
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-K**

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934
OR
 TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF
THE
SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2000

Commission file No. 0-23930

TARGETED GENETICS CORPORATION

(Exact name of Registrant as specified in its charter)

Washington
(State of Incorporation)

91-1549568
(IRS Employer Identification No.)

1100 Olive Way, Suite 100
Seattle, WA 98101
(Address of principal executive offices) (Zip Code)

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

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

PREFERRED STOCK PURCHASE RIGHTS, \$.01 PAR VALUE

Indicate by check mark whether the Registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes No

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

Indicate the aggregate market value of voting stock held by nonaffiliates of the Registrant as of March 9, 2001: \$162,536,000

Indicate the number of shares outstanding of each of the Registrant's classes of common stock as of March 9, 2001:

<u>Title of Class</u>	<u>Number of shares</u>
Common Stock, \$.01 par value	43,757,050

DOCUMENTS INCORPORATED BY REFERENCE

(1) Portions of the Proxy Statement for the Annual Meeting of Shareholders to be held on May 8, 2001, are incorporated by reference into Part III of this report.

PART I
ITEM 1. BUSINESS

Forward-Looking Statements

Some of our statements in this annual report on Form 10-K are forward-looking statements that involve risks and uncertainties. In making these statements, we rely on a number of assumptions and make predictions about the future. Our actual results could differ materially from our expectations 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 rely unduly on these forward-looking statements, which apply only as of the date of this report. We undertake no duty to publicly announce or report revisions to the statements as new information becomes available that would cause us to change our expectations of the future.

Overview

Targeted Genetics Corporation develops gene therapy products and technologies for treating acquired and inherited diseases. We have assembled a broad base of core technologies that we believe has the potential to address a significant number of these diseases and we believe that we have expertise that will enable us to develop products based on these technologies. We have two lead products under development for treating cystic fibrosis and cancer and a promising pipeline of product candidates focused on hemophilia A, arthritis, cancer, lysosomal storage disease, cardiovascular disease and AIDS prophylaxis. We believe that our success in developing these initial products would demonstrate the value of our core technologies and their potential to treat numerous other 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 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 gene delivery, or vector, technologies. Our viral vector development activities focus on adeno-associated viral (AAV) vectors and our synthetic vectors are based on lipids. Currently, we are the only company with both viral and synthetic vectors in clinical development. We believe these systems give 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 intellectual property in the area of retroviral vectors, which may have utility in the area of *ex vivo* gene delivery or cell therapy.

Build a strong product development infrastructure. We believe that an abundance of basic research is being conducted in the area of gene delivery, and that those who are capable of translating that research into cost-effective products will derive significant value from those products. A great deal of discovery research has been focused on gene delivery techniques, but much less effort has been focused on creating the product development infrastructure that is necessary to move gene delivery concepts through clinical trials into the commercial realm. We have therefore focused the majority of our efforts on establishing product development expertise in the areas of preclinical biology, process development, manufacturing, 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 sooner than our competitors with products having a higher likelihood of success.

Demonstrate clinical proof of concept. We believe that by providing strong evidence of the clinical benefit of our products, we will generate significant value enhancement for our shareholders. We believe that we have two lead product candidates with significant potential to demonstrate clinical proof of concept in the near term: tgAAV-CF for cystic fibrosis and tgDCC-E1A for cancer. Both of these products entered Phase II clinical trials in 2000 and we expect to have the resulting data available to us in mid-2002. We believe that proof of concept in cystic fibrosis and cancer will serve to demonstrate the value not only of these two lead product candidates but of our AAV and synthetic gene delivery technologies as well.

Build a strong pipeline of product candidates with significant market potential. We believe that there is tremendous long-term potential for the use of our gene delivery systems to treat additional diseases. The infrastructure we have built to support the development of tgAAV-CF and tgDCC-E1A is now becoming available to support the development of new products based on our AAV and synthetic gene delivery systems. Similarly, the knowledge and expertise we gain in developing our two initial products should apply directly to future products under development. We believe that we can derive significant future value by applying this infrastructure, knowledge and expertise to additional pipeline products. Currently, we have ongoing preclinical product development activities in the areas of cancer, rheumatoid arthritis, hemophilia, lysosomal storage diseases, HIV vaccines and cardiovascular disease.

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

The following table summarizes our product development programs:

Program/Product	Preclinical	Phase I	Phase II	Phase III	Collaborator
AAV Vectors: Cystic Fibrosis Rheumatoid Arthritis Hemophilia A Lysosomal Storage Disorders HIV Vaccine Hyperlipidemia	XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX XXXXXX	XXXX	XXXX		Celltech Group --- Genetics Institute Genzyme IAVI ---
Synthetic Vectors: Head and Neck Cancer (tgDCC-E1A) Ovarian Cancer (tgDCC-E1A) Metastatic Cancer (tgLPD-E1A)	XXXXXX XXXXXX XXXXXX	XXXX XXXX	XXXX XXXX		--- --- ---
Adenoviral Vectors: Glioma (brain cancer)	XXXXXX				Biogen, Inc.

In addition to our gene delivery technologies, we have patents and expertise in cell therapy that may prove to have significant value. We have established a subsidiary, CellExSys, Inc., to exploit these technologies. Our technology and expertise enables the isolation of potent, disease-specific cytotoxic T lymphocytes (CTLs) from small samples of patient blood, which can then be expanded to large numbers for reinfusion to the patient. We believe that this technology and expertise could support development of a series of immunotherapies to treat infectious diseases and cancer. Key to this technology is our proprietary rapid expansion method (REM), for which we received our first patent in 1998. Using REM, we can grow billions of CTLs from individual cloned cells over several weeks, while preserving the cells' specific disease-fighting capabilities. We also believe that REM also has utility in the areas of genomic target validation, antigen discovery and vaccine development. We intend to transfer our REM technology to CellExSys in 2001.

Acquisition of Genovo, Inc.

In September 2000, we acquired all of the outstanding shares of common stock of Genovo, Inc. in a merger valued at approximately \$66 million. The transaction combines our product development pipeline and processes and our expertise in several gene delivery methods with Genovo's expertise in rapid AAV-vector production techniques and its product development collaborations with two leading biotechnology companies. In addition, the acquisition broadens our AAV-vector intellectual property and patent positions.

Genovo's major assets included:

- Proprietary AAV-based product development programs in the areas of hyperlipidemia, atherosclerosis and hemophilia;
- A collaboration with Genzyme Corporation covering the development of viral-based products to treat lysosomal storage disorders; and
- Intellectual property related to production, composition of matter and use of AAV-based products and additional patents related to other viral vector systems

In addition, we negotiated a new agreement with Biogen, Inc. that replaced a collaboration established between Genovo and Biogen in 1995. The new agreement covers an ongoing product development program in the oncology field and up to four other product candidates to be determined by Biogen and us over the next three years. A detailed description of our collaborations with Biogen and Genzyme is included in this section of Item 1 under the caption entitled "Research and Development Collaborations."

Clinical Product Development Programs

tgAAV-CF

Cystic fibrosis is the most common single-gene deficiency 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 (CFTR) gene, which results in a build-up of mucus in the lungs, leading to chronic infections, loss of lung function and early death. Current treatments for cystic fibrosis relieve only symptoms of the disease, and cannot cure the disease or stop its progression.

Our cystic fibrosis product candidate, designated tgAAV-CF, is comprised of a functional CFTR gene delivered in an AAV vector. Based on our research and development to date, we believe that tgAAV-CF may be superior to other gene-based approaches for the treatment of cystic fibrosis, due to the duration of its effect and lack of toxicity. In preclinical studies, we have observed gene transfer 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.

Our early clinical trials involved the administration of a liquid form of tgAAV-CF 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 resulting inflammatory response or other side effects, even after repeat delivery. Additionally, in the clinical trial involving administration of the product to the maxillary sinus, we observed consistent gene transfer, persistence of the gene for at least 70 days after treatment, improvements in measurements of chloride transport in cells after treatment, and reduction of inflammatory cytokine levels in the treated sinuses compared to the untreated ones.

In November 1998, we entered into a license and collaboration agreement related to tgAAV-CF with Medeva Pharmaceuticals, Inc., a subsidiary of Celltech Group plc. Under this agreement, Celltech owns exclusive worldwide marketing rights to tgAAV-CF and provides significant funding to Targeted Genetics. The section below entitled “Research and Development Collaborations” provides a detailed description of this relationship.

In December 1998, we began a Phase I clinical trial to test the safety of aerosol delivery of tgAAV-CF to the whole lungs of CF patients. The clinical trial, for which patient enrollment was completed in early 2000, was conducted at three sites: Stanford University, the University of Washington, and Harvard University. We treated twelve patients with a single dose of tgAAV-CF in the study, three each at four increasing dosage levels. Data suggests that tgAAV-CF delivered via nebulizer was safe and well-tolerated at all doses evaluated. Additionally, by examining tissue samples obtained by bronchoscopy, we observed efficient gene transfer in all patients at the highest dose. These samples, taken from various regions of patients’ lungs, indicate that tgAAV-CF was well distributed throughout the upper airways of the patients. We also observed the presence of vector in some patients up to 90 days after a single administration of aerosolized tgAAV-CF. tgAAV-CF has been granted orphan drug status by the United States Food and Drug Administration (FDA).

In November 2000, we began a Phase II clinical trial to test the efficacy of aerosol delivery of tgAAV-CF to the lungs of cystic fibrosis patients. The double-blind, placebo-controlled study will evaluate the impact of tgAAV-CF on lung function and inflammatory proteins in patients with cystic fibrosis.

tgDCC-E1A

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

Our product candidate for the treatment of cancer uses our proprietary synthetic delivery system, called DC-Cholesterol, to deliver the E1A gene locally to cancer cells. We call this product tgDCC-E1A. E1A is a gene from the adenovirus type 5, a common respiratory virus. Researchers have performed tests that indicate that E1A can function as an inhibitor of the HER-2/*neu* oncogene, which is known to be overexpressed in many cancers. Other research has indicated that E1A has other anti-tumor effects unrelated to the inhibition of HER-2/*neu* expression. Preclinical studies in mice bearing tumors indicate that DCC-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. Researchers have also performed preclinical studies that indicate that tgDCC-E1A sensitizes tumor cells to killing by certain chemotherapeutic agents or radiation. We have exclusive worldwide rights to issued patents covering the use of the E1A gene in cancer therapy.

We completed a series of Phase I and II clinical trials of tgDCC-E1A as a single agent in several different cancers before testing the product in combination with chemotherapy and radiation. 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 that had failed standard therapy, we delivered tgDCC-E1A as a single agent by direct injection into their tumors. The results 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. Additionally, in 55% of the patients, growth of the tumor was arrested or reversed.

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, Taxol and Cisplatin at increasing dose levels. We anticipate enrolling up to 21 patients in this study, which is ongoing at several centers. In late 2000, we began a clinical trial of tgDCC-E1A administered together with radiation therapy in patients with recurrent or inoperable head and neck cancer. We may enroll up to 50 patients with the goal of 38 evaluable patients. We are treating subjects with twice-weekly injections of tgDCC-E1A throughout six to seven weeks of radiation therapy. Primary endpoints 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 in patients who did not receive tgDCC-E1A in all their tumors. This trial is a multi-center, open-label study. We expect to complete patient enrollment in both of these clinical trials during 2001.

Preclinical Product Development Programs

Rheumatoid Arthritis

Rheumatoid arthritis (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 American College of Rheumatology, RA affects more than two million Americans, with disease onset occurring most frequently in people between the ages of 20 and 45. Direct and indirect costs associated with RA reached \$65 billion in 1992. While the exact cause of the disease remains unknown, autoimmune and inflammatory processes lead to chronic and progressive joint damage. The cytokine TNF α plays a pivotal role in this disease process. Symptoms are treated with a variety of steroidal and nonsteroidal anti-inflammatory drugs and disease-modifying drugs such as methotrexate, cyclosporine and etanercept. There is no cure for RA.

Our interest in developing a gene therapy product for treating rheumatoid arthritis stems from our origins as a spinout from Immunex Corporation. As part of that spinout, Immunex granted us a license to certain Immunex technology for use in the field of genetic therapy. We believe that the characteristics of AAV vectors make them well-suited for delivery of genes to joints. We envision an AAV-based RA product (AAV-TNFR) as an attractive alternative to systemic RA protein therapy in patients susceptible to infection or with disease symptoms limited to one or several joints.

We have administered AAV-ratTNFR:Fc, a vector that expresses a soluble form of TNFR, to the muscle or the joint of rats with experimentally induced arthritis. Data from these studies show that a single administration of AAV-ratTNFR:Fc to one ankle joint suppressed joint inflammation, pannus formation and cartilage and bone destruction in the treated ankle as well as in the contralateral joint. A single injection of AAV-ratTNFR:Fc to either the muscle or the joint resulted in a normalization of circulating TNF- α levels. Administration of AAV-ratTNFR:Fc to the joint resulted in reduced expression of other pro-inflammatory cytokines, including IL-1, IL-6 and TGF- β .

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 live with hemophilia A in the United States. Worldwide, there are approximately 50,000 hemophilia A patients. Hemophilia A patients face spontaneous, uncontrolled internal bleeding that can lead to restricted mobility, pain and, if left untreated, death. These serious, acute bleeding incidents are generally treated with either recombinant or naturally derived Factor VIII protein. If slow, chronic bleeding is not treated, however, progressive irreparable physical damage results. In addition, both recombinant and naturally-derived Factor VIII proteins are expensive, and the naturally derived protein 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 bleeding incidents, for the following reasons:

- the disease results from a single gene defect that is well understood and has been validated by the development of a protein therapy;
- overproduction of Factor VIII has not been shown to be harmful, therefore eliminating the need for precise regulation of gene expression;
- researchers believe that production of just 5% of normal levels of Factor VIII could prevent the chronic bleeding incidents in hemophilia A patients;
- high costs and safety issues prevent protein therapies from being administered prophylactically, thereby creating an unmet need among hemophilia patients; 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 the most promising means of creating an effective gene therapy product for treating hemophilia A. The characteristics of AAV vectors, including their demonstrated 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 tgAAV-CF, which we believe can also be efficiently adapted to developing a Factor VIII AAV vector product.

