we received exclusive rights to an issued patent and other pending patent applications related to AAV vector manufacturing. The issued patent broadly covers a manufacturing method that we believe is key to making AAV-based products in a commercially viable, cost-effective manner. The license to this technology, first developed by Children s Hospital in Columbus, Ohio, covers the use of cell lines for manufacturing AAV vectors and expands a limited field license to these rights that we previously acquired. Under the terms of the license agreement, we issued to Alkermes 500,000 shares of common stock and two warrants, each to purchase 1,000,000 additional shares of common stock. The warrants expire in June 2007 and June 2009 and have an exercise price of $2.50 and $4.16 per share, respectively. 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 Immunex Corporation

Targeted Genetics was formed in 1989 as a subsidiary of Immunex, a biopharmaceutical company developing recombinant proteins as therapeutics. In connection with our formation, we issued Immunex shares of our preferred stock that were subsequently converted into 1,920,000 shares of common stock, in exchange for Immunex granting us 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.

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 United States Patent and Trademark Office, or USPTO, as well as 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 by the USPTO and foreign counterparts. 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 since 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, which we licensed from the National Institutes of Health, or NIH, and 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 was notified that the USPTO had declared an interference proceeding to determine whether

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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 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 Intellectual property disputes regarding third-party technology that we license may prevent or impair our ability to develop and commercialize our product candidates 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, however, 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.

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Competition

A number of companies and institutions are developing or considering the development of potential gene therapy and cell 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. 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 product 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 premarket approval procedures administered by the Food and Drug Administration, or 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 and cell therapy are both relatively new technologies that have not been extensively tested in humans. The FDA reviews all product candidates for safety and efficacy at each stage of clinical testing. Both safety and efficacy standards must be met before the FDA permits clinical testing to proceed to the next stage or 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 and cell therapy product candidates and commercialized products frequently 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 Institution Review Board 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

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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 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 NIH-funded clinical trial can begin, the Institutional Biosafety Committee 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. 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 or the RAC 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, as well as the approval of several other governmental and nongovernmental agencies, before we can market the product in the United States. 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.

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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

At December 31, 2001, we had 173 full-time-equivalent employees, of which 151 are directly involved in research and development, or support our research and development efforts. 31 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.

Competition among biotechnology and pharmaceutical companies for highly skilled scientific and management personnel is intense. We believe that we have compensation and benefit programs in place that will allow us to be competitive in this environment. If we are ineffective, however, in retaining our existing workforce and scientific advisors or in attracting additional qualified employees and advisors, our business will not succeed. None of our employees are covered by a collective bargaining agreement.

Item 2. ***Properties***

We currently occupy an aggregate of approximately 90,000 square feet of laboratory and office space in Seattle, Washington and Sharon Hill, Pennsylvania. The leases on our Seattle laboratory and office facilities expire in March 2004 and contain options for us to extend the terms for two additional five-year periods. The average annual rent payment during the current terms of the Seattle leases total approximately $1.4 million, including amounts related to landlord financing of leasehold improvement costs. The lease on our laboratory and office facilities in Sharon Hill expires in November 2005 and contains options for us to extend its term for two additional five-year periods. The annual rent payment during the current term of the Sharon Hill lease is approximately $353,000. In July 2000, we leased approximately 76,000 square feet of space in Bothell, Washington for future large-scale manufacturing of our products. The lease on this facility expires in September 2015 and contains an option for us to extend its term for one additional five-year period. The average annual rent payment during the current term of the Bothell lease is approximately $1.3 million. We believe that our current facilities in Seattle and Sharon Hill, together with additional expansion space available in our Bothell facility and the office complex adjoining our main Seattle building, will be adequate to meet our projected needs for the next several years. Within that time frame, however, we could be required to locate alternative facilities, depending on the extent of our growth and development.

Item 3. ***Legal Proceedings***

We are not a party to any material legal proceedings, although from time to time we may become involved in disputes in connection with the operation of our business.

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 2001.

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PART II

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

Our common stock trades on the Nasdaq National Market under the symbol TGEN. As of March 5, 2002, we had approximately 263 shareholders of record and approximately 19,700 beneficial holders of our common stock.

We have never paid cash dividends and do not anticipate paying them in the foreseeable future. In addition, our loan agreements with Biogen, Inc. and Celltech Group plc restricts the amount of cash dividends we can pay.

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

	High	Low
2001:		
4th Quarter	$ 3.50	$ 1.71
3rd Quarter	5.87	1.45
2nd Quarter	6.60	3.00
1st Quarter	9.25	2.38
2000:		
4th Quarter	12.81	6.38
3rd Quarter	17.00	9.00
2nd Quarter	15.00	5.31
1st Quarter	28.00	3.63

In connection with a private placement of common stock in 1998, we issued warrants to purchase a total of 4,333,333 shares of common stock at an exercise price of $2.00 per share. On January 18, 2001, The Equitable Life Assurance Company exercised warrants to purchase 1,000,000 shares of common stock. The transaction was exempt from registration under Section 4(2) of the Securities Act, on the basis that the transaction did not involve a public offering.

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Item 6. ***Selected Financial Data***

	Year Ended December 31,				
	2001	**2000**	**1999**	**1998**	**1997**
Statement of Operations Data					
Revenue	$ 18,880,000	$ 11,403,000	$ 6,848,000	$ 7,510,000	$ 1,328,000
Operating expenses	47,484,000	57,208,000	33,694,000	16,373,000	15,828,000
Loss from operations	(28,604,000)	(45,805,000)	(26,846,000)	(8,863,000)	(14,501,000)
Loss before cumulative effect of change in accounting principle	(27,170,000)	(43,973,000)	(26,655,000)	(8,687,000)	(14,188,000)
Cumulative effect of change in accounting principle (1)		(3,682,000)			
Net loss	$ (27,170,000)	$ (47,655,000)	$ (26,655,000)	$ (8,687,000)	$ (14,188,000)
Basic and diluted net loss per share:					
Loss before cumulative effect of change in accounting principle (2)	$ (0.62)	$ (1.16)	$ (0.83)	$ (0.33)	$ (0.70)
Cumulative effect of change in accounting principle (1)		(0.10)			
Net loss per basic and diluted common share (2)	$ (0.62)	$ (1.26)	$ (0.83)	$ (0.33)	$ (0.70)
Shares used in computing basic and diluted net loss per common share	43,927,822	37,752,164	32,173,756	26,637,823	20,196,325
Proforma amounts assuming the accounting change is applied retroactively:					
Net loss			$ (24,555,000)	$ (14,468,000)	
Net loss per common share			$ (0.77)	$ (0.54)	

	December 31,				
	2001	**2000**	**1999**	**1998**	**1997**
Balance Sheet Data					
Cash and cash equivalents	$ 25,186,000	$ 38,630,000	$ 7,153,000	$ 11,957,000	$ 5,038,000
Total assets	71,038,000	87,974,000	13,692,000	16,204,000	9,767,000
Long-term obligations	16,403,000	2,447,000	2,088,000	900,000	1,517,000
Redeemable preferred stock	12,015,000	12,015,000	12,015,000		
Total shareholders equity (3)	25,386,000	51,417,000	(5,049,000)	11,982,000	5,592,000

(1) Effective January 1, 2000, we changed our method of accounting for nonrefundable up-front license fees. See Note 1 to the consolidated financial statements.

(2) The net loss per common share for 2001, 2000 and 1999 has been restated to eliminate the 7% dividend previously accrued on the Series B Preferred Stock. See Note 1 to the consolidated financial statements.

(3) Shareholders equity for 2001, 2000 and 1999 has been restated to classify the Series B Preferred Stock outside of permanent equity. See Note 1 to the consolidated financial statements.

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

We develop gene therapy products and technologies to treat acquired and inherited diseases on our own and through various research and development collaborations with others. We have historically funded our product development efforts primarily through the sale of equity securities and through funding received from our product development partners. We have six major collaborations that provide ongoing funding for our research and development programs:

a cystic fibrosis product development collaboration with Medeva Pharmaceuticals, Inc., now a wholly owned subsidiary of Celltech Group plc;

an AAV-based AIDS vaccine development collaboration with the International Aids Vaccine Initiative;

a multiple-product gene therapy product development collaboration with Biogen, Inc.;

a lysosomal storage disorder product development collaboration with Genzyme Corporation;

an AAV-based hemophilia product development collaboration with Wyeth/Genetics Institute, a unit of Wyeth Pharmaceuticals; and

Emerald Gene Systems, Ltd., our joint venture with Elan International Services, Ltd., a wholly owned subsidiary of Elan Corporation plc, for the development of enhanced gene delivery technology.

Our development collaborations with other entities typically provide us with funding, including one or more purchases of our equity securities, loans, payments for reimbursement of research and development costs and milestone fees and payments. We and our partner will typically agree on a development plan for the product candidate, which often extends for multiple years. The product candidate s progress is periodically reviewed with the partner. Our development partners often coordinate clinical evaluation of product candidates and marketing rights for product candidates that are successfully developed. We generally maintain manufacturing and royalty-based interests in successfully developed product candidates.