In 1999, we entered into an agreement with the University of North Carolina at Chapel Hill to gain exclusive access to patent applications filed on a novel approach for using AAV vectors to deliver the Factor VIII gene. In November 2000, we entered into a collaboration with Genetics Institute, the biotechnology research division of Wyeth-Ayerst, a division of American Home Products Corporation, to develop gene therapy products for the treatment of hemophilia. Under this agreement, Genetics Institute owns exclusive worldwide marketing rights to any resulting products and provides us with significant funding. The section below entitled "Research and Development Collaborations" provides a detailed description of this relationship.

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 affects fewer than 5,000 to 10,000 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 upon completing our acquisition of Genovo. Genzyme and Genovo had initiated a research and development agreement in this area in 1999. In November 2000, we amended the research and development agreement to include our viral gene delivery capabilities. Under the terms of the agreement, we will work with Genzyme to develop gene therapies for lysosomal storage disorders and Genzyme will be responsible for clinical development and commercialization of any products resulting from the collaboration. We could receive milestone payments for future product advancement and royalties on sales. The section below entitled “Research and Development Collaborations” provides a detailed description of this relationship.

HIV Vaccine

According to the International AIDS Vaccine Initiative, (IAVI), more than 36 million people worldwide suffer from AIDS or are infected with HIV, the virus that causes AIDS, and an additional 14,500 men, women and children are infected daily. While current therapies such as protease inhibitors and reverse transcriptase inhibitors have helped many patients with AIDS to manage their disease, these therapies are not curative, have significant, and often treatment-limiting, side effects and are extremely costly. A prophylactic vaccine that would protect against infection by HIV is likely to have significant market potential. To date, no companies have 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 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 as a novel form of genetic immunization, with the goal of eliciting a protective immune response against the virus. Work to date in nonhuman primates suggests that AAV vector vaccines 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. This data provides the basis for moving forward with further preclinical development that will support Phase I testing in humans. Under terms of the public-private IAVI/Children’s collaboration, IAVI will fund development, preclinical and Phase I studies at Targeted Genetics and at Children’s in Ohio. IAVI has agreed to invest a minimum of \$6 million during the first three years of the collaboration, provided that specified milestones are achieved. We have the right to commercialize in industrialized countries any vaccine product 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.

Hyperlipidemia

We are exploring the field of cardiovascular disease by applying our AAV vector technology to the treatment of hyperlipidemia, the elevation of lipids in the bloodstream. Approximately four million people in the United States have a genetic predisposition to 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 myocardial infarction or stroke. Our collaborators have generated data showing reduction of total cholesterol in a mouse model using an AAV vector to administer the gene for the very-low-density lipoprotein receptor (VLDL_R). In this model of familial hypercholesterolemia, animals receiving AAV-VLDL_R showed significant reduction in total cholesterol levels and modest reduction in triglycerides and did not develop atherosclerosis, while control animals developed high cholesterol and consequently atherosclerotic disease. We are conducting further research studies to assess the clinical utility of AAV-VLDL_R in the treatment of hyperlipidemia. We have exclusive rights to certain intellectual property related to the use of AAV-based gene therapy for the treatment of hypercholesterolemia. We acquired our AAV- VLDL_R product development project as part of our September 2000 acquisition of Genovo.

Metastatic Cancer

Based on our clinical testing of tgDCC-E1A, we believe that we have demonstrated the potential of E1A as a tumor inhibitor. We therefore believe that if we were able to deliver E1A systemically and reach tumor sites throughout the body, we could significantly expand the utility of E1A as a cancer treatment. We have developed a new formulation of E1A, called tgLPD-E1A, that we believe has the potential to target cancer cells when administered systemically.

tgLPD-E1A is based on a gene delivery vehicle called LPD, which contains lipid, polycation and DNA, and results in the formation of small, stable particles encapsulated in a lipid shell. Several preclinical tests 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 with administration of Taxol, a chemotherapeutic drug. Additionally, in mice that received both Taxol and tgLPD-E1A, the inhibition of tumor growth was significantly better than with either agent alone. Based on these encouraging results, we are conducting preclinical studies and hope to begin a Phase I clinical trial in 2002.

Glioma

In connection with our acquisition of Genovo, we entered into an expanded collaboration with Biogen, Inc. and assumed responsibility for a program in glioma (brain cancer), which had been a part of an existing collaboration between Biogen and Genovo. Current treatment options for glioma, which affects 16,000 people each year, include surgery, radiation therapy, chemotherapy, or a combination of these treatments. We are collaborating with Biogen to deliver the gene encoding interferon beta to the brain as a treatment for glioma, using an adenoviral vector as the delivery system for this collaboration. 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 strong results in several animal cancer models validate this approach. Biogen owns worldwide rights to product candidates resulting from this research and anticipates starting clinical trials in 2001. We may provide Biogen with input on the manufacturing process for this potential product.

Core Technology Platform

We have assembled a broad range of core 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 type of cell to be modified, the duration of effect desired and the need for *in vivo* (inside the body) or *ex vivo* (outside the body) delivery. Accordingly, our strategy has been to develop multiple gene delivery systems based on AAV vector and synthetic vector technologies. In addition, through our Emerald Gene Systems joint venture, we are working to create enhanced delivery systems that would further extend the applicability of our technology base. We believe these systems will give us the flexibility to develop gene therapies for a broader range of diseases than we could develop using any single gene delivery system.

In the area of cell therapy, we believe that our technology and expertise in isolating and multiplying CTLs could lead to development of a series of immunotherapies to treat infectious diseases and cancer. In December 2000, we established CellExSys, Inc., a majority-owned subsidiary focusing on the research and development of our broad portfolio of intellectual property in the area of cell therapy and the generation of antigen-specific T-lymphocytes.

Gene Therapy

Overview. Gene therapy is an approach to the treatment and prevention of genetic and acquired diseases that involves inserting genetic information into target cells to produce specific proteins needed to correct or modulate disease conditions. Proteins are the fundamental components of all living cells and are essential to 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, or produce, a specific protein.

An alteration in the function of, or an absence of, specific genes can cause disease, including inherited diseases such as cystic fibrosis and certain types of cancer. Gene therapy may be used to treat these diseases by replacing a missing or defective gene to facilitate the normal protein production capabilities of cells. In addition, gene therapy may be used to enable cells to perform additional roles in the body, such as enhancing the function of the immune system to fight infectious diseases or cancer. Gene therapy may also be used to inhibit production of undesirable proteins or viruses within cells that cause disease.

A key factor in the progress of gene therapy has been the development of safe and efficient methods of transferring genes into cells. For transfer into cells, the gene is incorporated into a delivery system called a vector, which may be derived from either viral or synthetic systems. The most common gene delivery approach to date relies on viral gene transfer, in which modified viruses are used to transfer the desired genetic material into host cells. The process of gene transfer can be accomplished *ex vivo* (outside the body), whereby doctors remove cells from the patient, genetically modify the cells and reinfuse them into the patient, or *in vivo* (inside the body), whereby vectors are introduced directly into the patient's body.

The use of viruses takes advantage of their natural ability to introduce genes into host cells and use the host's metabolic machinery to produce proteins essential for the survival and function of the virus. In gene therapy applications, viruses are genetically modified to contain the desired genes and to inhibit the ability of the virus to reproduce. Successful viral gene transfer for diseases requiring long-term gene expression involves a number of essential technical requirements, including the ability of the vector to carry the desired genes, to transfer the genes into a sufficient number of target cells and to enable the delivered genes to persist in the host cell. A number of different viral vectors, including AAV, adenoviral and retroviral vectors, are being used for potential gene therapy applications requiring long-term gene expression.

Current synthetic vector systems generally consist of DNA incorporating the desired gene, combined with various compounds aimed at enabling the DNA to be taken up by the host cell. These *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 proteins that bind to the receptors.

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

- AAV does not cause human disease;
- AAV vectors contain no viral genes that could produce unwanted cellular immune responses leading to side effects or reduced efficacy;
- 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

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

We are building a proprietary position in AAV 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 tgAAV-CF clinical development program, we are conducting preclinical experiments to assess the potential for delivery of genes to other target cells using AAV vectors. Currently, we are evaluating the use of AAV vectors to deliver genes to cells of the cardiovascular system, joints, muscles and the liver. As resources become available to do so, we intend to examine, both internally and through academic collaborators, the use of AAV vectors in additional cell types. In connection with our acquisition of Genovo, we entered into an expanded collaboration with Biogen and assumed responsibility for a program in glioma, which had been a part of an existing collaboration between Biogen and Genovo. We are collaborating with Biogen to deliver the gene encoding interferon beta to the brain as a treatment for glioma. We are using an adenoviral vector as the delivery system for this collaboration.

Synthetic Vectors. 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 promote uptake of genes by cells. These vectors appear to be safe for use *in vivo*. We believe that synthetic vectors have several characteristics that make them particularly well suited for treating certain diseases, including:

- the ability to target a specific cell type;
- relative ease of manufacture; and
- the ability to transfer relatively large segments of DNA.

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 to generate particles of defined size that have significantly enhanced gene transfer efficiency and stability in the bloodstream. We therefore believe that LPD may be useful for delivery of genes by intravenous administration.

Enhanced Vectors. In July 1999, we began a collaborative effort with Elan Pharmaceutical Technologies, a division of Elan Corporation plc, to focus on developing enhanced gene delivery systems. We established Emerald Gene Systems, Ltd., a joint venture with Elan, to focus on combining our AAV and synthetic gene delivery technologies with Elan's drug delivery technologies. Elan's contributed technologies include targeting ligands and polymers. We plan to develop enhanced gene delivery systems that can be systemically or orally administered and that will target the desired cells within the body.

Cell Therapy

The human immune system is designed to recognize foreign antigens and eliminate diseased or virally infected cells from the body. The inherent properties of CTLs, a key effector of the cellular immune response, give these cells potential for treating a wide variety of diseases and broad application in identifying novel targets for drug discovery and development initiatives. Our 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 cellular therapy. We own or have rights to 79 issued patents and patent applications in the area of cell therapy and other applications of T-cell technology, including exclusive rights to a patent, issued to the Fred Hutchinson Cancer Research Center in October 1998, related to a process for rapidly expanding CTLs in culture to millions even billions of cells that retain their ability to recognize specific disease-related antigens. We believe that this proprietary rapid expansion method (REM) enables key effector cells of the immune system to be expanded in a timely and cost-effective manner and overcomes the hurdles previously associated with *ex vivo* cell therapy – the inability to culture sufficient numbers of antigen-specific cells. We believe that REM technology can be used to generate antigen-specific CTLs for use in adoptive immunotherapy to treat a variety of diseases, including cancer and infectious diseases, or for use in drug development initiatives.

We established CellExSys in December 2000 to create an environment in which to move our cell therapy technology forward independent of our core gene delivery business. The applications of the REM technology, an *ex vivo* therapeutic approach, are quite distinct from the *in vivo* gene delivery technologies that have become our primary focus. We plan to transfer our interests in our cell therapy- and ex-vivo therapy- related patents and patent applications to CellExSys in 2001. As a separate subsidiary focused on patient-specific cell therapy and other applications of the REM technology, we believe that CellExSys is well-positioned to identify and take advantage of appropriate product, partnership and financial opportunities that fall outside the field of *in vivo* gene delivery. CellExSys intends to fund expansion of its activities by selling stock to outside investors.

REM: *Technology Overview*

We and our collaborators have tested the REM technology in the laboratory and in clinical trials and have demonstrated that

- REM technology can produce at least a thousand-fold increase in antigen-specific T-cells in less than two weeks, a process that can generate millions and even billions of antigen-specific, disease-fighting cells in a matter of weeks;
- CTLs produced with the REM technology retain their antigen-specific function when returned to a patient's body, taking up their natural role of targeting and destroying specific diseased cells;
- CTLs produced with the REM technology are less likely to cause unacceptable side effects when returned to a patient's body, because they are homogeneous and native to the patient's own immune system and recognize only the disease antigens for which they were selected;
- REM technology can work to multiply very small numbers of cells, even a single T-cell, and is applicable to other important populations of T-cells, including so-called "helper" T-cells that assist CTLs in clearing the body of diseased cells;
- CTLs produced using REM technology can be used immediately or stored for later use; and
- REM technology is simple, easy and effective, and kits have been developed that enable researchers and clinical workers anywhere to apply REM technology themselves.

REM: *Therapeutic Potential*

The goal of cell therapy is to amplify the number of immune system cells in the body in order to enhance the body's natural ability to recognize and fight disease. Our REM technology can be used to identify the few cells that are capable of eliminating diseased cells and to expand these cells to numbers that allow the body to fight disease effectively. We and our collaborators have generated proof-of-principle data in clinical and preclinical

studies of several diseases, including melanoma (skin cancer), HIV, hepatitis B and cytomegalovirus (CMV) infections. Clinical trials were designed primarily to assess the safety of REM-based cell therapy and, in all cases, showed the administered cells to be safe and well-tolerated. In addition, the Phase I trials with HIV patients showed indications of biological effect and the Phase I CMV trial suggested evidence of benefit from REM-based cell therapy.

Our technology platform includes additional assets applicable to cell therapy, such as intellectual property rights relating to the ability to genetically modify antigen-specific CTLs in ways that could increase their potency as disease fighters.

REM: Commercialization Opportunities

Other potential applications of our cell therapy technology include:

- **Antigen discovery:** Because CTLs naturally identify the biologically active sites on diseased cells that promote an immune response, they can be used, if available in sufficient quantity, to identify new antigens. This furthers our understanding of disease processes and provides new targets for the development of therapeutic products.
- **Vaccine development:** REM technology may be used to assist in vaccine development in two key ways. First, CTLs could enable researchers to determine at the earliest stages of vaccine development those antigens that are the most potent stimulators of the immune response. Second, clinicians could use the REM technology to isolate and quantify antigen-specific CTLs that the body has produced after administration of a vaccine, enabling them to monitor the vaccines progress on an incremental basis. This, in turn, could enable clinicians to make more timely decisions about additional or alternative therapies. This approach also may speed the development of vaccines, as current approaches to evaluating the immune response to vaccines are neither efficient nor cost-effective.

Research and Development Collaborations

Medeva Pharmaceuticals, Inc./Celltech Group plc

In November 1998, we entered into agreements with Medeva Pharmaceuticals, Inc., now a wholly owned subsidiary of Celltech Group plc, to develop and commercialize tgAAV-CF, our gene therapy product candidate for the treatment of cystic fibrosis. Medeva committed to provide up to three years of funding, up to \$5 million per year, to support tgAAV-CF development and commercialization 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 to funding development and clinical support, Medeva agreed to pay the costs of Phase II and subsequent clinical trials of AAV-CF product candidates. While we are currently managing a Phase II clinical trial in the United States, Medeva will conduct all other trials and is responsible for securing worldwide registration of tgAAV-CF.