We have two lead product candidates in clinical trials, tgAAVCF for treating cystic fibrosis and tgDCC-E1A for treating cancer. tgAAVCF is currently in a Phase II clinical trial. tgDCC-E1A is currently in a Phase I clinical trial for treating ovarian cancer and a Phase II clinical trial for treating head and neck cancer. We are pursuing tgDCC-E1A initially as a company-funded program but anticipate entering into a strategic collaboration later in the development process. Our product candidates for treating hemophilia and lysosomal storage disorders, our potential vaccine to prevent HIV infection and the products we are developing with Elan and Biogen are all in preclinical development. Developing pharmaceutical products 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 degree of involvement by a development partner and the intended use of the product candidate. Our commencement and rate of completion of clinical trials may vary or be delayed for many reasons, including those discussed in the section of this Item 7 entitled Factors Affecting Our Operating Results, Our Business and Our Stock Price-Risks Related to Product Development and Regulatory Approval and elsewhere in this annual report. As a result, we are unable to predict whether we will be able to successfully develop any of our product candidates or the time or cost successful development will require.

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, milestone payments and licensing fees from current and 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

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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 may 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 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 will continue to fluctuate as we proceed with our current development collaborations, enter into potential new development collaborations and licensing agreements and earn milestone payments.

As of December 31, 2001, our accumulated deficit totaled $178.0 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 our staffing levels, outside costs for supplies and materials and clinical trial activities. We increased our staffing, outside costs and clinical trial activities in 2001 and 2000 as a result of the greater number, complexity and advancing development stages of our collaborations. We anticipate 2002 staffing and outside costs for supplies, materials and clinical trial activities will continue at levels similar to those in 2001. As described in the section of this Item 7 entitled Liquidity and Capital Resources, the initial development periods of three of our collaborations conclude in 2002 and 2003. If we and the collaborators do not agree to extend these collaborations, they will terminate. Absent new collaborative partnerships or extensions to our existing collaborative partnerships, we anticipate that both our research and development costs and our revenue will decrease in 2003. We will need to scale our research and development activities to match the levels of funding provided by our collaborators and other sources of capital available to us, which may be subject to fluctuation in the future.

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 and on acceptable terms, obtain and maintain corporate partnerships or complete acquisition transactions necessary or desirable to complete the development of our product candidates.

In September 2000, we acquired Genovo, Inc., a privately held biotechnology company focused on developing therapeutic products based on AAV vectors. The purchase price totaled $66.4 million, which consisted of 5,250,805 shares of our common stock, valued at $58.4 million, assumed Genovo options valued at $7.7 million and transaction costs of $600,000 less $300,000 allocated to the intrinsic value of unvested stock options that we assumed. In connection with the acquisition of Genovo, we recorded acquired in-process research and development, or IPR&D, expenses of $28.0 million and acquisition-related intangibles of $39.5 million, consisting of AAV vector know-how of $12.7 million, workforce in place of $1.6 million and goodwill of $25.2 million.

Significant Accounting Policies

There are several accounting policies that we believe are critical to the presentation of our consolidated financial statements. Note 1 to our consolidated financial statements *Description of Business and Summary of Significant Accounting Policies* summarizes each of our significant accounting policies. The most critical accounting policies include those related to revenue recognition, specifically as these policies relate to our collaborative development relationships with other companies, the accounting and presentation for our unconsolidated joint venture interest in Emerald, the application of assumptions and estimates in accounting for acquired IPR&D costs and the valuation of our intangible assets.

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We generate revenue from technology licenses, collaborative research arrangements and cost reimbursement agreements. Revenue under technology licenses and collaborative agreements typically consist 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 ratably over 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.

We own 80.1% of Emerald s common stock and 80.1% of Emerald s preferred stock and Elan owns the remaining 19.9% of Emerald s common and preferred stock. The common stock of Emerald held by Elan is similar in all respects to the common stock held by us, except that those shares held by Elan do not have voting rights. The common shares held by Elan may be converted into voting common shares at Elan s election. Although we currently own 100% of the voting stock, Elan and its subsidiaries have retained significant minority investor rights that are considered participating rights under the FASB s Emerging Issues Task Force 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 prevent us from exercising control over Emerald, we do not consolidate the financial statements of Emerald but instead account for our investment in Emerald under the equity method of accounting.

Our Series B preferred stock, which is currently valued at $12 million, is convertible into shares of our common stock or may be exchanged, at Elan s option, for the preferred shares we hold in Emerald, which represents 30.1% ownership interest in Emerald. If Elan exercises its exchange right, it must make a cash payment to us equal to 30.1% of the joint venture losses that we and Elan funded after its formation. We periodically monitor the redemption value of the Series B preferred stock, as measured by 30.1% of the fair value of the joint venture that Elan would receive, less the cash payable to us upon exchange by Elan. If and when the redemption value of the Series B preferred stock exceeds its then current carrying value, we will increase the carrying value of the Series B preferred stock to the redemption value and recognize a corresponding dividend to the Series B preferred shareholder. We will recognize subsequent increases or decreases in the redemption value of the Series B preferred stock; however, decreases will be limited to amounts previously recorded as increases, so as not to reduce the carrying amount of the Series B preferred stock below the original basis of $12 million. The exchange right currently expires in April 2003, but is subject to extension by our mutual agreement with Elan.

Our estimates are based on assumptions we believe to be reasonable at the time we perform these estimates. Changes in the underlying assumptions may result in substantially different accounting estimates. For example, when we acquired Genovo in September 2000, we assigned value to the acquired assets on the basis of several estimates and assumptions. Changes in these underlying estimates may result in substantially different allocation of the overall purchase price and the amount of expenses recorded on our balance sheet as acquired IPR&D and intangible assets. In addition, we will make assumptions and estimates on a periodic basis when we evaluate the carrying value of goodwill for evidence of impairment.

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

Results of Operations

Revenue

Revenue in 2001 totaled $18.9 million, compared to $11.4 million in 2000. This increase primarily resulted from our hemophilia product development collaboration with Wyeth/Genetics Institute and our multiple-product development collaboration with Biogen, both of which were established in late 2000. The increase also reflects growth in revenue earned from the Emerald joint venture and revenue earned under our AIDS vaccine collaboration with IAVI. The increase in revenue for 2001 was partially offset by a decrease in revenue earned under our development program with Celltech for a cystic fibrosis product candidate, under which we earned a $2 million milestone payment in 2000. Revenue increased to $11.4 million in 2000 from $6.8 million in 1999, reflecting amounts generated under our collaboration agreement with Celltech, a full year of providing research and development services to Emerald and, to a lesser degree, revenue generated from a partial year of product development efforts in our collaborations with Wyeth/Genetics Institute, Biogen and IAVI.

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We generated $2.8 million in revenue in 2001, $1.9 million in revenue in 2000 and $446,000 in revenue in 1999 from research and development activities performed for Emerald.

Operating Expenses

Research and Development. We incurred research and development expenses of $31.5 million in 2001, compared to $19.3 million in 2000. This increase resulted from increased research and development efforts in our hemophilia and AIDS vaccine product development collaborations, design costs associated with our large-scale manufacturing facility expansion and the addition of Genovo s research and development operations. The increase also reflects increased research and development activities to support our collaborations with Elan, as well as additional clinical and regulatory activities associated with the development for our cancer programs. Research and development expenses increased to $19.3 million in 2000 from $14.3 million in 1999, reflecting increased expenses related to our acquisition of Genovo s research and development operations, additional activities related to our collaborations with Wyeth/Genetics Institute and IAVI and, to a lesser extent, costs incurred to support the Emerald joint venture. The increase in total expenses in 2001 was partially offset by decreases in our tgDCC-E1A development expenses as tgDCC-E1A moved into clinical development.

Our research and development expenses for the years ended December 31, 2001, 2000 and 1999 were as follows:

	Year Ended December 31,		
	2001	**2000**	**1999**
Research and preclinical programs:	$ 18,693,000	$ 6,321,000	$ 1,440,000
Clinical programs:			
Cystic fibrosis	2,521,000	3,959,000	5,440,000
Cancer products	2,630,000	2,251,000	770,000
Indirect costs	7,702,000	6,781,000	6,641,000
Total Clinical Programs	12,853,000	12,991,000	12,851,000
Total research and development expense	$ 31,546,000	$ 19,312,000	$ 14,291,000

Research and development costs attributable to clinical programs include costs of salaries, benefits, clinical trial site costs, outside services, materials and supplies incurred to support the clinical programs. Indirect costs allocated to clinical programs include facility and occupancy costs, intellectual property-related expenses, including patent prosecution and maintenance, and license and royalty payments. Costs attributed to research and preclinical programs largely represent our product pipeline generating activities. Because of the large number of research projects we have ongoing at any one time, and our ability to utilize resources across several projects, the majority of our research and preclinical development costs are not directly assigned to individual projects and are instead allocated among multiple projects. For purposes of reimbursement from our collaboration partners, we capture the level of effort expended on a project through our project management system which is based primarily on human resource time allocated to each project, supplemented by an allocation of indirect costs and other specifically identifiable costs, if any. As a result, the costs we allocate to a project are not intended to, and do not necessarily, reflect the actual costs of the project.