Under the terms of our research and development funding agreement, we granted Medeva an exclusive worldwide license to sell tgAAV-CF, but retained responsibility for manufacturing and supplying bulk tgAAV-CF product to support clinical trials and product commercialization. Medeva agreed to loan us \$2 million to

partially fund the construction of a pilot-scale tgAAV-CF manufacturing facility. Medeva also agreed to loan us, under specified conditions, up to an additional \$10 million toward building a Good Manufacturing Practices (GMP) manufacturing facility for higher-volume production of tgAAV-CF.

Assuming successful commercialization of a tgAAV-CF product, we could receive a total of up to \$54 million in license fees, development funding, milestone payments, loans and equity investments connected with the tgAAV-CF agreements. We received a \$2 million milestone payment in 2000 at the start of our Phase II clinical trial. Under a related long-term supply agreement, we will also receive proceeds from sales of tgAAV-CF, assuming successful commercialization, based on a pricing formula intended to provide us with a significant percentage of Celltech's net revenue from tgAAV-CF product sales. The research and development funding agreement is effective through October 1, 2001, with an option to extend the term if both parties agree. The long-term supply agreement is effective for the term of the patents covering tgAAV-CF. Celltech may terminate our tgAAV-CF agreements at will with 180 days' notice. Should Celltech exercise its termination right, all rights related to tgAAV-CF would return to us.

Emerald Gene Systems, Ltd.

In July 1999, we formed a joint venture with Elan International Services, Ltd., a wholly owned subsidiary of Elan Corporation plc, named Emerald Gene Systems, Ltd. Emerald's purpose is to develop enhanced gene delivery systems based on a combination of our gene delivery technologies and Elan's drug delivery technologies. The joint venture is based in Bermuda and currently is owned 80.1% by us and 19.9% by Elan. Although we hold 100% of the voting common shares, as Elan's shares are non-voting, Elan and its subsidiaries have retained significant minority investor rights that prevent us from exercising control over Emerald. Accordingly, we do not consolidate the financial statements of Emerald but instead account for our investment in Emerald under the equity method of accounting.

Generally, Emerald's research and development is conducted under contract by Elan and us, and Emerald reimburses each company for the costs of research and development plus a profit percentage. Elan and Targeted Genetics fund the expenses of Emerald in proportion to their ownership interests.

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

- a \$5 million purchase of common stock at the closing of the agreements and an additional \$5 million purchase of common stock one year later; and
- a \$12 million purchase of convertible exchangeable preferred stock at the closing of the agreements, the proceeds of which we used to make our initial investment in Emerald and Emerald used to purchase a license from Elan.

At Elan's option, the convertible exchangeable preferred stock can be converted into our common stock or exchanged for an additional 30.1% ownership in Emerald, which would result in a 50/50 ownership of Emerald.

Elan has also agreed to provide up to \$12 million of take-down financing 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 and total draws on this note cannot exceed our cumulative investment in Emerald. Any draws on this convertible note:

- bear interest at 12% per year, compounded semi-annually;
- are payable semi-annually in cash or interest that can be capitalized and added to the principal amount outstanding; and
- are due July 21, 2005.

At Elan's option, the convertible note can be converted into our common stock at a conversion price equal to the 150% of the average closing price of our common stock for a specified period of time before the date of each draw on the note. We also have the option to convert the note into shares of our common stock at a conversion price equal to the lesser of the then-current market price and the Elan conversion price. As of December 31, 2000, we had not drawn any amounts against the convertible note.

Biogen, Inc.

In September 2000, we established a multiple-product development and commercialization collaboration with Biogen, Inc. Under the terms of our agreements with Biogen, we will collaborate 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 next three years. In addition, we will provide process development assistance related to Biogen's manufacturing an existing gene therapy product candidate currently in clinical development for the treatment of glioma, resulting in a total of up to five products covered by the collaboration. Under the terms of the collaborative agreement, we granted Biogen an exclusive worldwide license to sell any products developed in the collaboration and assumed responsibility for manufacturing and supplying bulk vector supplies to Biogen to support product development, clinical trials and product commercialization.

Biogen paid us \$8 million upon initiation of the collaboration and will provide us with a minimum of \$3 million in research and development funding over three years, at a rate of \$1 million per year. The \$8 million up-front payment made by Biogen included prepaid research and development funding of \$3 million. Biogen also agreed to provide us with loans of up to \$10 million over the next five years and to purchase up to \$10 million of our common stock, each at our discretion. We may make up to five draws against the \$10 million loan amount, with any draws bearing interest at market rates. We can elect to have Biogen purchase the common stock in one or more tranches during the first three years of the agreement. 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 will receive royalties for any sales of products that result from the collaborative product development efforts. Alternatively, we will sell product resulting from the collaboration to Biogen at transfer prices that include sales-based and cost-based components.

The research and development funding agreement is effective to September 30, 2003, with an option to extend the term if both parties agree. The product manufacturing and supply provisions of the agreement are effective for the term of the patents covering our technology. Although Biogen may terminate the development and commercialization agreement any time after the first anniversary of the agreements, Biogen's obligation under the related funding agreement to pay minimum annual project funding of \$3 million over three years would continue.

We are amortizing the \$5 million up-front fee paid by Biogen over the three-year research and development performance period. We will recognize revenue on the remaining \$3 million of up-front payment and the \$1 million minimum annual project funding as we perform specified research and development efforts. We performed no research and development efforts attributable to the Biogen collaboration agreements in 2000.

Genetics Institute

In November 2000, we entered into a collaboration to develop gene therapy products for the treatment of hemophilia with Genetics Institute, the biotechnology research division of Wyeth-Ayerst, a division of American

Home Products Corporation. Under the terms of the agreement, we will collaborate on the development of AAV vector-based products for hemophilia A and, potentially, for hemophilia B.

Genetics Institute has agreed to pay us \$5 million in up-front payments, \$500,000 for research we performed before the collaboration, up to \$15 million over the next three years for developing a hemophilia A product candidate, and, subject to our achieving of specified objectives, development and commercialization milestone payments of up to \$60 million. We also granted Genetics Institute an option to collaborate on developing a hemophilia B product candidate, which, if developed, would trigger additional payments to us. Genetics Institute has also agreed to manage and fund the costs of clinical trials and related regulatory filings required for product approval and marketing. Genetics Institute will retain global marketing rights for any products resulting from the alliance.

Genetics Institute also has agreed, upon the occurrence of specified events, to enter into an agreement, to loan us up to \$10 million to finance manufacturing facility expansions. In addition, 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, to be extended should regulatory agencies approve a product for commercial use. Genetics Institute has the right to terminate both agreements at will, with 180 days' notice. Should Genetics Institute exercise this right to terminate, all rights that we have granted or otherwise extended to Genetics Institute related to the hemophilia technology would return to us.

Genzyme Corporation

On August 30, 1999, Genovo entered into a development and license agreement with Genzyme Corporation, under which Genovo was committed to perform, at its own cost, up to \$2.9 million per year of research and development activities, for up to three years. A separate agreement also provided for Genzyme to purchase up to \$11.4 million of Genovo equity, of which \$3.4 million had been purchased as of September 30, 2000. The agreement also required Genzyme, upon the achievement of specified regulatory milestones, to pay Genovo milestone payments and royalties on sales of any products developed. We assumed the Genzyme agreements when we acquired Genovo. The initial term of the agreement is three years, cancellable by Genzyme at any time with notice. None of the milestones had been reached as of December 31, 2000.

On November 3, 2000, we entered into an expanded agreement with Genzyme to amend the development and license agreement originally established with Genovo. The amended agreement expands the collaboration's technological scope and financial terms and establishes a development plan for the second year of the three-year collaboration. After the execution of the amended agreement, Genzyme exercised its option to purchase 311,295 shares of our common stock at a price of \$12.8495 per share, providing us with \$4.0 million of proceeds.

International AIDS Vaccine Initiative

In February 2000, we entered into a collaboration to develop a vaccine to prevent AIDS with the International AIDS Vaccine Initiative (IAVI) and Children's Research Institute on the campus of Children's Hospital in Columbus, Ohio to develop a vaccine to prevent AIDS. The vaccine will utilize our AAV vectors to deliver HIV genes as a novel form of genetic immunization. Under the terms of the public-private collaboration, IAVI will fund development, preclinical studies and Phase I clinical trials at our facility in Seattle and at Children's Hospital in Columbus. IAVI has agreed to invest at least \$6 million in research funding during the first three years of the collaboration, provided that specified milestones are achieved. Vaccine candidates will be constructed based on subtypes of the virus most prevalent in Southern and Eastern Africa and are expected to be field-tested in those

regions. AAV vectors will be used to deliver selected HIV genes with the goal of eliciting a protective immune response against the virus.

We expect to manufacture the vaccine and will retain exclusive worldwide commercialization rights to any product that may stem from the collaboration. In return for the IAVI funding, and in keeping with IAVI's philanthropic mission, IAVI has secured rights to ensure that any successful vaccine will be distributed in developing countries at a reasonable price. The price will take a number of factors into consideration, including the income level of the country, and is expected to be substantially lower than prices in industrialized countries. Under the terms of the agreement, if we decline to produce the vaccine for developing countries in reasonable quantity 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, should we develop a successful vaccine, we will have exclusive rights to commercialize the vaccine in industrialized countries.

Alkermes, Inc.

In June 1999, we entered into a strategic alliance with Alkermes, Inc. in which we received exclusive rights to an important 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 previously acquired limited field license to these rights. Under the terms of our agreement, we issued to Alkermes 500,000 shares of common stock and warrants to purchase two million additional shares of common stock at significant premiums over the market price at the time of the original transaction. Alkermes will also receive milestone payments and royalties on the sale of any products manufactured using the licensed technology.

Relationship With Immunex Corporation

Targeted Genetics was formed in 1989 as a subsidiary of Immunex, a biopharmaceutical company developing recombinant proteins as therapeutics. In February 1992, we spun off as a separate company from Immunex and entered into a technology license agreement with Immunex. In exchange for shares of our preferred stock that were converted into 1,920,000 shares of common stock at the time of our initial public offering, Immunex granted us an exclusive worldwide field-of-use license for Immunex proprietary technology specifically applicable to our gene therapy business. This technology relates to gene identification and cloning, panels of retroviral vectors, packaging cell technology, recombinant cytokines, DNA constructs, cell lines, promoter/enhancer elements and immunological assays. In addition, the agreement required Immunex to disclose to us, until February 1999, information concerning improvements discovered or developed by Immunex relating to the transferred technology, such as new techniques, biological materials, inventions or developments. We have the option to acquire a nonexclusive, worldwide, fully paid, royalty-free license and, in some cases, an opportunity to negotiate the conversion of a nonexclusive license into an exclusive license, for these improvements. Immunex currently owns approximately 6% of our outstanding common stock.

Patents and Proprietary Rights

Patents and licenses are important to our business. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that we consider important to developing our business. We also rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. To date, we have filed or exclusively licensed 397 patent applications with the United States Patent and Trademark Office (USPTO), as well as foreign counterparts of some of these applications in Europe, Japan and other countries. Of these patent applications, 125 patents have been issued or allowed by the USPTO. The substantial increase in the number of patent applications outstanding

in 2000 covering our product technology development programs reflects the addition of intellectual property from our acquisition of Genovo. In 2001, our total number of patent applications may decrease as we align the collected body of acquired patent applications with our existing patent portfolio and our product and technology development programs.

In addition to the intellectual property that we own or have exclusively licensed, we have licensed on a nonexclusive basis the 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 (NIH) and the University of Florida Research Foundation. In addition, we have acquired nonexclusive rights to the CFTR gene being delivered in our tgAAV-CF product.

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. The coverage claimed in a patent application may be significantly reduced before a patent is issued. Consequently, patent applications may not result in the issuance of patents and, 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. Since patent applications in the United States are maintained in secrecy until patents issue and patent applications in 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 any licensor was the first creator of inventions covered by pending patent applications or the first to file patent applications for these inventions.

We are currently indirectly involved in a patent interference proceeding declared by the USPTO to determine priority of invention of the CFTR gene delivered in our tgAAV-CF product candidate, for which we have a nonexclusive license. Should another party prevail in this proceeding, costs associated with securing and maintaining a license from the prevailing party could be substantial and would include ongoing royalties in excess of those currently payable under our existing CFTR gene license.

A number of pharmaceutical and biotechnology companies and research and academic institutions have developed technologies, filed patent applications or received patents on various 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 that cover our activities are issued to other companies, we may be required to either obtain a license under those patents or to develop or obtain alternative technology. A license may not be available on acceptable terms, if at all, and we may not be able 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 upon 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. Similarly, litigation 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 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.

In addition to patent protection, we rely upon trade secret protection for our confidential and proprietary information. To protect our trade secrets, we 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. These agreements, however, may not provide meaningful protection of our trade secrets or adequate remedies in the event of unauthorized use or disclosure of this confidential information. Other parties may gain access to our trade secrets and disclose our technology, however, or may independently develop substantially equivalent proprietary information and techniques.

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, fully integrated pharmaceutical companies, universities, research institutions, governmental agencies and other healthcare providers. In addition, our potential products will compete with existing pharmaceutical products based on established technologies. We also compete with others to acquire products or technology from research institutions or universities. Many of our competitors have substantially more financial and other resources, larger research and development staffs and more experience and capabilities in researching, developing and testing products in clinical trials, obtaining FDA and other regulatory approvals and manufacturing, marketing and distributing products. In addition, the competitive positions of other companies may be strengthened through collaborative relationships with large pharmaceutical companies or academic institutions. Our competitors may develop, obtain patent protection for, receive FDA and other regulatory approvals for, or commercialize products more rapidly than we do. 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. 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. Our competitors may manufacture and market their products more successfully than our potential products. These developments could render our potential products less competitive or obsolete.