Costs associated with our preclinical program activities increased each year, reflecting the addition of the AIDS vaccine collaboration with IAVI in early 2000, the hemophilia collaboration with Wyeth/Genetics Institute and the lysosomal storge disorder collaboration with Genzyme in late 2000 and increased activity in our self- funded RA and gene delivery technology development programs. Costs associated with our clinical program activities were relatively stable as increases in costs attributable to our cancer research and development programs were offset by decreases in costs attributable to our cystic fibrosis research and development costs.

Equity in Loss of Unconsolidated, Majority-Owned Research and Development Joint Venture. Our equity in the net loss of the Emerald joint venture increased to $3.7 million in 2001 from $2.5 million in 2000. Losses in both years reflect our 80.1% equity share in the loss generated by Emerald s research and development and licensing activities performed by Elan and us. In 1999, our equity in the net loss of Emerald was $12.6 million, which included our 80.1% share of a $15.0 million charge for an exclusive license to Elan s drug delivery technology and our 80.1% share of Emerald s 1999 collaboration costs.

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In-Process Research and Development. In 2000, we recorded $28.0 million in IPR&D expenses, which reflects the portion of the purchase price paid to acquire Genovo that was allocated to acquired IPR&D. In 1999, we incurred an expense of $3.2 million to acquire from Alkermes, Inc. an exclusive sublicense to a patent and patent applications related to the manufacture of AAV vectors. We acquired this license in exchange for shares of our common stock and warrants to purchase shares of our common stock.

We acquired ongoing IPR&D projects from Genovo in the fields of AAV manufacturing platforms, lysosomal storage disorders, glioma, hemophilia and hyperlipidemia. The amount recorded as IPR&D expense for the Genovo acquisition represents the present value of the estimated after-tax cash flows that we believe may be generated by the purchased technology that, as of the acquisition date, had not yet reached technological feasibility. We based the cash flow projections for revenue on estimates of growth rates and the aggregate size of the markets for each product, the probability of technical success given the stage of development at the time of acquisition, royalty rates based on prior licensing agreements, product sales cycles and the estimated life of the product s underlying technology. We deducted our estimated operating expenses and income taxes from our estimated revenue projections to arrive at our estimated after-tax cash flows. The rate that we used to discount projected cash flows for in-process technologies ranged from 30% to 45%, depending on the relative risk of each in-process technology, and were based primarily on internal rates of return, cost of capital, rates of return for research and development and our weighted average cost of capital at the time of acquisition. The acquired IPR&D projects consisted of the following:

AAV manufacturing platform projects related to hyperlipidemia, hemophilia, lysosomal storage disorders, and glioma, which pursue manufacture of AAV as a stable gene therapy vector capable of delivering genes to a variety of dividing and nondividing cells. Genovo estimated that the additional research and development costs to complete the AAV manufacturing platform projects in 2007 would be approximately $23.8 million. Since the acquisition of Genovo, we have continued to perform preclinical development of the AAV manufacturing platform program we acquired from Genovo.

Technology in the area of lysosomal storage disorders, which is a family of approximately 40 genetic diseases, are normally single-gene defects that prevent the production of one or more lysosomal enzymes, which leads to abnormal deposits of substrates within lysosomal vacuoles. Genovo estimated the additional costs to complete these technologies at approximately $9.0 million, with a targeted completion date in 2007. Since the acquisition of Genovo, we have been developing with Genzyme Corporation a product candidate for treating Fabry disease, which is currently in preclinical development.

Glioma technology, intended to treat brain tumors in adults. These tumors, which are highly malignant, are nearly always fatal and currently have no known curative treatment. Genovo had been developing a gene therapy product to treat glioma with Biogen. Genovo estimated that the additional costs to complete its glioma technology at approximately $750,000, with a targeted completion date in 2006. Since our acquisition of Genovo, Biogen has begun a Phase I clinical trial of its gene therapy product candidate to treat glioma.

Technologies for treating hemophilia, which is a genetic disorder that results in prolonged external and/or internal bleeding. Genovo estimated the additional costs to complete its hemophilia technologies at approximately $12.0 million, with a targeted completion date in 2009. We are working with Wyeth/ Genetics Institute to develop a gene therapy product candidate to treat hemophilia A, which is currently in preclinical development.

Technologies for treating hyperlipidemia, which is an elevation of lipids in the bloodstream that are transported as part of large molecules called lipoproteins. Genovo estimated that its hyperlipidemia technology would be completed in 2007, at an additional cost of approximately $16.0 million. We currently have limited preclinical development activities focused on hyperlipidemia.

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Genovo based all of these estimates and projections on assumptions believed to be reasonable at the time of the acquisition, but that are inherently uncertain and unpredictable. If we do not successfully develop these projects, our business, operating results and financial condition may be adversely affected. As of the date of the acquisition, we concluded that Genovo s technologies under development, once completed, can be economically used only for their specifically intended purposes and that these in-process technologies have no alternative future use after taking into consideration the overall objectives of the project, progress toward the objectives and uniqueness of developments to these objectives. Given the uncertainties involved in developing these product candidates, we are unable to predict whether we will be able to successfully develop any of these product candidates or the time or costs involved in doing so. The risk of untimely completion includes the risk that competitors will develop alternative products.

General and Administrative. We incurred general and administrative expenses of $6.2 million in 2001 as compared to $5.7 million in 2000. This increase is attributable to higher business development and legal costs, including expenses related to the spin-out of our majority-owned cell therapy subsidiary, CellExSys, Inc., and increased administrative support for our growing number of collaborative partnerships. General and administrative expenses increased to $5.7 million in 2000 from $3.6 million in 1999. This increase reflected the addition of Genovo administrative costs, costs associated with integrating Genovo s operations into our own and greater business-development and legal costs related to establishing new development collaborations.

Amortization of Acquisition-Related Intangibles. We recorded amortization expenses of $6.1 million in 2001, compared to $1.7 million in 2000, for goodwill, noncompetition agreements and assembled workforce that we acquired when we purchased Genovo. We recorded no expenses related to amortization of acquired intangibles in 1999. In July 2001, the Financial Accounting Standards Board, or FASB, issued Statement of Financial Accounting Standards, or SFAS, No. 142, Goodwill and Other Intangible Assets, which requires use of a nonamortization approach to account for purchased goodwill and certain intangibles, effective January 1, 2002. Under this nonamortization approach, goodwill and certain intangibles will not be amortized into operating results, but instead will be reviewed for impairment and written down and charged to operating results only in the periods in which the carrying value of goodwill and certain intangibles is more than its fair value. Assembled workforce will be reclassified into goodwill in accordance with SFAS No. 142 and will be evaluated accordingly. We will continue to amortize noncompetition agreements over each agreement s estimated remaining useful life. We expect adoption of SFAS No. 142 to substantially reduce our amortization of goodwill and intangibles commencing January 1, 2002.

Other Income and Expense

Investment Income. Our investment income from marketable securities, all of which are cash equivalents, was $1.9 million in 2001, compared to $2.1 million in 2000 and $426,000 in 1999. These fluctuations result from fluctuations in the level of our cash and investments during the periods and, to a lesser degree, from fluctuations in interest rates. Most of our cash is invested in a short-term bond mutual fund.

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 increased to $452,000 in 2001 from $265,000 in 2000 and $235,000 in 1999. The increase in 2001 is primarily due to higher average outstanding principal balances during the second half of the year, when we drew $13.0 million on available loans and notes. We expect our interest expense to increase in 2002, to reflect our increased level of borrowings during 2001.

Accounting Change

In the fourth quarter of 2000, we adopted the provisions of the SEC s Staff Accounting Bulletin No. 101, or SAB 101, *Revenue Recognition in Financial Statements*. SAB 101 generally provides that nonrefundable up- front fees for licenses and rights to product candidates must be deferred and recognized as revenue over the product development period in which we are providing continuing services related to product development. Previously, we recognized revenue from nonrefundable up-front license fees when the technology was transferred and we had fulfilled all of our significant contractual obligations relating to the fees. The cumulative effect on prior years of implementing SAB 101 resulted in a noncash charge of $3.7 million and a corresponding increase in deferred revenue. This cumulative effect adjustment was calculated as of January 1, 2000 and included in our financial results for 2000. We recognized $1.6 million of revenue in 2001 and $2.1 million in 2000 related to this change in accounting.