Governmental Regulation

All of our potential products will require regulatory approval by U.S. federal and applicable foreign governmental agencies before they can be commercialized. Human therapeutic products are subject to rigorous preclinical and clinical testing and other premarket approval procedures administered by the U.S. 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 both are relatively new technologies and have not been extensively tested in humans. The FDA reviews all product candidates for safety and efficacy, and both standards must be met before the FDA grants product approval. Obtaining approval from the FDA and other regulatory authorities for a new therapeutic product candidate is likely to take several years, if approval is ever obtained. 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, could and do involve substantial expenditures of financial and other resources.

To secure regulatory approval to market a new therapeutic agent in the United States, the product candidate must be subjected to preclinical testing. Preclinical tests must be conducted in accordance with the FDA's Good Laboratory Practice regulations and generally require studies in the laboratory or in animals to assess the potential product's safety and effectiveness. Preclinical tests 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. 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, then the potential product will undergo clinical trials to test the therapeutic agent in humans. Human clinical trials are subject to numerous governmental regulations that provide detailed procedural and administrative requirements designed to protect the trial participants. Each institution that conducts human clinical trials has an institutional review board charged with evaluating each trial and any trial amendments to ensure that the trial is ethical, patients are protected and the trial meets the institutional requirements. These evaluations include reviews of how the institution will communicate the risks inherent in the clinical trial to potential participants, so that the patients may give their informed consent. Clinical trials must be conducted in accordance with the FDA's Good Clinical Practices regulations, under protocols we establish 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 rules 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 or efficacy.

The NIH also requires each institution conducting our clinical trials to evaluate the proposed study with respect to compliance with NIH guidelines before initiating the trial. These evaluations are generally performed by the institution's biosafety committee. In addition, if the NIH is providing any type of funding to an institution performing a clinical trial of our product candidate, the clinical trial involving our products is subject to a review by the NIH's Office of Biotechnology Activities Recombinant DNA Advisory Committee. 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 recommend a public review. Should the committee 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 NIH committee review process can impede the trial process, even if the FDA has reviewed the trial and approved its initiation.

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, multicenter, 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 the modification, suspension or termination of the clinical trial if it deems patient risk too high. The length of the clinical trial period, the number of trials conducted and the number of enrolled patients per trial vary, depending on our results and FDA requirements for the particular clinical trial. Although we and other companies in our industry, have made progress in the field of gene therapy, we cannot predict what the FDA will require in any of these areas to establish to its satisfaction the safety and effectiveness of the product candidate.

After successful completion of clinical trials for a product candidate, we must obtain FDA approval, as well as the approval of several other governmental and nongovernmental agencies, to market the product in the U.S. Current FDA regulations relating to biologic therapeutics require us to submit a Biologics License Application (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 and 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; or
- perform additional testing.

As in clinical trial review, the FDA's criteria for BLA approval vary. 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.

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 of 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 of product approval and on a continuing basis. In complying with these requirements, we must expend time, money and effort in production, record keeping and quality control. Our manufacturing facilities are subject to periodic inspections by the FDA. Failure to pass these inspections could subject us to possible FDA 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.

Human Resources

At December 31, 2000, we had 132 full time-equivalent employees, of which 103 are directly involved in research and development and 25 have Ph.D. or M.D. degrees. 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.

ITEM 2. PROPERTIES

We currently occupy an aggregate of approximately 71,000 square feet of laboratory and office space in Seattle, Washington and Sharon Hill, Pennsylvania. The leases on our Seattle laboratory and office facilities expire on March 31, 2004 and have options to extend their terms for two additional five-year periods. The average annual rent payment during the current terms of the Seattle leases total approximately \$700,000, including amounts related to landlord financing of leasehold improvement costs. The lease on our Sharon Hill laboratory and office facilities expires on November 30, 2005, has options to extend its term for two additional five-year periods and has an early termination option allowing for termination of the lease on November 30, 2001, with advance notice. The annual rent payment during the current term of the Sharon Hill lease is approximately \$350,000. In July 2000, we leased approximately 76,000 square feet of expansion space in Bothell, Washington. The lease on this facility expires on October 1, 2015 and has an option to extend its term for an additional five-year period. The average annual rent payment during the current term of the Bothell lease is approximately \$1.4 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, 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.

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 2000.

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. At March 1, 2001, we had approximately 250 shareholders of record and approximately 18,200 beneficial holders of our common stock. We have never paid cash dividends and do not anticipate paying them in the foreseeable future. In addition, we are restricted as to the amount of dividends we can pay under our loan agreement with Celltech Group plc.

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
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
1999		
4th Quarter	\$ 4.88	\$ 1.25
3rd Quarter	2.75	1.50
2nd Quarter	1.81	1.44
1st Quarter	3.06	1.31

On November 3, 2000, we sold 311,295 unregistered shares of our common stock to Genzyme Corporation at a price of \$12.8495 per share, upon its exercise of an option we assumed in connection with our acquisition of Genovo. The transaction was exempt from registration under Section (2) of the Securities Act, on the basis that the transaction did not involve a public offering.

ITEM 6. SELECTED FINANCIAL DATA

	Year Ended December 31,				
	2000 (1) (2)	1999	1998	1997	1996
Results of Operations					
Revenue	\$ 11,402,700	\$ 6,847,993	\$ 7,510,252	\$ 1,327,585	\$ 1,330,458
Expenses	54,734,291	21,084,502	16,372,987	15,828,094	27,894,811
Loss from operations	(43,331,591)	(14,236,509)	(8,862,735)	(14,500,509)	(26,564,353)
Loss before cumulative effect of change in accounting principle	(43,974,004)	(26,655,135)	(8,687,049)	(14,187,774)	(26,038,042)
Cumulative effect of change in accounting principle	(3,681,687)	-	-	-	-
Net loss	(47,655,691)	(26,655,135)	(8,687,049)	(14,187,774)	(26,038,042)
Net loss applicable to common shareholders	(48,540,956)	(27,030,648)	(8,687,049)	(14,187,774)	(26,038,042)
Basic and diluted net loss per share:					
Loss before cumulative effect of change in accounting principle	(1.19)	(0.84)	(0.33)	(0.70)	(1.59)
Cumulative effect of change in accounting principle	(0.10)	-	-	-	-
Net loss applicable to common shareholders	(1.29)	(0.84)	(0.33)	(0.70)	(1.59)
Shares used in computing basic and diluted net loss per share	37,752,164	32,173,756	26,637,823	20,196,325	16,407,928
Balance Sheet Data					
Cash, cash equivalents and securities available for sale	\$ 38,630,216	\$ 7,153,269	\$ 11,956,796	\$ 5,037,821	\$ 19,051,070
Total assets	87,974,042	13,692,478	16,204,083	9,767,084	25,139,052
Long-term obligations, including current portion	3,284,319	3,248,382	2,072,044	2,547,324	3,378,420
Shareholders' equity	63,431,597	6,965,514	11,981,759	5,591,587	19,507,788

- (1) Expenses and net loss applicable to common shareholders increased in 2000 due to the acquisition of Genovo and the resulting \$28.0 million write-off described in further detail in Item 7 of this annual report, "Management's Discussion and Analysis," in the subsection entitled "Operating Expenses - - In-Process Research and Development."
- (2) Net loss also increased as a result of a \$3.7 million cumulative-effect adjustment related to a change in the method of accounting for revenue recognition, as described in "Management's Discussion and Analysis" in the subsection entitled "Accounting Change."

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

Our goal is to research and develop gene and cell therapy products to treat acquired and inherited diseases. We have two lead product candidates in clinical trials, tgAAV-CF for treating cystic fibrosis and tgDCC-E1A for treating cancer, and several additional product candidates in preclinical development. We focus our efforts on product development, which we have funded primarily through the sale of equity securities and proceeds from our product development collaborations.

In September 2000, we completed the acquisition of Genovo, Inc., a privately held biotechnology company focused on developing therapeutic products based on AAV vectors. We purchased Genovo for approximately \$66.4 million, consisting of 5,250,805 shares of our common stock and assumed stock options to purchase 1,302,034 shares of common stock valued at \$65.8 million in the aggregate, plus transaction costs of \$0.6 million. We intend that the transaction, which was accounted for as a purchase, will qualify as a tax-free reorganization. We recorded acquired in-process research and development (IPR&D) of \$28.0 million and acquisition-related intangibles of \$39.5 million, including AAV-vector know-how of \$12.7 million, workforce in place of \$1.6 million and goodwill of \$25.2 million.

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;
- a gene delivery technology development joint venture with Elan International Services, Ltd. (Elan), a wholly owned subsidiary of Elan Corporation plc, named Emerald Gene Systems, Ltd. (Emerald);
- an AAV-based AIDS vaccine development program with the International Aids Vaccine Initiative (IAVI);
- a multiple-product gene therapy product development collaboration with Biogen, Inc.;
- a lysosomal storage disease product development collaboration with Genzyme Corporation; and
- an AAV-based hemophilia product development collaboration with Genetics Institute, the biotechnology research division of Wyeth-Ayerst.

Although 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 have any commercial product revenues for at least the next several years. Through December 31, 2000, our accumulated losses totaled approximately \$150.8 million, of which \$28.0 million is attributable to the write-off of IPR&D costs associated with the acquisition of Genovo. We expect to generate substantial additional losses in the future, due primarily to the costs of our preclinical and clinical development programs, developing our manufacturing capabilities and preparing our products under development for commercialization. We may never become a profitable company.

Results of Operations

Revenue

Our revenue results have fluctuated from year to year and will likely continue to be volatile as we establish and complete collaborations, enter into licensing agreements and recognize varying amounts of revenue from our research and development activities. We had revenue of \$11.4 million in 2000, compared with \$6.8 million of

revenue in 1999. Revenue increases in 2000 were generated from our tgAAV-CF collaboration agreement with Celltech, from a full year of providing research and development services to the Emerald joint venture and from revenue generated from our new product development collaborations with Genetics Institute, Biogen and IAVI. Year 2000 revenue was also impacted from an accounting change, as described below under the caption "Accounting Change."

We had revenue of \$7.5 million in 1998. This amount included \$6.0 million in fees earned when we established the Celltech collaboration and approximately \$1.0 million earned from Celltech for product development efforts in the fourth quarter of 1998.

We expect revenue from our collaborative agreements to increase in 2001, reflecting the addition of our hemophilia collaboration with Genetics Institute, increased AIDS vaccine development activities in connection with our IAVI collaboration and revenue generated from the amortization of nonrefundable up-front fees we received when we initiated the Genetics Institute, Biogen and Celltech collaborations.

Operating Expenses

Research and Development. Research and development expenses increased to \$19.3 million in 2000 from \$14.3 million in 1999. This increase reflects increased expenses related to our acquisition of Genovo's research and development operations, hiring additional research scientists to support our Emerald, Genetics Institute and IAVI collaborations and hiring additional clinical and regulatory personnel to administer our cystic fibrosis and cancer clinical trials. Current year expenses also reflect greater preclinical product development efforts in our cancer, hemophilia and arthritis programs.

Research and development expenses increased to \$14.3 million in 1999 from \$13.3 million in 1998, reflecting increased expenses related to our tgAAV-CF collaboration with Celltech and, to a lesser extent, costs incurred to support the Emerald joint venture. The increases in 1999 were partially offset by decreases in tgDCC-E1A development expenses. In 1999, we had lower expenses related to the development of manufacturing methods for tgDCC-E1A and paid Celltech \$1.0 million in common stock as a milestone payment at the start of Phase II clinical trials.

We expect research and development expenses to increase in 2001 as a result of increased staffing in 2000 and the first half of 2001 to support the Genetics Institute, Genzyme and IAVI projects, projected increases in facilities operating expenses and expanded preclinical and clinical activities.

In-Process Research and Development. In September 2000, we incurred IPR&D expenses of \$28.0 million, which reflects the amount allocated to IPR&D we acquired when we purchased Genovo. We incurred no IPR&D expenses in 1999 or 1998.

The IPR&D from the Genovo acquisition represents the present value of the estimated after-tax cash flows that we expect to 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. Our projected operating expenses include general and administrative expenses and research and development costs.

At the acquisition date, we acquired ongoing IPR&D projects from Genovo in the fields of AAV manufacturing platform, hyperlipidemia, lysosomal storage disorders (LSD), glioma and hemophilia. Of the IPR&D amount, approximately \$19.6 million is related to AAV manufacturing platform projects, approximately \$7.5 million is related to hyperlipidemia projects, approximately \$538,000 is related to hemophilia projects, approximately \$217,000 is related to LSD projects and approximately \$177,000 is related to glioma projects. We assigned values to these programs based on the discounted cash flows currently projected from the technologies acquired. If we do not successfully develop these programs, our business, operating results, and financial condition may be adversely affected.

- Genovo's AAV manufacturing platform projects are efforts to manufacture AAV as a stable gene therapy vector capable of delivering genes to a variety of dividing and nondividing cells. Several companies are studying AAV vectors for gene transfer in a broad range of chronic disease indications. Genovo has identified both patient populations for potential projects and potential partner candidates for using its early-stage manufacturing platform to develop specific AAV vectors to deliver candidate genes. Genovo estimated that the additional research and development costs to complete the AAV manufacturing platform projects in 2007 will be approximately \$23.8 million. Additional AAV platform projects in early development stages are scheduled for completion by 2008 and 2009. As of the acquisition date, Genovo had made progress in this field in the areas of bench processes, Good Laboratory Practices-grade processes and scale-up processes. Significant risk for the AAV manufacturing platform projects relate to completing scale-up efforts and establishing, validating and commercializing Good Manufacturing Practices-grade processes.
- Hyperlipidemia is an elevation of lipids in the bloodstream that are transported as part of large molecules called lipoproteins. Genovo's hyperlipidemia technology targets patient populations requiring treatment of elevated cholesterol and patients with existing cardiovascular disease. Genovo plans to develop with a partner a gene therapy product to treat hyperlipidemia. Genovo estimates that its hyperlipidemia technology will be completed in 2007, at a cost of an additional \$16.0 million in research and development. As of the acquisition date, Genovo had made progress in this field in the areas of discovery, research and preclinical work.
- Lysosomal storage disorders, a family of approximately 40 genetic diseases, are normally single-gene defects that prevent the production of one or more lysosomal enzymes, leading to abnormal deposits of substrates within lysosomal vacuoles. These deposits cause a loss of function in many crucial areas of the body, which may result in mental and physical disability. Genovo is developing with a partner a gene therapy product to treat LSD. Genovo estimates the additional costs to complete its LSD technologies at \$9.0 million, with a targeted completion date in 2007. As of the acquisition date, Genovo had made progress in this field in the areas of discovery, research and preclinical work.
- Genovo's glioma technology is 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 is developing with a partner a gene therapy product to treat glioma. Genovo estimates the additional costs to complete its glioma technology at \$750,000, with a targeted completion date in 2006. As of the acquisition date, Genovo had made progress in this field in the areas of discovery, research and preclinical work.
- Hemophilia, an x-chromosome linked recessive clotting disorder caused by a mutation in one of the body's plasma proteins, results in prolonged external and/or internal bleeding. Genovo plans to develop with a partner a gene therapy product to treat hemophilia. Genovo estimates the additional costs to complete its hemophilia technologies at \$12.0 million, with a targeted completion date in 2009. As of the acquisition date, Genovo had made progress in this field in the areas of discovery, research and preclinical work.