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Restatement of Financial Information

The consolidated balance sheets as of December 31, 2001 and 2000 and the consolidated statements of redeemable preferred stock and shareholders equity for each of the three years in the period ended December 31, 2001, have been restated to present our Series B convertible exchangeable preferred stock, with a carrying amount of $12.0 million, outside of permanent shareholders equity, as a result of the adoption of EITF Topic D-98, *Classification and Measurement of Redeemable Securities*. We issued the Series B preferred stock in connection with the formation of Emerald Gene Systems, our joint venture with Elan. Shares of Series B preferred stock are exchangeable for a portion of our investment in Emerald. The effect of this restatement is to reduce total shareholders equity by $12 million for the periods described and to reflect the Series B preferred stock outside of permanent equity.

Net loss per common share for the years ended December 31, 2001, 2000 and 1999 has been restated to eliminate the 7% dividends previously accrued on the Series B preferred stock and included in the net loss applicable to common shareholders. Because dividends would only be payable in common shares upon conversion of the Series B preferred stock into common stock, the amounts previously recorded as dividends actually represent adjustments to the conversion price that are accounted for under EITF Issue 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios*. Because the commitment date fair value of the maximum number of common shares that could be issued pursuant to conversion of the Series B preferred stock is less than the proceeds of issuance of the Series B preferred stock, the Series B preferred stock does not contain a beneficial conversion feature that should be added to the net loss when determining net loss applicable to common shareholders. This restatement does not affect net loss for any periods previously reported.

Liquidity and Capital Resources

In the last three years, we have financed our operations primarily through proceeds from public and private sales of our equity securities, which have totaled approximately $47.5 million and through cash payments received from our development partners to fund the development of our product candidates, which totaled approximately $60.2 million. To a lesser degree, we have also financed our operations through grant funding, interest earned on cash, cash equivalents and short-term investments and funding under equipment leasing agreements. These financing sources have historically allowed us to maintain adequate levels of cash and investments.

Our combined cash and cash equivalents totaled $25.2 million at December 31, 2001 compared with $38.6 million at December 31, 2000. During 2001, we used $23.5 million to fund our operations, $4.4 million to purchase capital equipment, $2.8 million to fund our share of the operations of the Emerald joint venture and $1.1 million to repay scheduled debt payments. The primary financing sources of our cash and cash equivalents in 2001 were $13.0 million borrowed under debt financing commitments from our corporate partners, $3.1 million in proceeds from the sale of common stock and $2.4 million received under equipment financing agreements.

Our future cash requirements will depend on many factors, including the rate and extent of scientific progress in our research and development programs, the scope and results of clinical trials, the time and costs involved in obtaining regulatory approvals, the costs of our success in filing, prosecuting and enforcing patents, competing technological and market developments and the cost and success of product commercialization. We do not expect to generate positive cash flow from our operations for at least the next several years, because all of our product candidates are in pre-clinical and clinical development and we expect to continue incurring significant expense in advancing our research and development programs and commercializing our product candidates. Assuming our research efforts for existing collaborations are continued for the full research term, as of December 31, 2001 we have total committed funding of approximately $65 million. This amount consists of i) $25 million of cash on hand, ii) $17 million expected to be received in 2002 under loan and equity commitments from our strategic partners, of which approximately $4 million must be spent on the project sponsored by the partner providing the commitment, and iii) $23 million in collaborative funding that we expect to receive from our development partners primarily in 2002 and 2003 to help fund costs associated with the development programs that they sponsor. In general, the obligation of our corporate collaborators to provide research funding can be terminated by our partners with notice.

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In the case of such an event, the collaboration agreements specify the rights, if any, that each party will retain. We also have warrants outstanding to purchase 3.3 million shares of our common stock at $2.00 per share, which expire in April 2003. These warrants, if exercised would provide us with proceeds of up to $6.7 million. The holder of these warrants, however, may not elect to exercise the warrant to purchase shares of our common stock.

Because internally generated cash flow will not be sufficient to fund development and commercialization of our product candidates, grow our business and expand research and development of our product candidates for treating additional diseases, we will require substantial additional financial resources. We may be unable to obtain funding when needed on acceptable terms, if at all. A significant portion of our operating expenses are funded through our collaborative development agreements with third parties. The initial development periods of our collaborations with Genzyme and Elan will conclude in 2002 and the initial development periods of our other collaborations will conclude in 2003. These development collaborations typically provide for extension options to continue development of product candidates. Absent new collaborative partnerships or extensions to our existing collaborative partnerships, our research and development revenue and funding will decrease in 2003. We may also need to scale a large portion of our future research and development activities to match the levels of funding provided by our collaborators or from other funding that may be available to us. Assuming that we conduct our currently planned operating activities and receive the funding anticipated from our collaborative partners, and that we are able to scale our operations to reflect any lesser amount of funding, we expect that our available cash, anticipated interest income and collaborative funding will be sufficient to finance our operations to 2004. We may require additional capital before that time, however, as a result of unanticipated loss of funding from collaborative partners, the implementation of additional research and development programs or other factors discussed in the section of this Item 7 entitled Factors Affecting Our Operating Results, Our Business and Our Stock Price. We may be unable to obtain financing when needed on acceptable terms, if at all.

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 is convertible until July 2005, at Elan s option, into shares of our common stock, at an initial conversion price of $3.32 per share. Compounding dividends accrue semi-annually at 7% per year on the $1,000 per share face value of the stock, plus dividends. Dividends are not paid in cash but rather result in an increase in the number of shares of common stock issuable upon conversion. At the expiration of the convertibility period, the Series B preferred stock would be convertible into approximately 5.47 million shares, at an effective conversion price of $2.20 per share. Alternatively, Elan may exchange the Series B preferred stock for all shares of preferred stock that we hold in Emerald, which would increase Elan s ownership in the joint venture to 50%. If Elan exercises its exchange right, it must make a cash payment to us equal to 30.1% of the total funding that we and Elan provided to Emerald after its formation. We periodically monitor the redemption value of the Series B preferred stock, as measured by 30.1% of the fair value of the joint venture that Elan would receive, less the cash payable to us upon exchange by Elan. If and when the redemption value of the Series B preferred stock exceeds its then current carrying value, we will increase the carrying value of the Series B preferred stock to the redemption value and recognize a corresponding dividend to the Series B preferred shareholder. We will recognize subsequent increases or decreases in redemption value of the Series B preferred stock; however, decreases will be limited to amounts previously recorded as increases, so as not to reduce the carrying amount of the Series B preferred stock below the original basis of $12.0 million. The exchange right currently expires in April 2003, but is subject to extension by our mutual agreement with Elan.

We intend to take advantage of additional funding opportunities as they arise. If we fail to receive substantial amounts of our currently anticipated collaborative funding or fail to secure additional collaborative agreements, or if we fail to obtain alternative financing when needed, we will need to substantially reduce the scope and size of our operations. We may also need to reduce or terminate business development or other operating activities, or delay, curtail or terminate research and development of one or more of our product candidates.

The following are our contractual commitments associated with our debt and lease obligations:

	Payments Due by Period				
	Total	2002	2003-2005	2006-2007	After 2007
Contractual Obligations					
Lease commitments	$ 23,853,000	$ 2,903,000	$ 6,300,000	$ 2,725,000	$ 11,925,000
Long term obligations	17,711,000	1,308,000	5,876,000	10,527,000	
Total	$ 41,564,000	$ 4,211,000	$ 12,176,000	$ 13,252,000	$ 11,925,000

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Impact of New Accounting Pronouncements

In June 2001, the FASB issued SFAS No. 141, *Business Combinations* and SFAS No. 142, *Goodwill and Other Intangibles*. SFAS No. 141 requires that business combinations be accounted for using the purchase method of accounting, effective July 1, 2001. SFAS No. 142 requires the use of a nonamortization approach to account for goodwill and certain intangibles, effective January 1, 2002. Under this nonamortization approach, goodwill and certain intangibles will not be amortized into results of operations, but instead will be reviewed for impairment and written down through a charge to operations only in the periods in which the carrying value of goodwill and certain intangibles is more than its fair value. As of January 1, 2002, of the $31.8 million of net goodwill and other purchased intangibles, $31.4 million will be classified as goodwill and will no longer be amortized. The remaining $0.4 million will be classified apart from goodwill and will continue to be amortized over its estimated remaining useful life. We expect adoption of this accounting standard to substantially reduce our amortization of purchased goodwill and intangibles commencing January 1, 2002. The amount of goodwill amortization that would have been recorded in 2002 is approximately $5.6 million. Since future impairment reviews will be based on events and estimations in the future, we are currently unable to estimate the effect that such review may have on our consolidated financial statements.

The FASB also recently issued SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, which is applicable to financial statements issued for fiscal years beginning after December 15, 2001. SFAS No. 144 supersedes SFAS No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of*, and portions of Accounting Principles Bulletin Opinion No. 30, *Reporting the Results of Operations*. SFAS No. 144 provides a single accounting model for disposal of long-lived assets and significantly changes the criteria for classification of an asset as held-for-sale. If assets are classified as held-for-sale, they are not depreciated and are stated at the lower of fair value and carrying amount. SFAS No. 144 also requires us to display expected future operating losses from discontinued operations in the period or periods in which the losses are incurred, rather than as of the measurement date, as presently required. We do not expect the provisions of SFAS No. 144 to have a significant effect on our financial position or operating results as we currently do not hold any of our assets as held-for sale and we have no indication that an impairment of any of our long-lived assets exists.

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 Product Development and Regulatory Approval

If we are unable to successfully complete preclinical and clinical development of our product candidates, we will be unable to generate sufficient capital to maintain our business.

All of our potential products are either in research and development or in early-stage clinical trials. Our ability to apply for and obtain regulatory approval of our potential products depends upon successful completion of additional research and development and testing, in both preclinical and clinical trials. A product candidate that appears promising at an early stage of research or development may not result in a commercially successful product. Our trials may fail to demonstrate the safety and efficacy of a prospective product, for example, or we may encounter unacceptable side effects or other problems during or after clinical trials. Should this occur, we may have to delay or discontinue development of the potential product, and corporate partners that support development of that product candidate may terminate their support. If we are unable to successfully complete preclinical and clinical development of some or all of our product candidates, we may be unable to generate sufficient product revenue to maintain our business.

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Completion of clinical trials may take several years or more. The number and cost of clinical trials and the length of time necessary to complete trials generally varies substantially according to the type, complexity, novelty and intended use of the product candidate. The commencement, cost and rate of completion of our clinical trials may vary or be delayed for many reasons, including the risks discussed under the subheading below entitled Risks Related to Our Industry and Clinical Trials and elsewhere in this Factors Affecting Our Operating Results, Our Business and Our Stock Price section.

Failure to timely obtain regulatory approval for our product candidates could prevent or impair our ability to commercialize our products.

Even if our clinical trials are successful, commercializing any product in the United States or abroad requires regulatory approval from the Food and Drug Administration, or FDA, and applicable state and foreign regulators. Moreover, the FDA and other applicable regulatory bodies must conclude at each stage of clinical testing that our clinical data suggest acceptable levels of safety and efficacy in order for us to proceed to the next stage of clinical trials. In addition, gene therapy clinical trials that receive funding from the 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 an NIH-funded clinical trial can begin, the NIH s Institution Biosafety Committee must review the proposed clinical trial to ensure that there are no safety issues associated with the trial. The regulatory process in the gene therapy industry is costly, time consuming and subject to unpredictable delays, and regulatory requirements governing gene and cell therapy products frequently change. In addition, 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 among trials and potential products. 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. To our knowledge, no gene therapy products have received regulatory approval in the United States or in other countries. Because our product candidates involve new and unproven technologies, we believe that regulatory approval may proceed more slowly than clinical trials involving traditional drugs. We do not expect any of our product candidates to be approved for commercial sale for at least several years. Some or all of our product candidates may never receive regulatory approval or may not receive approval for all of the clinical applications for which we seek approval. 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 product sales or royalty revenue.

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

Our manufacturing operations are subject to the current Good Manufacturing Practices requirements of the FDA, as well as to other federal, state and local regulations such as the Occupational Health and Safety Act and the Environmental Protection Act. While we currently anticipate that we will be able to manufacture products that meet applicable regulatory requirements, we may be unable to attain or maintain compliance with current or future regulations. If we discover previously unknown manufacturing, contamination, product side effect or other problems after we receive regulatory approval for a potential product or fail to comply with applicable requirements, we may suffer restrictions on our ability to market the product or be required to withdraw the product from the market. Either of these, or an unexpected increase in the cost of compliance, could make it more difficult to maintain or improve our financial condition.

Risks Related to Our Business Operations

If we lose significant collaborative funding or we are unable to raise additional capital when needed, we may be unable to develop our potential products and conduct our operations.

Because internally generated cash flow will not fund development and commercialization of our products, we will require substantial additional financial resources to develop and commercialize our potential products. A significant portion of our operating expenses are funded through our collaborative development agreements with third parties. If a current or future collaborator were to terminate its financial or scientific support of a potential product, we may be unable to complete development and commercialization of that product candidate. We currently

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have collaborations with five pharmaceutical and biotechnology companies and a public health organization that provide expertise and funding to develop our product candidates. The initial development periods of three of these collaborations Emerald Gene Systems for enhanced gene delivery systems, Genzyme Corporation for lysosomal storage disorders and IAVI for AIDS vaccines will conclude in 2002 or early 2003. Each of these agreements will terminate unless we and the collaborator agree to extend the agreement. Substantially all of our revenue and substantially all of our expected revenue for the next several years, are derived from our collaborations to develop product candidates. If we were to lose this revenue, or other sources of funding that our corporate partners provide, we may be unable to continue our research and development program for the potential product covered by the collaboration and our business would suffer. Assuming that we conduct our currently planned operating activities and receive the funding anticipated from existing corporate partners, and that we are able to scale our operations to reflect any lesser amount of funding, we expect that our available cash, anticipated interest income and collaborative funding will be sufficient to finance our operations to 2004. We may require additional capital before that time, however, as a result of unanticipated loss of funding from collaborative partners, the implementation of additional research and development programs or other factors discussed in this Factors Affecting Our Operating Results, Our Business and Our Stock Price section or elsewhere in this annual report. We may be unable to obtain financing when needed on acceptable terms, if at all.

We intend to take advantage of additional funding opportunities as they arise. Sources of additional funding could include one or more of the following:

- product development and funding collaborations;
- technology sales;
- technology licenses;
- issuing debt; or
- issuing equity.

If we lose significant amounts of collaborative funding or we are unable to obtain additional financing when needed, we will be forced to make substantial reductions in the scope and size of our operations. We may be forced to delay or terminate one or more research and development programs, curtail capital expenditures or reduce or terminate business development and other operating activities.

We have a history of losses and may never become profitable, which could result in a decline in the value of our common stock and a loss of your investment.

We have generated small amounts of revenue and incurred significant net losses since inception. As of December 31, 2001, we had an accumulated deficit of $178.0 million. We expect to continue to incur substantial additional losses in the future, primarily due to the following factors:

- we will not generate any product revenue for at least several years because all of our product candidates are in preclinical and clinical development and have not received regulatory approval for commercial sale; and
- we will continue to incur significant expense for the foreseeable future to develop our research and development programs, conduct preclinical and clinical trials, seek regulatory approval for our product candidates and provide general and administrative support for these activities.

We may never generate profits and, if we do become profitable, we may be unable to sustain or increase profitability.

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

We have entered into various license agreements, both exclusive and nonexclusive, 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 and those of our partners. If we are unable to maintain our current licenses or obtain additional licenses on acceptable terms for technology used in our potential products, we and our corporate partners may be required to expend significant time and resources to develop or in-license replacement technology. If we are unable to do so, we may be unable to develop or commercialize some or all of our potential products. In addition, the license agreements for technology for which we hold exclusive licenses typically contain provisions requiring us to meet minimum development milestones in order to maintain the license on an exclusive basis. If we do not meet these requirements, our licensors may convert the license to a nonexclusive license or terminate the license.

We may be unable to develop and commercialize some of our potential products if our relationships with scientific consultants and corporate collaborators are not successful.

Our success depends on the continued availability of outside scientific consultants and corporate collaborators to perform research and to provide or develop technology and processes to advance and augment our internal efforts. Competition for scientific consultants and corporate collaborators in gene therapy is intense. If we are unsuccessful in establishing additional and maintaining existing relationships with individual and corporate collaborators, we could experience delays in our research and development or loss of access to important enabling technology. We may be unable to enter into additional collaborations on acceptable terms, if at all. Even if we maintain our current scientific collaborations or establish new relationships, they may never result in the successful development of product candidates.

The development and commercialization of many of our potential products, and therefore, the success of our business, substantially depends on the performance of these scientific consultants and corporate collaborators. Because they are not our employees, we have limited control over their activities and the amount of time they devote to our business. If our scientific consultants do not dedicate sufficient time, or if our corporate partners do not commit sufficient financial and technical resources, to our research and development programs or the commercialization of our potential products, the preclinical or clinical development related to the collaboration could be delayed or terminated. Even if substantial time and resources are dedicated to developing our product candidates, we may be unable to successfully complete development and commercialization of our product candidates. Our current or future collaborators may provide scientific expertise, technology or funding for, or develop or market, competing products or alternative technologies.

Any rights in inventions or processes discovered by a scientific consultant may be contractually subject to the rights of his or her research institution in that work. Some consultants may have obligations to other entities under consulting or other agreements that may potentially conflict with their obligations to us. Disputes, and potentially litigation, may arise with respect to ownership of technology invented or discovered by a scientific consultant or with respect to a product candidate developed under corporate collaborations. We may be unable to secure our rights with respect to these technology or product candidates.