We based all of these estimates and projections on assumptions we 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. If the projects fail, the economic contribution we project the IPR&D to make will not materialize. The risk of untimely completion includes the risk that competitors will develop alternative products.

Technology License Fee. We incurred a noncash expense of \$3.2 million in 1999 to acquire from Alkermes, Inc. an exclusive sublicense to a patent and patent applications related to the manufacture of AAV vectors, which we use in our tgAAV-CF cystic fibrosis program, among others. In exchange for this license, we issued to Alkermes 500,000 shares of our common stock and warrants to purchase up to 2.0 million additional shares. We valued these securities at \$3.2 million, based on the market value of the common stock exchanged and using the Black-Scholes model to determine the value of the warrants. While the technology we acquired under the exclusive license has promise, we expensed the entire value of the securities, which was the value we assigned to the license, because this technology is in the early stages of development and its feasibility has not been established. We had no technology license fee expenses in 2000 or 1998.

General and Administrative. General and administrative expenses increased to \$5.7 million in 2000 from \$3.6 million in 1999. This increase reflects the addition of Genovo operating costs, nonrecurring costs associated with assimilating Genovo's operations, higher business-development and legal costs and increased administrative support for our growing number of collaborative partnerships. General and administrative expenses increased to \$3.6 million in 1999 from \$3.0 million in 1998. This increase was primarily attributable to increased personnel costs, increased business development activity and investor communications costs related to the formation of the Emerald joint venture.

Amortization of Acquisition-Related Intangibles. We recorded amortization expense of \$1.7 million in 2000 for goodwill, noncompetition agreements and work force know-how that we acquired when we purchased Genovo. We had no expenses related to the amortization of acquired intangibles in 1999 or 1998.

Other Income and Expense

Equity in Loss of Joint Venture. Our equity in the losses of the Emerald joint venture decreased to \$2.5 million in 2000 from \$12.6 million in 1999. Losses in each year reflect our 80.1% equity share in the loss generated by Emerald's research and development and licensing activities. Emerald's losses in 2000 and 1999 were generated by research and development efforts performed by each joint venture partner; in addition, Emerald's losses for 1999 included a \$15.0 million noncash charge for an exclusive license to Elan's drug delivery technology. We expect to record additional equity in losses of Emerald in 2001 and for the foreseeable future.

Investment Income. Income from marketable securities increased to \$2.1 million in 2000 from \$426,000 in 1999 and \$440,000 in 1998. The increase in 2000 resulted from higher average cash and cash-equivalent balances. Most of our cash resides in a short-term bond mutual fund that earns a steady rate of return.

Interest Expense. Interest expense has remained fairly level over the past three years, at \$266,000 in 2000, \$235,000 in 1999 and \$265,000 in 1998. This expense relates to obligations under the capital leases and installment loans we use to finance purchases of laboratory and computer equipment, furniture and leasehold improvements. We expect our interest expense to increase in 2001 as we finance an expansion of our clinical

manufacturing facility and finance additional asset purchases with leases and loans. We borrowed \$1.0 million under a loan agreement with Celltech in late 1999 and we may elect to borrow additional amounts in the future under existing loan commitments from Biogen, Celltech, Elan or Genetics Institute.

Accounting Change

In the fourth quarter of 2000, we adopted the provisions of the Securities Exchange Commission's Staff Accounting Bulletin No. 101 (SAB 101), *Revenue Recognition in Financial Statements*. SAB 101 generally provides that nonrefundable up-front fees, for licenses and rights to product candidates are deferred and recognized as revenue over the product development period when 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. As a result of the implementation of SAB 101, we recognized \$7.7 million less revenue than under our previous revenue recognition policy. The cumulative effect on prior years of changing the accounting policy for recognizing of up-front fees was a noncash charge of \$3.7 million, calculated as of January 1, 2000 and included in the results for 2000.

Impact of New Accounting Pronouncements

In June 1998, the Financial Accounting Standards Board (the "FASB") issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities*. Statement No. 133, which is effective beginning in 2001, establishes accounting and reporting standards for derivative instruments, including certain derivative instruments imbedded in other contracts, and for hedging activities. We do not expect the impact of this new statement to be material.

Liquidity and Capital Resources

As of December 31, 2000, we had cash, cash equivalents and securities available for sale totaling \$38.6 million, compared with \$7.2 million as of December 31, 1999 and \$12.0 million in 1998. Working capital increased to \$29.5 million at December 31, 2000 from \$4.6 million in 1999 and \$9.1 million in 1998. During 2000, we used \$605,000 of net cash in our operations, compared with \$9.6 million in 1999 and \$5.8 million in 1998. The decrease in 2000 in cash used for operations was primarily due to our receipt of a total of \$10.6 million of up-front nonrefundable license and technology access fees from Biogen and Genetics Institute and to our increased collaborative activity in 2000. Our financing activities provided \$37.4 million in 2000, compared with \$7.4 million in 1999 and \$12.9 million in 1998. The increase in 2000 in cash from financing activities was primarily due to net proceeds of \$28.1 million from our March 2000 private placement of 2,164,285 shares of common stock, proceeds of \$5.0 million from our July 2000 sale of 382,739 shares of our common stock to Elan in connection with the Emerald joint venture and proceeds of \$4.0 million from our November 2000 sale of 311,295 shares of our common stock to Genzyme. These cash inflows were partially offset by outflows in 2000 of \$2.8 million for capital expenditures, including expenditures for the construction of an expanded clinical manufacturing suite. Our investing activities used \$2.2 million in 2000, compared with cash provided of \$4.5 million in 1999 and cash used of \$6.2 million in 1998. The decrease in cash used in 1999 compared with 1998 is primarily a result of the proceeds from our April 1998 private placement of common stock.

Although we expect our expenses to continue to increase in 2001, we expect cash generated from our collaborations with Genetics Institute, Biogen, Emerald and IAVI to increase as well, partially offsetting our expense increases. We also have contractual commitments for the following cash resources:

- a \$10.0 million equity investment by Biogen;
- a \$10.0 million loan agreement with Biogen;
- funds available under a \$12.0 million convertible loan from Elan; and

- an additional \$1.0 million of proceeds under our loan agreement with Celltech.

We also have warrants outstanding for 4.3 million shares, which will provide us with proceeds of \$8.7 million when exercised. Genzyme also has an exercisable option in 2001 to purchase 311,295 shares of our common stock, at an aggregate purchase price of \$4.0 million.

Our business strategy includes entering into additional collaborative relationships with corporate partners to generate license fees, milestone payments, research and development funding and, potentially, equity investments, all of which would be used to fund our ongoing operations. We may be unsuccessful in establishing any additional collaborative relationships or in maintaining our existing relationships. Over the long term, regardless of our partnering success, we expect that we will need to raise substantial additional funds to continue developing and commercializing our products.

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

In addition to the other information contained in this annual report, you should read and consider the following risk factors. If any of these risks actually occur, our business, operating results or financial condition could be adversely affected and the trading price of our stock could decline.

If we are unable to secure financing on terms acceptable to us for future capital needs, we will be unable to fund continuing operations.

Developing and commercializing our potential products will require substantial additional financial resources. Because internally generated cash flow will not fund development and commercialization of our products, we will look to outside sources for funding. These sources could involve one or more of the following types of transactions:

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

If we cannot obtain additional financing when needed or on acceptable terms, we will be unable to fund continuing operations.

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 we began business. As of December 31, 2000, we have incurred cumulative losses of \$150.8 million. We expect to continue to incur substantial additional losses in the future, primarily due to the following factors:

- all of our products are in a testing phase and have not received regulatory approval; and
- we will spend significant amounts on operating expenses.

We may never generate profits, and if we do become profitable, we may be unable to sustain or increase profitability on a quarterly or annual basis. As a result, the trading price of our stock could decline and you could lose all or part of your investment.

If our preclinical and clinical trials are unsuccessful or we do not receive regulatory approval for our products, most of which are in the early stage of product development, we may be unable to generate sufficient revenue to maintain our business.

Almost all of our potential products are in research and development or in early-stage clinical trials. We cannot apply for regulatory approval of our potential products until we have performed additional research and development and testing, both in preclinical and clinical trials. Our trials may not demonstrate the safety and efficacy of any potential product, and we may encounter unacceptable side effects or other problems. Should this occur, we may have to delay or discontinue development of the potential product. After a successful clinical trial, we cannot market any product in the United States or abroad until we receive regulatory approval from the FDA and applicable state and foreign regulators. If we are unable to gain regulatory approval of any product after successful clinical trials, we may be unable to generate sufficient product revenue to maintain our business.

Delays or unexpected costs in obtaining approval of our potential products or complying with governmental regulatory requirements could make it more difficult to maintain or improve our financial condition.

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 requirements of the FDA, NIH and other agencies for clinical trials and the criteria regulators use to determine 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. Delays in bringing a potential product to market or unexpected costs in obtaining regulatory approval could decrease our ability to generate product sales revenue. In addition, all manufacturing operations are subject on an ongoing basis to the current Good Manufacturing Practices requirements of the FDA, as well as to other federal, state and local regulations. While we currently anticipate that we will be able to manufacture products that meet these requirements, we may be unable to attain or maintain compliance with current or future regulatory requirements. If we discover previously unknown problems after we receive regulatory approval of a potential product or fail to comply with applicable requirements, we may suffer restrictions on our ability to market the product, including mandatory withdrawal of the product from the market. This, or an unexpected increase in the cost of compliance, could make it more difficult to maintain or improve our financial condition.

Failure to recruit patients could delay or prevent clinical trials of our potential products, which could cause a delay or inability to develop our 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. Delays in recruiting or enrolling patients to test our products could result in increased costs, delays in advancing our product development, delays in proving the effectiveness of our technology or termination of the clinical trials altogether. Any of these could delay or prevent the development of our product candidates.

Our business will not succeed if our technology and products fail to achieve market acceptance.

Even if our potential products or those of our corporate partners succeed in clinical trials and are approved for marketing, these products may never achieve market acceptance. Competing gene delivery products or alternative treatment methods, including more traditional approaches to treating disease, may be more effective or may be more economically feasible than our products. Moreover, doctors, patients, the medical community in general or the public may never accept or use any products based on gene delivery or other technologies that we or our corporate partners develop.

We may be unable to adequately protect our proprietary rights, which may limit our ability to compete effectively.

Our success depends in part on our ability to protect our proprietary rights. We own or exclusively license patents and patent applications for a number of genes, processes, practices and techniques critical to our present and potential products. 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 failure of our licensors to obtain and maintain patent protection for technology they license to us could similarly harm our business. 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 the patent may be reduced both before and after the patent is issued. Even if we secure a patent, the patent may not provide significant protection and may be circumvented or invalidated.

We also rely on unpatented proprietary technology and technology that we have licensed on a nonexclusive basis. While we take precautions to protect our proprietary unpatented technology, we may be unable to meaningfully protect this technology from unauthorized use or misappropriation by a third party. In any event, other companies may independently develop substantially equivalent proprietary information and techniques.

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

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, litigation may be necessary to enforce our intellectual property rights or determine the rights of others. Defending these claims, regardless of their merit, would be costly and would likely divert management's attention and resources away from our operations. If we infringe on another company's patented processes or technology, we may have to pay damages. We may also be required to obtain a license, or develop or obtain alternative technology, in order to continue manufacturing or marketing the affected product or using the affected process. If we are unable to obtain a license on acceptable terms or obtain or develop alternative technology, we may be unable to develop or commercialize some or all of our product candidates and our business could be harmed.

Our potential tgAAV-CF product uses our proprietary AAV delivery technology to deliver a normal copy of a CFTR gene to which we have rights under a nonexclusive license. The United States Patent and Trademark Office has declared an interference proceeding to determine the priority of invention of this gene. If the eventual outcome does not favor our licensor, we will have to pay increased license fees to the prevailing party to secure and maintain access to the CFTR gene to continue with development of tgAAV-CF. The costs of licensing the CFTR gene could be substantial. If we cannot maintain access to the CFTR gene, we may be unable to develop or deliver our potential tgAAV-CF product, which could result in decreased ability to generate revenue and difficulty in obtaining additional financing to fund our operations.

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

Our success depends on the continued availability of outside scientific and corporate collaborators to perform research and develop processes to advance and augment our internal efforts and to fund our development programs. Competition for collaborators in gene therapy is intense. If we are unsuccessful in recruiting or maintaining our relationships with scientific collaborators and other corporate partners, we could experience delays in our research and development or loss of access to important enabling technology. Even if we maintain our current or establish new scientific collaborations or other partnerships, however, 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 our collaborators. If our corporate partners do not commit sufficient financial and technical resources to our research and development programs or the commercialization of our products, the preclinical or clinical development related to the collaboration could be delayed or terminated. Our current or future collaborators may develop, market or provide funding for competing products or alternative technologies. In addition, disputes may arise with respect to ownership of technology or product candidates developed under our collaborations. Moreover, our corporate partners may terminate any existing partnerships, and we may be unable to enter into additional collaborations on acceptable terms, or at all.

If we are unable to license necessary technology from third parties, 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. Our success depends on our ability to obtain and maintain these kinds of licensing arrangements. Disputes may arise regarding rights to inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and or scientific collaborators. In addition, many of our in-licensing agreements contain milestone-based termination provisions. If we or any of our corporate partners fail to meet agreed milestones, the licensor could terminate the relevant agreement.

If we are unable to maintain our current licenses and obtain additional licenses in the future on acceptable terms, 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 develop alternative technology or obtain a replacement license on acceptable terms, we may be unable to develop or commercialize some or all of our potential products and our business may suffer.