Risks Related to Our Industry and Clinical Trials

Adverse events in the field of gene therapy could damage public perception of our prospective 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 November 1999, a patient with a rare metabolic disorder died in a gene therapy trial using an adenoviral vector to deliver a therapeutic gene. Genovo, a company we later acquired, was providing partial funding for this investigator-sponsored trial conducted at the University of Pennsylvania. Other patient deaths, though unrelated to gene therapy, have occurred in other clinical trials. These deaths 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. For example, there has been concern in the past regarding the potential safety and

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efficacy of gene therapy products derived from pathogenic viruses like adenoviruses. While our product candidates use AAV vectors, which are nonpathogenic, and nonviral vectors, the public and the medical community nonetheless may conclude that our technology is unsafe. Moreover, to the extent that unfavorable publicity or negative public perception arising from other biotechnology-related fields such as human cloning and stem-cell research are linked in the public mind to gene therapy, our industry will be harmed.

Future adverse events in or negative public perception regarding gene therapy or the biotechnology industry could also result in greater governmental regulation, 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.

The success of our early clinical trials are based on small numbers of patients over the short term and may not be indicative of results in a large number of patients or long-term efficacy.

Results in early-stage clinical testing are based on limited numbers of patients. Our reported progress and results from our early phases of clinical testing 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 will have a lasting effect. If a larger group of patients does not experience positive results, or any favorable results do not demonstrate a lasting effect, the product candidate may not receive approval from the FDA for further studies or commercialization. In addition, 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.

Failure to recruit patients could delay or prevent clinical trials of our potential products, which could cause a delay or inability to develop those potential products.

Identifying and qualifying patients to participate in testing our potential products is critical to our near-term success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our products. We have experienced delays in our previous and current clinical trials, and we may experience similar delays in the future. If negative publicity as a result of adverse events in the biotechnology industry affects the willingness of patients to participate in our gene therapy trials, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products will be delayed. Delays in recruiting or enrolling patients to test our products result in increased costs, delays in advancing our product development and delays in proving the effectiveness of our technology, and could result in termination of the clinical trials altogether. Any of these events could delay or prevent the development of our product candidates.

The success of our technology in animal models does not guarantee that the same results will be replicated in humans.

Because animals are different from humans, the successful results of our technology in animal models may not be predictive of the results that we will see in our clinical trials with humans. If successful results for a potential product in animal models are not replicated in human clinical trials, we may have to expend greater resources to pass the clinical trial stage and obtain regulatory approval of the product candidate or abandon its development.

Risks Related to Our Intellectual Property

We may be unable to adequately protect our proprietary rights, which may limit our ability to successfully market any products.

Our success substantially depends 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 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.

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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 substantially 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 could suffer a reduction in sales or be forced out of the market.

Intellectual property disputes regarding third-party technology that we license may prevent or impair our ability to develop and commercialize our product candidates.

We have licensed technology underlying several issued and pending patents, and have acquired rights to the gene delivered in our product candidate for cystic fibrosis. 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 competitors could market competing products using the intellectual property. Licensing of intellectual property critical to our business 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 scientific collaborators; 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. For example, in 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. Our tgAAVCF product candidate for treating cystic fibrosis uses our proprietary AAV delivery technology to deliver a normal copy of the CFTR gene. Interference proceedings before the USPTO are confidential, involving the opposing parties only, and can take several years to complete. Although we are not a party to the interference proceeding, its outcome could affect our license to the CFTR gene and related vector. The USPTO could rule that our licensor has priority of invention on both the CFTR gene and vector that we license, that our licensor has priority of invention on neither the gene nor the vector, or that our licensor has priority of invention on only the gene or only the vector. If the USPTO or 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.

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If our licensor does not retain its rights to the CFTR gene and the vector, and we cannot maintain 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.

Intellectual property claims and litigation could strain our resources and subject us to significant liability for damages and invalidation of our proprietary rights.

As the biotechnology industry expands, the risk increases that other companies may claim that our processes and potential products infringe on their patents. 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 a litigation or 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.

Risks Related to the Capital Markets and Dilution

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

In recent years, 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. Our common stock has experienced, and is likely to continue to experience, price fluctuations that cause the market price of our common stock to decline. 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. Market fluctuations in the price of our common stock could adversely affect our collaborative opportunities and our future ability to sell equity securities at a price we deem appropriate, and you could lose all or part of your investment.

Our future capital-raising activities could involve the issuance of equity securities, which would dilute your investment and could result in a decline in the trading price of our common stock.

To meet our long-term funding requirements, we may sell securities in the public or private equity markets if and when conditions are favorable, even if we do not have an immediate need for additional capital at that time. Furthermore, we may enter into financing transactions at prices that represent a substantial discount to market price. Raising funds through the issuance of equity securities will dilute the ownership of our existing shareholders. A negative reaction by investors and securities analysts to any discounted sale of our equity securities could result in a decline in the trading price of our common stock.

Additional Risks Related to Our Industry

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. Although we believe that our safety procedures for handling, storing and disposing of these materials comply with applicable laws and regulations, we cannot eliminate the risk of accidental contamination or injury from hazardous materials. If a hazardous material accident occurred, we could be held liable for any resulting damages. This liability could exceed our financial resources. These hazardous materials are subject to federal, state and local regulations. We may be required to incur significant costs to comply with future environmental or other laws. Accidents unrelated to our operations could cause federal, state

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or local regulatory agencies to restrict our access to hazardous materials needed in our research and development efforts. If our access to these materials is limited, we could experience 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 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, drugs and other pharmaceutical products. 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 we are able to market or result in our products failing to achieve market acceptance.

Gene therapy is a new and rapidly evolving field and is expected to continue to undergo significant and rapid technological change and competition. Our competitors may develop new technologies and products that are available for sale before our potential products or that may be more effective than our potential products. 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 could impair our ability to successfully commercialize our potential products and become profitable.

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 these proposals 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.

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Our ability to successfully commercialize our product candidates will substantially depend on the willingness of third-party payors to provide adequate reimbursement for the cost of our products.

Sales of medical products and treatments substantially depend, both domestically and abroad, on the availability of reimbursement to the consumer from third-party payors. Considerable pressure to reduce healthcare costs may cause reimbursement to become more restricted in the future. 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.

Additional Risks Related to Our Business Operations

Our business will not succeed if our product candidates fail to achieve market acceptance.

Even if our potential products succeed in clinical trials and are approved for marketing, these products may never achieve market acceptance. If marketing our products is unsuccessful 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 in this section or elsewhere in this annual report, we will be unable to generate sufficient product revenues to maintain our business.

Our limited manufacturing capability may limit our ability to successfully introduce our potential products.

We currently do not have the capacity to manufacture large-scale commercial quantities of our potential products. To do so, we will need to expand our current facilities and staff or supplement them through the use of contract providers. Our current manufacturing facility, which is designed for manufacturing our AAV vectors for clinical and development purposes, is subject to initial and ongoing regulation by the FDA and other government agencies, and 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. If we are unable to obtain and maintain the necessary manufacturing capabilities, either alone or through third parties, we will be unable to manufacture sufficient product to sustain our business. In addition, we are unlikely to become profitable if we or our contract providers are unable to manufacture our products in a cost-effective manner.

If we do not attract and retain qualified personnel, we will be unable to successfully develop our potential products.

Our future success depends in large part on our ability to attract and retain key technical and management employees and scientific advisors. We have programs in place to retain personnel, including competitive compensation packages and programs to create a positive work environment. Because other companies, research and academic institutions and other organizations in our field compete intensely for employees, however, we may be unable to retain our existing personnel or attract additional qualified employees and advisors. If we experience excessive turnover or difficulties in recruiting new personnel, our research and development could be delayed and we could experience difficulties in generating sufficient revenue to maintain our business.

If we do not develop adequate 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.

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 corporate partners to utilize their mature marketing and distribution capabilities. However, we may be unable to enter into marketing and distribution agreements on favorable terms, if at all. While we believe that our corporate partners will be motivated to market and distribute our potential products, our current and potential future partners may not commit sufficient resources to commercializing our products and technology on a timely basis. If our corporate partners do not adequately market and distribute our products 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.

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Product liability and other claims and product recalls could exceed our insurance coverage and damage our reputation, which could significantly harm our financial condition.

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. 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, health care providers or other sellers or users of our products. We may also face product recalls and adverse publicity resulting from a product recall or a liability claim against us or a collaborative partner. 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, 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.

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

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 neither employ any derivative or other financial instruments or derivative commodity instruments to hedge any market risks nor plan to employ these instruments in the future. At December 31, 2001, we held $25.2 million in cash and cash equivalents, which are primarily invested in a short-term bond fund invested in securities that, on the average, mature in less than 12 months. An analysis of the impact on these instruments of a hypothetical 10% change in short-term interest rates compared to interest rates at December 31, 2001, indicates that such change would not have a significant impact on expected fiscal year 2002 earnings.