If we or our business partners are unable to successfully market and distribute any potential product, our business will be harmed.

We have no experience in sales and marketing. To market any products that may result from our development programs, we will need to develop marketing and sales capabilities, either on our own or with others. We intend to enter into collaborations with corporate partners to utilize the mature marketing and distribution capabilities of our partners. While we believe that these collaborative 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 technology on a timely basis. If our business partners do not successfully market and distribute our products and we are unable to develop sufficient marketing and distribution capabilities on our own, our business will be harmed.

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 presently face competition from other companies and institutions developing gene therapy and cell therapy technologies and from companies using more traditional approaches to treating human diseases. We also compete with other companies to acquire products or technology from research institutions or universities. Most of our competitors have substantially more financial and infrastructure resources and experience than we do in the following areas:

- research and development;
- clinical trials;

- obtaining FDA and other regulatory approvals;
- manufacturing; and
- marketing and distribution.

In addition, the competitive positions of other companies may be strengthened through collaborative relationships. Consequently, our competitors may be able to commercialize and obtain regulatory approval for new products more rapidly than we do, or manufacture and market competitive products more successfully than we do. This could result in pricing pressures or our products failing to achieve market acceptance. In addition, gene therapy is a new and rapidly evolving field and is expected to continue to undergo significant and rapid technological change. Rapid technological development by our competitors, including development of technologies, products or processes that are more effective than those we have developed, could result in our actual and proposed technologies, products or processes losing market share or becoming obsolete.

If we do not attract and retain qualified personnel, we will be unable to successfully and timely 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 competition for employees in our field is intense, 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.

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 clinical or 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. We have recently leased a building for the purpose of developing a facility to manufacture AAV vectors for Phase III and early commercial purposes. This manufacturing facility, if successfully developed, as well as any future manufacturing facilities that we may construct, will be subject to initial and ongoing regulation by the FDA and other governmental agencies. 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 introduce sufficient product to sustain our business.

Our use of hazardous materials to develop our potential products exposes us to liability risks and the risk of regulatory limitation of our use of these materials, either of which could reduce our ability to generate revenue and make it more difficult to fund our operations.

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 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 would be liable for any resulting damages. This liability could exceed our financial resources. Additionally, hazardous materials are subject to regulatory oversight. Accidents unrelated to our operations could cause federal, state or local regulatory agencies to restrict our access to hazardous materials needed in our research and development efforts. 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 costs of product liability and other claims and product recalls could exceed the amount of our insurance, which could significantly harm our financial condition or our reputation.

Our business activities expose us to the risk of liability claims or product recalls and any adverse publicity that might result from a liability claim against us. We currently have only limited amounts of liability insurance, and the amounts of claims against us may exceed our insurance coverage. Liability insurance is expensive and may not continue to be available on acceptable terms. A product liability or other claim not covered by insurance or in excess of our insurance or a product recall could significantly harm our financial condition or our reputation. In addition, a liability claim against one of our corporate partners or another gene therapy company could also harm our reputation.

Our recent acquisition of Genovo and any future acquisitions could be costly, difficult to integrate and disruptive to our business.

In September 2000, we acquired Genovo, a privately held biotechnology company specializing in viral gene delivery. In the future, we may acquire additional complementary companies, products or technologies. Managing the Genovo acquisition and any future acquisition may entail numerous operational and financial risks and strains, including:

- difficulties in assimilating the operations, technologies, products or potential products and personnel of the acquired company;
- loss of key employees of the acquired company;
- disruption of our business;
- diversion of management's attention from our core business;
- assumption of known and unknown liabilities;
- higher-than-expected acquisition and integration costs and charges against earnings; and
- potentially dilutive issuances of equity securities.

We may be unable to successfully integrate Genovo or any future acquisitions with our existing operations or successfully develop any acquired product candidates or technologies. We may not gain any substantial benefit from the Genovo acquisition or any products, technologies or businesses that we acquire in the future, notwithstanding the expenditure of a significant amount of time and financial, personnel and other resources.

Market fluctuations or volatility could cause the market price of our common stock to decline.

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, these fluctuations in price, regardless of our performance. These fluctuations could cause the market price of our common stock to decline.

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 nominal. At present, we do not employ any derivative or other financial instruments or derivative commodity instruments to hedge any market risks and we do not currently plan to employ them in the future. At December 31, 2000, we held \$38.6 million in cash and cash equivalents, primarily invested in a short-term bond fund owning securities that, on the average, mature in less than one year.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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, 2000 and 1999, and the related consolidated statements of operations, shareholders' equity, and cash flows for each of the three years in the period ended December 31, 2000. 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, 2000 and 1999, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2000 in conformity with accounting principles generally accepted in the United States.

As discussed in Note 2 to the financial statements, in 2000 the Company changed its method of accounting for revenue recognition.

ERNST & YOUNG LLP

Seattle, Washington
February 12, 2001

TARGETED GENETICS CORPORATION

CONSOLIDATED BALANCE SHEETS

ASSETS

	December 31,	
	2000	1999
Current assets:		
Cash and cash equivalents	\$ 38,630,216	\$ 4,100,798
Securities available for sale	-	3,052,471
Accounts receivable	3,086,534	1,391,394
Receivable from joint venture	177,088	445,818
Prepaid expenses and other	291,435	269,864
Total current assets	42,185,273	9,260,345
Property, plant and equipment, net	6,206,276	4,021,466
Goodwill and other purchased intangibles, net	37,821,059	-
Other assets	1,761,434	410,667
	\$87,974,042	\$13,692,478

LIABILITIES AND SHAREHOLDERS' EQUITY

Current liabilities:		
Accounts payable	\$4,000,084	\$ 2,278,338
Payable to joint venture	261,743	594,699
Accrued payroll and other liabilities	679,739	605,545
Deferred revenue	6,906,174	-
Current portion of long-term obligations	838,245	1,160,174
Total current liabilities	12,685,985	4,638,756
Long-term obligations, less current portion	947,508	1,088,208
Long-term note payable	1,498,566	1,000,000
Deferred revenue	9,410,386	-
Shareholders' equity:		
Preferred stock, 6,000,000 shares authorized		
Series A preferred stock, \$.01 par value, 400,000 shares authorized, none issued and outstanding	-	-
Series B preferred stock, \$.001 par value, 12,015 shares authorized, issued and outstanding at December 31, 2000 and 1999	13,275,778	12,390,513
Common stock, \$.01 par value, 80,000,000 shares authorized, 42,608,943 and 34,019,175 shares issued and outstanding at December 31, 2000 and 1999, respectively	200,968,429	97,747,409
Accumulated deficit	(150,812,610)	(103,156,919)
Accumulated other comprehensive loss	-	(15,489)
Total shareholders' equity	63,431,597	6,965,514
	\$87,974,042	\$ 13,692,478

See accompanying notes to the consolidated financial statements.

TARGETED GENETICS CORPORATION
CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2000	1999	1998
Revenue:			
Collaborative agreements	\$ 9,552,835	\$ 6,402,175	\$ 7,192,048
Collaborative agreements with affiliates	1,849,865	445,818	-
Other revenue	-	-	318,204
Total revenue	<u>11,402,700</u>	<u>6,847,993</u>	<u>7,510,252</u>
Operating expenses:			
Research and development	19,311,790	14,291,066	13,327,152
Acquired in-process research and development	28,029,000	-	-
Technology license fee	-	3,200,000	-
Amortization of acquisition-related intangibles	1,685,943	-	-
General and administrative	5,707,558	3,593,436	3,045,835
Total operating expenses	<u>54,734,291</u>	<u>21,084,502</u>	<u>16,372,987</u>
Loss from operations	(43,331,591)	(14,236,509)	(8,862,735)
Equity in loss of joint venture	(2,474,154)	(12,609,699)	-
Investment income	2,097,392	425,726	440,478
Interest expense	(265,651)	(234,653)	(264,792)
Loss before cumulative effect of change in accounting principle	(43,974,004)	(26,655,135)	(8,687,049)
Cumulative effect of change in accounting principle	(3,681,687)	-	-
Net loss	(47,655,691)	(26,655,135)	(8,687,049)
Dividend on preferred stock	(885,265)	(375,513)	-
Net loss applicable to common shareholders	<u>\$ (48,540,956)</u>	<u>\$ (27,030,648)</u>	<u>\$ (8,687,049)</u>
Basic and diluted net loss per share:			
Loss before cumulative effect of change in accounting principle	\$ (1.19)	\$ (0.84)	\$ (0.33)
Cumulative effect of change in accounting principle	\$ (0.10)	\$ -	\$ -
Net loss applicable to common shareholders	<u>\$ (1.29)</u>	<u>\$ (0.84)</u>	<u>\$ (0.33)</u>
Shares used in computation of basic and diluted net loss per share	<u>37,752,164</u>	<u>32,173,756</u>	<u>26,637,823</u>

See accompanying notes to the consolidated financial statements.

TARGETED GENETICS CORPORATION
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY

	Preferred Stock Shares	Preferred Stock Amount	Common Stock Shares	Common Stock Amount	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Shareholders' Equity
Balance at January 1, 1998	-	\$ -	20,211,114	\$ 73,401,141	\$ (67,814,735)	\$ 5,181	\$ 5,591,587
Net loss - 1998	-	-	-	-	(8,687,049)	-	(8,687,049)
Unrealized gains on securities available for sale	-	-	-	-	-	23,224	23,224
Comprehensive loss	-	-	-	-	-	-	(8,663,825)
Sale of common stock and warrants, net of issuance costs of \$158,046	-	-	8,666,667	12,841,954	-	-	12,841,954
Sale of common stock to Medeva, net of issuance costs of \$153,100	-	-	750,000	1,129,400	-	-	1,129,400
Issuance of shares as milestone payment	-	-	875,134	1,000,000	-	-	1,000,000
Exercise of stock options	-	-	149,460	82,643	-	-	82,643
Balance at December 31, 1998	-	-	30,652,375	88,455,138	(76,501,784)	28,405	11,981,759
Net loss - 1999	-	-	-	-	(26,655,135)	-	(26,655,135)
Unrealized gains on securities available for sale	-	-	-	-	-	(43,894)	(43,894)
Comprehensive loss	-	-	-	-	-	-	(26,699,029)
Issuance of Series B convertible exchangeable preferred stock	12,015	12,015,000	-	-	-	-	12,015,000
Dividend on Series B preferred stock	-	375,513	-	(375,513)	-	-	-
Sale of common stock to Medeva, net of issuance costs of \$13,548	-	-	677,392	1,486,452	-	-	1,486,452
Sale of common stock to Elan, net of issuance costs of \$57,347	-	-	2,148,899	4,942,653	-	-	4,942,653
Issuance of common stock and warrants to Alkermes, net of issuance costs of \$17,500	-	-	500,000	3,182,500	-	-	3,182,500
Exercise of stock options	-	-	40,509	56,179	-	-	56,179
Balance at December 31, 1999	12,015	12,390,513	34,019,175	97,747,409	(103,156,919)	(15,489)	6,965,514
Net loss - 2000	-	-	-	-	(47,655,691)	-	(47,655,691)
Unrealized losses on securities available for sale	-	-	-	-	-	15,489	15,489
Comprehensive loss	-	-	-	-	-	-	(47,640,202)
Dividend on Series B preferred stock	-	885,265	-	(885,265)	-	-	-
Sale of common stock, net of issuance costs of \$2,181,314	-	-	2,164,285	28,118,676	-	-	28,118,676
Issuance of common stock to Elan, net of issuance costs of \$3,670	-	-	382,739	4,996,330	-	-	4,996,330
Issuance of common stock in Genovo acquisition	-	-	5,250,805	66,129,733	-	-	66,129,733
Exercise of stock options	-	-	730,765	4,606,812	-	-	4,606,812
Exercise of warrants	-	-	61,174	254,734	-	-	254,734
Balance at December 31, 2000	12,015	\$ 13,275,778	42,608,943	\$ 200,968,429	\$ (150,812,610)	\$ -	\$ 63,431,597

See accompanying notes to the consolidated financial statements.

TARGETED GENETICS CORPORATION
CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2000	1999	1998
Operating activities:			
Net loss	\$ (47,655,691)	\$ (26,655,135)	\$ (8,687,049)
Adjustments to reconcile net loss to net cash used in operating activities:			
Cumulative effect adjustment of change in accounting principle	3,681,687	-	-
Equity in loss of joint venture	2,474,154	12,609,699	-
In-process research and development	28,029,000	-	-
Expenses paid with common stock	-	3,200,000	1,000,000
Depreciation and amortization	1,473,377	1,614,019	1,635,797
Amortization of intangibles	1,685,943	-	-
Amortization of deferred compensation	301,297	-	-
Increase in deferred revenue	12,634,873	-	-
Increase in accounts receivable	(1,695,140)	(1,289,035)	(59,198)
Increase (decrease) in current liabilities	(607,867)	1,180,892	485,259
Increase in other assets	(800,000)	-	-
Decrease (increase) in prepaid expenses and other	(439,933)	62,347	(143,769)
Decrease (increase) in accounts receivable from joint venture	268,730	(445,818)	-
Decrease (increase) in accrued interest on securities available for sale	44,026	79,608	(65,746)
Net cash used in operating activities	<u>(605,544)</u>	<u>(9,643,423)</u>	<u>(5,834,706)</u>
Investing activities:			
Maturities and sales of securities available for sale	3,023,934	7,392,996	11,693,951
Investment in joint venture	(2,807,110)	(594,699)	-
Purchases of property, plant and equipment	(2,796,979)	(1,856,199)	(238,623)
Purchases of securities available for sale	-	(483,014)	(17,664,960)
Net cash acquired in acquisition	358,892	-	-
Increase in other assets	-	-	(15,000)
Net cash provided by (used in) investing activities	<u>(2,221,263)</u>	<u>4,459,084</u>	<u>(6,224,632)</u>
Financing activities:			
Net proceeds from sale of capital stock	37,976,552	6,467,784	14,053,997
Payments under capital leases and loans	(1,291,921)	(1,347,877)	(1,311,952)
Proceeds from leasehold improvement and equipment financing	671,594	1,294,389	176,289
Loan proceeds from collaborative partner	-	1,000,000	-
Net cash provided by financing activities	<u>37,356,225</u>	<u>7,414,296</u>	<u>12,918,334</u>
Net increase in cash and cash equivalents	34,529,418	2,229,957	858,996
Cash and cash equivalents, beginning of year	4,100,798	1,870,841	1,011,845
Cash and cash equivalents, end of year	<u>\$ 38,630,216</u>	<u>\$ 4,100,798</u>	<u>\$ 1,870,841</u>
Cash paid for interest	\$ 244,851	\$ 202,883	\$ 264,702
Supplemental disclosure of noncash investing and financing activities:			
Common stock issued in acquisition	66,129,733	-	-
Preferred stock issuance in exchange for interest in joint venture	-	12,015,000	-
Preferred stock dividend	885,265	375,513	-
Equipment financed through renewal of capital lease	-	-	594,983

See accompanying notes to the consolidated financial statements.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Operations

Targeted Genetics Corporation is developing gene therapy products and technologies for the treatment of certain acquired and inherited diseases. Targeted Genetics was incorporated in the state of Washington in March 1989.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements include the accounts of Targeted Genetics and its wholly-owned subsidiaries Genovo, Inc., TGCF Manufacturing Corporation and CellExSys, Inc. All intercompany transactions have been eliminated. Targeted Genetics' operations constitute one business segment.