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

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REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

The Board of Directors and Shareholders
Targeted Genetics Corporation

We have audited the accompanying consolidated balance sheets of Targeted Genetics Corporation as of December 31, 2001 and 2000, and the related consolidated statements of operations, redeemable preferred stock and shareholders equity, and cash flows for each of the three years in the period ended December 31, 2001. 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 auditing standards generally accepted in the 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 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, 2001 and 2000, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2001 in conformity with accounting principles generally accepted in the United States.

As described in Note 1 to the consolidated financial statements, in 2000 the Company changed its method of accounting for revenue recognition.

As described in Note 1 to the consolidated financial statements, the Company has restated its consolidated balance sheets as of December 31, 2001 and 2000 and its consolidated statements of operations and redeemable preferred stock and shareholders equity for each of the three years in the period ended December 31, 2001.

ERNST & YOUNG LLP

Seattle, Washington
February 14, 2002, except for the
last two paragraphs of Note 1,
as to which the date is
July 29, 2002

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TARGETED GENETICS CORPORATION

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2001	2000
	(restated)	(restated)
ASSETS		
Current assets:		
Cash and cash equivalents	$ 25,186,000	$ 38,630,000
Accounts receivable	2,475,000	3,087,000
Receivable from unconsolidated, majority-owned research and development joint venture	893,000	177,000
Prepaid expenses and other	935,000	292,000
Total current assets	29,489,000	42,186,000
Property and equipment, net	8,308,000	6,206,000
Goodwill and other purchased intangibles, net	31,752,000	37,821,000
Other assets	1,489,000	1,761,000
	$ 71,038,000	$ 87,974,000
LIABILITIES AND SHAREHOLDERS EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	$ 3,452,000	$ 3,579,000
Payable to unconsolidated, majority-owned research and development joint venture	1,123,000	262,000
Accrued employee expenses	1,114,000	696,000
Deferred revenue	4,631,000	6,906,000
Current portion of long-term obligations	1,308,000	838,000
Total current liabilities	11,628,000	12,281,000
Deferred rent	640,000	404,000
Long-term obligations	16,403,000	2,447,000
Deferred revenue	4,966,000	9,410,000
Commitments		
Series B convertible exchangeable preferred stock	12,015,000	12,015,000
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; 12,015 shares designated, issued and outstanding		
Common stock, $0.01 par value, 80,000,000 shares authorized, 44,125,677 shares issued and outstanding at December 31, 2001 and 42,608,943 shares at December 31, 2000	441,000	426,000
Additional paid-in capital	202,927,000	201,803,000
Accumulated deficit	(177,982,000)	(150,812,000)
Total shareholders equity	25,386,000	51,417,000
	$ 71,038,000	$ 87,974,000

See accompanying notes to the consolidated financial statements.

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TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2001	2000	1999
Revenue:			
Collaborative agreements	$ 16,117,000	$ 9,553,000	$ 6,402,000
Collaborative agreement with unconsolidated, majority-owned research and development joint venture	2,763,000	1,850,000	446,000
Total revenue	18,880,000	11,403,000	6,848,000
Operating expenses:			
Research and development	31,546,000	19,312,000	14,291,000
Equity in net loss of unconsolidated, majority-owned research and development joint venture	3,666,000	2,474,000	12,610,000
Acquired in-process research and development		28,029,000	3,200,000
Amortization of acquisition-related intangibles	6,069,000	1,686,000	
General and administrative	6,203,000	5,707,000	3,593,000
Total operating expenses	47,484,000	57,208,000	33,694,000
Loss from operations	(28,604,000)	(45,805,000)	(26,846,000)
Investment income	1,886,000	2,097,000	426,000
Interest expense	(452,000)	(265,000)	(235,000)
Loss before cumulative effect of change in accounting principle	(27,170,000)	(43,973,000)	(26,655,000)
Cumulative effect of change in accounting principle		(3,682,000)	
Net loss	$ (27,170,000)	$ (47,655,000)	$ (26,655,000)
Computation of basic and diluted net loss per common share:			
Loss before cumulative effect of change in accounting principle (restated)	$ (0.62)	$ (1.16)	$ (0.83)
Cumulative effect of change in accounting principle		(0.10)	
Net loss per common share (restated)	$ (0.62)	$ (1.26)	$ (0.83)
Shares used in computation of basic and diluted net loss per common share	43,927,822	37,752,164	32,173,756

See accompanying notes to the consolidated financial statements.

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TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF REDEEMABLE PREFERRED STOCK AND SHAREHOLDERS EQUITY
(Restated)

	Series B Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Shareholders Equity
	Shares	Amount	Shares	Amount				
Balance at January 1, 1999		$	30,652,375	$ 307,000	$ 88,149,000	$ (76,502,000)	$28,000	$11,982,000
Net loss 1999						(26,655,000)		(26,655,000)
Unrealized gains on securities available for sale							(44,000)	(44,000)
Comprehensive loss								(26,699,000)
Issuance of Series B convertible exchangeable preferred stock for interest in unconsolidated, majority-owned research and development joint venture	12,015	12,015,000						
Sale of common stock to Celltech for cash, net of issuance costs of $14,000			677,392	7,000	1,480,000			1,487,000
Sale of common stock to Elan, net of issuance costs of $57,000			2,148,899	21,000	4,921,000			4,942,000
Issuance of common stock and warrants to Alkermes for technology rights, net of issuance costs of $18,000			500,000	5,000	3,177,000			3,182,000
Exercise of stock options			40,509		56,000			56,000
Balance at December 31, 1999	12,015	12,015,000	34,019,175	340,000	97,783,000	(103,157,000)	(16,000)	(5,050,000)
Net loss 2000						(47,655,000)		(47,655,000)
Unrealized losses on securities available for sale							16,000	16,000
Comprehensive loss								(47,639,000)
Sale of common stock for cash, net of issuance costs of $2,181,000			2,164,285	22,000	28,097,000			28,119,000
			382,739	4,000	4,992,000			4,996,000

Issuance of common stock to Elan for cash, net of issuance costs of $4,000								
Issuance of common stock in Genovo acquisition			5,250,805	53,000	66,077,000			66,130,000
Exercise of stock options			730,765	7,000	4,600,000			4,607,000
Exercise of warrants			61,174		254,000			254,000
Balance at December 31, 2000	12,015	12,015,000	42,608,943	426,000	201,803,000	(150,812,000)		51,417,000
Net loss and comprehensive loss 2001						(27,170,000)		(27,170,000)
Cancellation of shares held in escrow related to Genovo acquisition			(155,649)	(2,000)	(1,998,000)			(2,000,000)
Exercise of stock options			672,383	7,000	1,052,000			1,059,000
Exercise of warrants			1,000,000	10,000	1,990,000			2,000,000
Stock based compensation					80,000			80,000
Balance at December 31, 2001	12,015	$12,015,000	44,125,677	$ 441,000	$ 202,927,000	$ (177,982,000)	$	$25,386,000

See accompanying notes to the consolidated financial statements.

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TARGETED GENETICS CORPORATION

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2001	2000	1999
Operating activities:			
Net loss	$ (27,170,000)	$ (47,655,000)	$ (26,655,000)
Adjustments to reconcile net loss to net cash used in operating activities:			
Cumulative effect of change in accounting principle adjustment		3,682,000	
Equity in net loss of unconsolidated, majority-owned research and development joint venture	3,666,000	2,474,000	12,610,000
Acquired in-process research and development		28,029,000	3,200,000
Depreciation and amortization	2,623,000	1,473,000	1,614,000
Amortization of acquisition-related intangibles	6,069,000	1,686,000	
Stock-based compensation expense	80,000	301,000	
Changes in assets and liabilities:			
Increase (decrease) in deferred revenue	(6,719,000)	12,635,000	
Increase in accounts receivable	(1,388,000)	(1,695,000)	(1,289,000)
Decrease (increase) in accounts receivable from unconsolidated, majority-owned research and development joint venture	(716,000)	269,000	(446,000)
Decrease (increase) in prepaid expenses and other	(643,000)	(396,000)	62,000
Increase (decrease) in current liabilities	241,000	(972,000)	626,000
Increase in deferred rent	236,000	364,000	40,000
Increase (decrease) in other assets	178,000	(800,000)	
Net cash used in operating activities	(23,543,000)	(605,000)	(10,238,000)
Investing activities:			
Purchases of property and equipment	(4,411,000)	(2,797,000)	(1,856,000)
Investment in unconsolidated, majority-owned research and development joint venture	(2,805,000)	(2,807,000)	
Maturities and sales of securities available for sale		3,024,000	7,393,000
Purchases of securities available for sale			(483,000)
Net cash acquired in acquisition		359,000	
Net cash provided by (used in) investing activities	(7,216,000)	(2,221,000)	5,054,000
Financing activities:			
Loan proceeds from collaborative partners	13,000,000		1,000,000
Net proceeds from sales of capital stock	3,059,000	37,976,000	6,468,000
Proceeds from leasehold improvements and equipment financing arrangements	2,401,000	671,000	1,294,000
Payments under leasehold improvements and equipment financing arrangements	(1,145,000)	(1,292,000)	(1,348,000)
Net cash provided by financing activities	17,315,000	37,355,000	7,414,000
Net increase (decrease) in cash and cash equivalents	(13,444,000)	34,529,000	2,230,000
Cash and cash equivalents, beginning of year	38,630,000	4,101,000	1,871,000
Cash and cash equivalents, end of year	$ 25,186,000	$ 38,630,000	$ 4,101,000
Supplemental information:			
Cash paid for interest	$ 269,000	$ 245,000	$ 203,000
Acquisition-related common stock issued (recovered)	(2,000,000)	66,130,000	
Preferred stock dividend	945,000	885,000	376,000
Preferred stock issuance in exchange for interest in unconsolidated, majority-owned research and development joint venture			12,015,000

See accompanying notes to the consolidated financial statements

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TARGETED GENETICS CORPORATION

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 operate our business in one reportable segment, research and product development. On both our own behalf and in connection with various collaborative agreements with others, we conduct research and development of gene therapy products and technologies for treating acquired and inherited diseases.

Basis of Presentation

Our consolidated financial statements include the accounts of Targeted Genetics, our wholly owned subsidiaries Genovo, Inc. and TGCF Manufacturing Corporation, and our majority owned subsidiary, CellExSys, Inc. The consolidated financial statements do not include Emerald Gene Systems, Ltd. our unconsolidated, majority-owned research and development joint venture with Elan International Services Ltd., a wholly owned subsidiary of Elan Corporation plc, because we do not have operating control of the joint venture. All significant inter-company transactions have been eliminated in consolidation.

Cash Equivalents

We consider to be cash equivalents all short-term investments that have a maturity at the time of purchase of three months or less, are readily convertible into cash and have insignificant interest rate risk. Our cash equivalents, recorded at cost, which approximates fair market value, consist principally of money market accounts and shares of a short-term, limited-maturity mutual 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

Our financial statements present property and equipment at cost less accumulated depreciation, which includes the amortization of assets recorded under equipment financing leases. We compute depreciation of property and equipment using the straight-line method over the asset s estimated useful life, which ranges from three to seven years. Leasehold improvements are amortized over the asset s estimated useful life or the lease term, whichever is shorter.

Purchased Intangible Assets

Purchased intangible assets consist of acquired technology that is core to our development programs and goodwill. We amortize our purchased intangibles on the straight-line method over periods ranging from two to seven years.

Long-Lived Assets

In accordance with Statement of Financial Accounting Standards (SFAS) No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed Of*, we review the carrying value of intangible assets and other long-lived assets on a regular basis for the existence of facts or circumstances, both internal and external, that may indicate impairment. 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. To date, we have no indication that an impairment of our intangible and other long-lived assets exists.

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TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Series B Convertible Exchangeable Preferred Stock

Our Series B convertible exchangeable preferred stock, which is currently valued at $12 million, is convertible into shares of our common stock or may be exchanged, at Elan s option, for a 30.1% ownership interest in Emerald. If Elan exercises its exchange right, it must make a cash payment to us equal to 30.1% of the total funding that we and Elan provided to Emerald after its formation. We periodically monitor the redemption value of the Series B preferred stock, as measured by 30.1% of the fair value of the joint venture that Elan would receive, less the cash payable to us upon exchange by Elan. If and when the redemption value of the Series B preferred stock exceeds its then current carrying value, we will increase the carrying value of the Series B preferred stock to the redemption value and recognize a corresponding dividend to the Series B preferred shareholder. We will recognize subsequent increases or decreases in redemption value of the Series B preferred stock; however, decreases will be limited to amounts previously recorded as increases, so as not to reduce the carrying amount of the Series B preferred stock below the original basis of $12.0 million. The exchange right currently expires in April 2003, but is subject to extension by our mutual agreement with Elan.

Stock Compensation

As permitted by the provisions of Financial Accounting Standards Board (FASB) Statement No. 123, *Accounting for Stock-Based Compensation*, we have elected to follow Accounting Principles Board (APB) Opinion No. 25, Accounting for Stock Issued to Employees, and related interpretations in accounting for employee stock option grants, and we apply the disclosure-only provisions to account for our stock option plans. 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. Options granted to consultants are recorded as an expense over their vesting term based on their fair value, which is determined using the Black-Scholes method.

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 recognized ratably over 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. Payments received in excess of amounts earned are classified as deferred revenue.

We previously recognized nonrefundable, up-front license fees as revenue when the technology was transferred and when all of its significant contractual obligations relating to the fees had been fulfilled. Effective January 1, 2000, we changed our method of accounting for nonrefundable up-front license fees to recognize such fees over the term of the related research and development collaboration arrangement on a straight-line basis, as this method best matches the effort provided. We believe that this change in accounting principle is preferable, based on guidance provided in the SEC s Staff Accounting Bulletin (SAB) No. 101, Revenue Recognition in Financial Statements. The $3.7 million cumulative effect of the change in accounting principle, calculated as of January 1, 2000, was reported as a charge for the year 2000. The cumulative effect was recorded as deferred revenue that was recognized as revenue over the remaining term of the research and development collaboration agreements. $2.1 million ($0.06 per share) of the $3.7 million cumulative effect was amortized as deferred revenue in 2000 and $1.6 million ($0.04 per share) was amortized in 2001. Had the change in accounting been in effect retroactively to January 1, 1999, net loss for 1999 would have decreased by $2.1 million ($0.07 per share).

Relationships with Strategic Partners

In connection with our collaborations with Biogen, Inc., Celltech Group plc and Genzyme Corporation and our joint venture with Elan, each strategic partner purchased shares of our common stock. The number of shares of our common stock that we issued to each of our strategic partners represented less than 10% of our total shares then outstanding. We cannot control or monitor shares of our stock that these partners may buy or sell in open market transactions. Although each of our collaborative partners influence the activities specific to their collaborations with us, our partners do not influence our management or operating policies generally or otherwise significantly influence our operating activities.

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TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Significant Revenue Relationships and Concentration of Risk

Four companies accounted for 100% of the revenue we recorded from collaborative agreements in 2001 and 2000. One company accounted for 100% of our revenue from collaborative agreements in 1999. Emerald Gene Systems, our 80.1% unconsolidated, majority-owned research and development joint venture with Elan, accounted for all of our revenue from collaborative agreements with unconsolidated joint ventures. A change in the level of work or funding received from any one of these collaborative partners could disrupt our business and adversely affect our cash flow and results of operations.

Research and Development Costs

Research and development costs are expensed as incurred. Costs and expenses related to programs conducted under collaborative agreements that result in collaborative revenue totaled $11.4 million in 2001, $6.6 million in 2000 and $6.7 million in 1999. See Notes 6 and 7 for more detailed information.

Net Loss Per Common Share

Net loss per common share is based on net loss after giving effect to preferred stock dividends, 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 13,535,778 shares in 2001, 14,028,623 shares in 2000 and 12,632,797 shares in 1999.

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.

Recent Accounting Pronouncements

In June 2001, the FASB issued SFAS No. 141, *Business Combinations* and SFAS No. 142, *Goodwill and Other Intangibles*. SFAS No. 141 requires that business combinations be accounted for using the purchase method of accounting, effective July 1, 2001. SFAS No. 142 requires the use of a nonamortization approach to account for goodwill and certain intangibles, effective January 1, 2002. Under this nonamortization approach, goodwill and certain intangibles will not be amortized into results of operations, but instead will be reviewed for impairment and written down through a charge to operations only in the periods in which the carrying value of goodwill and certain intangibles is more than its fair value. As of January 1, 2002, of the $31.8 million of net goodwill and other purchased intangibles, $31.4 million will be classified as goodwill and will no longer be amortized. The remaining $0.4 million will be classified apart from goodwill and will continue to be amortized over its estimated remaining useful life. We expect adoption of this accounting standard to substantially reduce our amortization of purchased goodwill and intangibles commencing January 1, 2002. The amount of goodwill amortization that would have been recorded in 2002 is approximately $5.6 million. Since future impairment reviews will be based on events and estimations in the future, we are currently unable to estimate the effect that such review may have on our consolidated financial statements. The following table reconciles the results of operations we reported for the years ended December 31, 1999, 2000 and 2001 to the amounts adjusted for the elimination of goodwill amortization that we would have recorded had we adopted SFAS No. 142 as of the beginning of each of those periods:

	Year ended December 31,		
	2001	2000	1999
Net loss	$ (27,170,000)	$ (47,655,000)	$ (26,655,000)
Elimination of goodwill amortization	5,564,000	1,547,000	