Cash Equivalents

Targeted Genetics considers as cash equivalents all short-term investments with a purchased maturity of three months or less that are readily convertible into cash and have insignificant interest rate risk. Cash equivalents, valued at cost that approximates fair market value, consist principally of money market accounts and shares of a short-term limited-maturity mutual fund. All other investments are reported as securities available for sale.

Securities Available for Sale

Securities available for sale consist primarily of corporate debt securities and U.S. government notes that, on the average, mature within one year. Targeted Genetics classifies all of its securities investments as securities available for sale. Securities held are stated at market value, with any unrealized gains and losses included as a component of shareholders' equity. The cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity, which are included in investment income. Realized gains and losses and declines in value on securities available for sale judged to be other than temporary are also included in investment income. The cost of securities sold is calculated using the specific identification method.

Fair Value of Financial Instruments

The carrying amounts of financial instruments such as cash and cash equivalents, securities available for sale, investments, accounts receivable and accounts payable reasonably approximate fair value, because of the short-term nature of these items. Targeted Genetics believes the carrying amounts of the note payable and capital lease obligations approximate fair value because the interest rates on these instruments change with, or approximate, market interest rates.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Long-Lived Assets

Property, plant and equipment are stated at cost. Depreciation of furniture and equipment is provided using the straight-line method over the assets' estimated useful lives, which range from three to seven years. Furniture and equipment under capitalized leases are amortized over the life of the lease. Leasehold improvements are amortized over the life of the improvements or the term of the lease, whichever is shorter. Amortization of assets recorded under capital leases is included with depreciation expense.

Intangible assets consist of assembled workforce, employment contracts, acquired AAV core technology and goodwill and are amortized on the straight-line method over periods ranging from two to seven years.

In accordance with SFAS No. 121 *Accounting for the Impairment of Long-Lived Assets and for Long-Live Assets to be Disposed of*, the carrying value of intangible assets is reviewed on a regular basis to determine whether factors are present that may indicate impairment. To date, no factors are present that would indicate impairment. Should impairment exist in the future, the impairment would be measured based on the excess of the carrying value of the assets over the discounted future cash flows expected to be generated by the impaired assets.

Stock Compensation

As permitted by the provisions of Financial Accounting Standards Board ("FASB") Statement No. 123, *Accounting for Stock-Based Compensation*, Targeted Genetics has elected to follow Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees*, and related interpretations in accounting for its employee stock option grants and to apply the disclosure-only provisions to account for its stock option plans. Targeted Genetics does not recognize any compensation expense related to the plans because all options are granted at fair market value on the date of grant. Options granted to consultants are accounted for using the Black-Scholes method prescribed by Statement No. 123 and are subject to periodic revaluation over their vesting terms.

Revenue Recognition under Collaborative Agreements

Targeted Genetics generates revenues 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. Advance payments received in excess of amounts earned are classified as deferred revenue.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Targeted Genetics 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, Targeted Genetics changed its 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. Targeted Genetics believes that this change in accounting principle is preferable, based on guidance provided in the SEC's Staff Accounting Bulletin 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 will be recognized as revenue over the remaining term of the research and development collaboration agreements. In September 2000, Targeted Genetics recognized a nonrefundable, up-front fee of \$5.0 million. This amount has been reversed and will be recognized over the term of the related research and development arrangement, of which \$430,000 has been recognized during 2000. In November 2000, the Company received another nonrefundable up-front fee of \$5.0 million. This amount will be recognized over the term of the related research and development arrangement. For 2000, the impact of the change in accounting was to increase net loss by \$11.4 million, or \$0.30 per share, comprised of the \$3.7 million cumulative effect of the change as described above (\$0.10 per share), net of \$2.1 million of related deferred revenue that was recognized as revenue during the year (\$0.06 per share), and \$10.5 million of revenue deferred under the agreements executed in September 2000 and November 2000, less \$704,000 recognized during 2000. The remainder of the related deferred revenue will be recognized as revenue approximately as follows: \$5.0 million in 2001, \$3.4 million in 2002 and \$3.0 million in 2003. Had the change in accounting been in effect retroactively to January 1, 1999, net loss for 1999 would have decreased by \$2.1 million, or \$0.07 per share. The pro forma amounts shown on the statement of operations have been adjusted for the effects on revenue that would have applied had the new method been in effect during the periods presented.

Net Loss Per Share

Basic net loss per share is computed based on the weighted average number of common shares outstanding during the period after giving effect to preferred stock dividends. Targeted Genetics' diluted net loss per share is the same as its basic net loss per share because all stock options, warrants and other potentially dilutive securities are antidilutive and are therefore excluded from the calculation of diluted net loss per share. The total number of shares excluded from this calculation of diluted net loss per share, prior to the application of the treasury stock method for options, was 14,552,758, 13,807,922 and 6,982,589 for 2000, 1999 and 1998, respectively.

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. Actual results may differ from those estimates.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

New Accounting Pronouncements

In June 1998, the FASB issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities*. Statement No. 133, which is effective beginning in 2001, establishes accounting and reporting standards for derivative instruments, including certain derivative instruments embedded in other contracts, and for hedging activities. Because Targeted Genetics does not currently hold derivative instruments or engage in hedging activities, the impact of Statement No. 133 is not expected to be material.

Reclassifications

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

3. Business Combinations

On September 19, 2000, Targeted Genetics acquired all of the outstanding shares of capital stock of Genovo, Inc., a development-stage biotechnology company specializing in viral gene delivery. Targeted Genetics accounted for the acquisition of Genovo as a purchase transaction. The total purchase price for the acquisition was approximately \$66.4 million, which consisted of the following:

Issuance of 5,250,805 shares of common stock	\$ 58,461,000
Fair value of options to purchase 1,302,034 shares of common stock	7,668,000
Transaction costs	<u>584,000</u>
Total consideration	66,713,000
Less: intrinsic value of unvested stock options	<u>(301,000)</u>
Purchase price	<u>\$ 66,412,000</u>

The aggregate purchase price was allocated, based on estimated fair values on the acquisition date, as follows:

Tangible assets acquired	\$ 1,850,000
Liabilities assumed	(2,974,000)
Acquired in-process research and development	28,029,000
Assembled work force	605,000
Employment contracts	1,010,000
Acquired AAV core technology	12,723,000
Goodwill	<u>25,169,000</u>
Total purchase price	<u>\$ 66,412,000</u>

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The acquired assets associated with the Genovo purchase are being amortized as follows:

Acquired asset:	Amortization period:
Assembled work force	4 years
Employment contracts	2 years
Tangible assets acquired	remaining life
Acquired AAV core technology	7 years
Goodwill	7 years

Of the 5,250,805 shares issued in the merger, 550,872 shares are held in escrow for the benefit of former Genovo stockholders. Subject to the fulfillment of specified representations and warranties in the merger agreement, all or a portion of the escrowed shares will be released to the stockholders in accordance with the terms of the merger agreement during the 18-month period following the merger date.

Under two circumstances, Targeted Genetics may issue additional shares of its common stock as merger consideration, as follows:

- Because specified Genovo licensing arrangements were unresolved at the time of the merger, Targeted Genetics and Genovo agreed to establish an escrow of 700,000 shares. These shares are held in escrow for the benefit of former Genovo stockholders. All, a portion, or none of the escrowed shares, depending on whether and the extent to which Targeted Genetics successfully renegotiates these license terms, will be release to the former Genovo stockholders no later than 18 months after the merger.
- In connection with the merger and an August 1999 collaborative research agreement between Genzyme Corporation and Genovo, Targeted Genetics assumed Genzyme's outstanding option to purchase Genovo capital stock in two tranches. After the merger, Genzyme exercised the first option tranche to purchase 311,295 shares of Targeted Genetics common stock, at a price of \$12.8495 per share. In August 2001, Genzyme may exercise the second option tranche and acquire up to an additional 311,295 shares of Targeted Genetics common stock (as successor company to Genovo), also at a price of \$12.8495 per share. If, at that time, Genzyme should elect to purchase fewer than 311,295 shares of Targeted Genetics common stock, the former Genovo shareholders and optionholders will receive additional purchase price consideration in the form of shares equal to one-half the difference between the number of shares purchased by Genzyme and the 311,295 shares purchasable by Genzyme.

In each of the above circumstances, the fair value of the shares issued to the former Genovo shareholders, if any, will be determined on the date of resolution of the matter described and will be reflected as additional purchase price. No amounts related to these contingencies have been included in the purchase price to date.

Certain stock options assumed by the Company were subject to continuing employment. The intrinsic value of the invested options of \$301,000 was recorded as deferred compensation. As of December 31, 2000 all of the deferred compensation had been earned and recognized as expense.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Acquired in-process research and development (IPR&D) in the acquisition was evaluated utilizing the present value of the estimated after-tax cash flows expected to be generated by the purchased technology, which had not reached technological feasibility at the effective time of the acquisition. The cash flow projections for revenue are based on estimates of growth rates and the aggregate size of the markets for each product or technology; 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. Estimated operating expenses and income taxes were deducted from estimated revenue projections to arrive at estimated after-tax cash flows. The rates utilized to discount projected cash flows for in-process technologies were 30% to 45%, depending on the relative risk of each in-process technology, and were based primarily on Targeted Genetics' internal rates of return, cost of capital, rates of return for research and development and the weighted average cost of capital at the time of acquisition. Projected operating expenses include general and administrative expenses and research and development costs.

Targeted Genetics based all of the foregoing estimates and projections regarding the Genovo acquisition on assumptions that it believed to be reasonable at the time of the acquisition but that are inherently uncertain and unpredictable. If Targeted Genetics does not successfully develop the projects and technologies considered in these estimates, its business, operating results and financial condition may be adversely affected. As of the date of the acquisition, management concluded that the technologies under development, once completed, could be economically used only for their specifically intended purposes and that the in-process technology had 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. If Targeted Genetics fails in these development efforts, no alternative economic value will result from these technologies and the economic contribution projected to be made by the IPR&D will not materialize. The risk of unsuccessful or untimely completion includes the risk that Targeted Genetics' competitors will develop alternative gene delivery technologies or will develop more effective or economically feasible technologies using more traditional approaches to treating human diseases.

The following table reflects unaudited consolidated pro forma results of operations for the year ended December 31, 2000, which give effect to the Genovo acquisition as if it had occurred on January 1, 2000, and for the year ended December 31, 1999, which give effect to the Genovo acquisition as if it had occurred on January 1, 1999. These pro forma amounts are not necessarily indicative of what the actual consolidated results of operations would have been if the acquisition had been effective at the beginning of each of these periods. The pro forma information does not include the one-time charges for acquired IPR&D related to the acquisition of Genovo.

	For the year ended <u>December 31, 2000</u>	For the year ended <u>December 31, 1999</u>
Revenue	\$ 15,262,000	\$12,241,000
Net loss	(29,671,000)	(38,820,000)
Basic and diluted net loss per share	(0.77)	(1.04)
Shares used in computation of basic and diluted net loss per common share	38,372,000	37,425,000

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

4. Significant Concentrations

Targeted Genetics' collaborative agreement with Celltech Group plc (as successor to Medeva Pharmaceuticals, Inc.) provided 56%, 87% and 88% of revenue in 2000, 1999 and 1998, respectively. See Note 9. At December 31, 2000 and 1999, amounts receivable from Celltech represented 59% and 76%, respectively, of Targeted Genetics' accounts receivable balance. Targeted Genetics does not require collateral or security related to receivables and has historically had no losses on uncollectible accounts. Accordingly, no allowance for bad debts has been recorded.

5. Securities Available for Sale

Targeted Genetics held no securities available for sale at December 31, 2000. At December 31, 1999, securities available for sale consisted of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
December 31, 1999:				
U.S. Treasury securities and obligations of U.S. government agencies	\$ 3,067,960	\$ -	\$ (15,489)	\$ 3,052,471

6. Long-Lived Assets

Property, plant and equipment consisted of the following:

	December 31,	
	2000	1999
Furniture and equipment	\$ 7,287,890	\$ 5,522,248
Leasehold improvements	7,389,268	5,567,091
	14,677,158	11,089,339
Less accumulated depreciation and amortization	(8,470,882)	(7,067,873)
	\$ 6,206,276	\$ 4,021,466

Depreciation expense totaled \$1.4 million in 2000, \$1.5 million in 1999 and 1.5 million in 1998.

Targeted Genetics leases furniture and equipment, primarily laboratory equipment under agreements deemed to be capital leases. The total cost of leased furniture and equipment capitalized at December 31, 2000 and 1999 was \$5.3 million and \$3.8 million, respectively, with related accumulated amortization of \$1.5 million and \$2.5 million at December 31, 2000 and 1999, respectively.

Targeted Genetics acquired goodwill and other purchased intangibles totaling \$39.5 million in connection with its September 2000 acquisition of Genovo. Amortization expense for acquired goodwill and purchased intangibles was \$1.7 million in 2000.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

7. Long-Term Obligations

Long-term obligations consisted of the following:

	December 31,	
	2000	1999
Capitalized lease obligations (See Note 11)	\$ 1,731,563	\$ 2,055,062
Note payable to Celltech	1,000,000	1,000,000
Note payable to Biogen	498,566	-
Other	54,190	193,320
	3,284,319	3,248,382
Less current portion	(838,245)	(1,160,174)
	\$ 2,446,074	\$ 2,088,208

Future aggregate principal payments related to long-term obligations are \$838,245 in 2001, \$605,244 in 2002, \$1,285,581 in 2003, \$43,252 in 2004 and \$511,997 in 2005.

Under an agreement with Celltech, subject to specified circumstances, Celltech will loan Targeted Genetics up to \$2.0 million. Loan proceeds are unsecured and are required to be used to partially finance the cost of establishing tgAAV-CF manufacturing facilities for the supply of bulk product to be used in Phase III clinical trials and for initial commercial launch. As of December 31, 2000 and 1999, Targeted Genetics had \$1.0 million in loans outstanding under this agreement. Interest on borrowings is payable annually in arrears at a rate that is 150 basis points over the one-month LIBOR rate, but neither less than 5% nor more than 7% per year. Targeted Genetics recognized \$70,000 of Celltech loan interest expense in 2000 and \$19,000 in 1999. Principal is due and payable in November 2003, or earlier if the cumulative net product sales of Targeted Genetics' cystic fibrosis product equal or exceed \$60.0 million. The loan agreement contains financial covenants including limits on Targeted Genetics' ability to declare or pay dividends. Targeted Genetics can, at its option and with Celltech's consent, repay the loan with its common stock at any time during the loan term, at a conversion price equal to the average closing price of the common stock over a 20-day period preceding the repayment date.

In September 2000, as part of its acquisition of Genovo, Targeted Genetics assumed promissory notes with an outstanding principal amount of \$650,000 previously issued by Genovo to Biogen. The notes bear no interest and are due in September 2005. At the time of the acquisition, Targeted Genetics discounted the notes to reflect market interest rates, using an imputed interest rate of 5.6%. In 2000, Targeted Genetics recognized \$8,000 of interest expense relating to the Biogen promissory notes.

8. Shareholders' Equity

Series B Preferred Stock

In July 1999, Elan International Services, Ltd. purchased \$12,015,000 of Targeted Genetics' Series B preferred stock in conjunction with the formation of the Emerald Gene Systems Ltd. joint venture. See Note 14. This preferred stock bears an annual dividend of 7%, accrued semi-annually and added to principal. As of December 31, 2000 and 1999, Targeted Genetics had accrued dividends of \$1.3 million and \$376,000, respectively. The Series B preferred stock is convertible until July 2005, at Elan's option, into Targeted Genetics

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

common stock, at a price of \$3.32 per share. Elan's holdings of the Series B preferred stock were convertible into 3,998,375 shares of the common stock as of December 31, 2000. Targeted Genetics would issue 5,740,548 shares of its common stock if Elan were to elect to convert its preferred stock into shares of common stock as of July 21, 2005, the expiration of the conversion option. Alternatively, Elan has an option to exchange the Series B preferred stock and all accumulated dividends for a 30.1% interest in Emerald. This exchange option is exercisable up to six months after the completion of a research and development program that is currently anticipated to be 36 to 48 months in length. This exchange right will terminate if the preferred stock is converted into common stock, unless the conversion occurs as a result of a liquidation or specified transactions involving a change of control of Targeted Genetics.

Should Targeted Genetics liquidate or wind-up its operations, Targeted Genetics' articles of incorporation give preferred shareholders priority over common shareholders with respect to the assets legally available for distribution to shareholders. The Series B shareholders' liquidation preference is at the original purchase price. Targeted Genetics has redemption rights to these shares only in certain instances involving a change of control. Holders of Series B preferred stock are not entitled to vote together with holders of common stock with respect to election of directors or other corporate governance matters.

Warrants

In June 1999, Targeted Genetics issued warrants to purchase 2,000,000 shares of its common stock to Alkermes, Inc. These warrants were issued in two tranches of 1,000,000 shares each. The warrants expire in June 2007 and June 2009 and have an exercise price of \$2.50 and \$4.16 per share, respectively. See Note 10.

In 1998, Targeted Genetics completed a private placement of common stock and warrants, which resulted in net proceeds of approximately \$12.8 million. Warrants to purchase a total of 4,333,333 shares of common stock were issued in the transaction, with an exercise price of \$2.00 per share and an expiration of April 2003.

Targeted Genetics has outstanding warrants to purchase a total of 64,842 shares related to equipment financing and consulting agreements. These warrants have a weighted average price of \$4.66 per share and expire between May 2001 and March 2004.

At December 31, 2000, 6,398,175 shares of common stock were reserved for issuance upon the conversion of all outstanding warrants.

Shareholder Rights Plan

Targeted Genetics has adopted a shareholder rights plan, under which it has distributed a dividend of one right for each outstanding share of common stock. These rights could cause substantial dilution to persons or groups that attempt to acquire Targeted Genetics on terms not approved by its Board of Directors.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Stock Options

Targeted Genetics has four stock option plans. Beginning in 1999, Targeted Genetics began granting all options from its 1999 Stock Option Plan (the "1999 Plan"), and discontinued grants from two other plans existing at that time. In 2000, in connection with the acquisition of Genovo, Targeted Genetics established the Genovo, Inc. Roll-over Stock Option Plan (the "Genovo Plan").

The 1999 Plan provides for option grants of up to a maximum of 1.5 million shares of common stock to employees, directors and officers of Targeted Genetics and to consultants, agents, advisors and independent contractors who provide services to Targeted Genetics or its subsidiaries. Generally, options vest in even quarterly or annual increments over a three- to five-year period. All options expire ten years from date of grant. As of December 31, 2000, options to purchase 524,135 shares were available for future grant under the 1999 Plan.

The Genovo Plan was established to convert Genovo employees' options to purchase shares of common stock of Genovo into options to purchase common stock of Targeted Genetics. Targeted Genetics issued options to purchase 679,444 shares of Targeted Genetics common stock under the Genovo Plan to the former employees of Genovo, based on their option holdings in Genovo before the acquisition. These options are fully vested and expire ten years from the date that the underlying Genovo stock options were granted. The Genovo Plan is subject to approval by the shareholders of Targeted Genetics.

The following table summarizes activity related to Targeted Genetics stock option plans:

	Shares	Weighted Average Exercise Price
Balance, January 1, 1998	1,696,702	\$ 3.62
Granted	1,269,277	1.49
Exercised	(149,460)	0.55
Canceled	(955,933)	3.61
Balance, December 31, 1998	1,860,586	2.42
Granted	835,265	1.94
Exercised	(40,509)	1.39
Canceled	(214,000)	2.51
Balance, December 31, 1999	2,441,342	2.26
Granted	694,272	9.90
Assumed in acquisition	679,444	1.30
Exercised	(419,470)	1.45
Canceled	(74,810)	6.13
Balance, December 31, 2000	<u>3,320,778</u>	3.66

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Options to purchase 1,782,082, 1,094,420 and 628,785 shares were exercisable at December 31, 2000, 1999 and 1998, respectively.

In 1998, Targeted Genetics offered active employees, except executive officers, the opportunity to cancel previously awarded stock option grants with exercise prices greater than the current market price of common stock and to be granted the same number of new options at the closing market price on the grant date. Substantially all eligible employees elected to replace their previously awarded stock option grants, resulting in the cancellation of options to purchase 531,550 shares, at an average price of \$3.77 per share, and the issuance of options to purchase the same number of shares at \$1.22 per share. The new options awarded under this offer vest over a three-year period, ending in February 2001.

The following table summarizes information for outstanding and exercisable options at December 31, 2000:

Range of Exercise Prices	Outstanding			Exercisable	
	Shares Subject to Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life	Shares Subject to Options	Weighted Average Exercise Price
\$0.50 - \$1.22	752,201	\$0.95	6.95	668,182	\$0.94
1.38 - 1.94	770,591	1.72	7.72	321,302	1.73
2.18 - 3.00	692,602	2.28	8.11	336,023	2.33
3.94 - 8.56	741,984	6.20	6.44	438,236	5.16
8.88 - 21.38	363,400	10.80	9.55	18,339	13.42
\$0.50 - \$21.38	<u>3,320,778</u>	3.66	7.54	<u>1,782,082</u>	2.51

Pro forma information regarding net loss and net loss per share is as follows. The pro forma information is provided as if Targeted Genetics had accounted for its stock options granted to employees under the fair value method, as required by Statement 123.

	2000	1999	1998
Net loss, as reported	\$ (48,540,956)	\$ (27,030,648)	\$ (8,687,049)
Net loss, pro forma	(54,578,982)	(27,985,273)	(9,512,398)
Basic net loss per share, as reported	(1.29)	(0.84)	(0.33)
Basic net loss per share, pro forma	(1.45)	(0.87)	(0.36)

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

	2000	1999	1998
Expected dividend rate	Nil	Nil	Nil
Expected stock price volatility	1.661	0.908	0.814
Risk-free interest rate	6.47%	5.05%	5.38%
Expected life of options from vest date	3 years	3 years	3 years

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The weighted average fair value of options granted during 2000, 1999 and 1998 was \$9.90, \$1.94 and \$1.11 per share, respectively. Compensation expense included in these pro forma amounts may not be representative of the effects on pro forma earnings for future years.

In connection with the Genovo acquisition and an August 1999 collaborative research agreement between Genzyme and Genovo, Targeted Genetics assumed Genzyme's outstanding option to purchase Genovo capital stock in two tranches. As discussed in Note 3, Genzyme exercised the first option tranche after the merger and purchased 311,295 shares of Targeted Genetics common stock, at a purchase price of \$12.8495 per share. Genzyme has a remaining option to purchase an additional 311,295 shares for \$4.0 million, exercisable in August 2001.

As of December 31, 2000, Targeted Genetics had reserved a total of 14,552,758 shares of common stock for issuance upon the conversion of outstanding preferred stock, stock options and warrants, as listed below:

	Shares reserved for issuance
Stock options issued	3,320,778
Stock options available for future grant	524,135
Warrants	6,398,175
Emerald Gene Systems joint venture preferred stock	3,998,375
Genzyme collaboration options	311,295
Total	14,552,758

In January 2001, Targeted Genetics' board of directors unanimously approved an increase to the 1999 Plan to provide for option grants to purchase up to an additional 2.0 million shares of common stock. The increase in the number of shares subject to stock option grants is subject to approval by Targeted Genetics' shareholders.

9. Collaborative Agreements

Celltech Group Agreement

In 1998, Targeted Genetics entered into a series of agreements with Medeva Pharmaceuticals, Inc. In January 2000, Medeva merged with Celltech/Chiroscience to become part of Celltech Group plc. Celltech has assumed Medeva's rights and responsibilities under these agreements, under which Targeted Genetics and Celltech will collaborate to develop on a worldwide basis Targeted Genetics' tgAAV-CF gene therapy product for the treatment of cystic fibrosis. Under a research and development funding agreement, Targeted Genetics received a license and technology access fee of \$5.0 million at the time of signing and a milestone payment of \$1.0 million related to the start of Phase I clinical trials for the aerosolized version of the tgAAV-CF product. In addition, Celltech will pay up to \$5.0 million per year for three years to fund Targeted Genetics' tgAAV-CF research and development activities and certain Phase I clinical trial expenses and will pay the costs of Phase II and subsequent clinical trials of the product candidate. Assuming successful development and regulatory approval, Celltech will have the exclusive right to market the product on a worldwide basis. Under a long-term supply agreement, Targeted Genetics will manufacture and supply bulk product to Celltech under a pricing formula constructed to compensate Targeted Genetics with a fixed percentage of Celltech's net product sales.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The research and development funding agreement is effective from October 1998 to October 2001, with an option to extend the term if both parties agree. The long-term supply agreement is effective for the term of the patents covering Targeted Genetics' tgAAV-CF technology. Celltech has the option to terminate the agreements at will with 180 days' notice. Should Celltech exercise this right to terminate, all rights related to tgAAV-CF technology would return to Targeted Genetics.

Targeted Genetics recognized \$6.7 million, \$6.4 million and \$7.0 million of revenue under the Celltech agreements in 2000, 1999 and 1998, respectively. As a result of implementing SAB 101, \$2.1 million of revenue from amortization of a nonrefundable up-front fee received in 1998 is included in the \$6.7 million recognized in 2000.

Under related agreements, Celltech agreed to purchase \$3.0 million of Targeted Genetics common stock and, as described below, to loan Targeted Genetics up to \$12.0 million for the construction of manufacturing facilities. Celltech purchased \$3.0 million of Targeted Genetics common stock in two tranches: 750,000 shares of common stock for \$1.5 million upon signing the agreements in 1998 and 677,392 shares of common stock for \$1.5 million in 1999. Under the agreements, subject to specified conditions, Targeted Genetics can draw up to \$2.0 million to partially fund construction of facilities to support Phase III clinical trials and initial commercialization of tgAAV-CF product candidates. At December 31, 2000, Targeted Genetics had drawn \$1.0 million. Celltech will also loan Targeted Genetics, under specified conditions, up to an additional \$10.0 million toward building a manufacturing facility compliant with the FDA's Good Manufacturing Practices guidelines for higher-volume production of tgAAV-CF. No amounts have been drawn under this commitment.

Emerald Gene Systems Joint Venture

In July 1999, Targeted Genetics and Elan International Services, Ltd. formed Emerald Gene Systems, Ltd., a joint venture to develop enhanced gene delivery technology and products.

Elan has agreed to loan Targeted Genetics up to \$12.0 million, in the form of a convertible promissory note, to support Targeted Genetics' share of Emerald's research and development costs. The note has a six-year term and any draws made under the note accrue interest at 12% per year. The note and related accrued interest are convertible, at Elan's option, into Targeted Genetics common stock at a conversion price equal to 150% of the average closing price of Targeted Genetics common stock for the 60 trading days ending two business days before the draws. Alternatively, the note agreement includes provisions allowing Targeted Genetics, at its option, to convert the note into common stock at the lesser of the then-current market price and the Elan conversion price. As of December 31, 2000 and 1999, Targeted Genetics had not drawn on the note.

Targeted Genetics also entered into an agreement with Elan that requires Elan to purchase up to \$10.0 million of Targeted Genetics common stock. Elan purchased \$5.0 million of common stock (2,148,899 shares) at the closing of the joint venture transaction and purchased the remaining \$5.0 million of common stock (382,739 shares) in July 2000, the one-year anniversary of the agreement.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Biogen Agreement

In September 2000, Targeted Genetics established a multiple-product development and commercialization collaboration with Biogen, Inc. Biogen paid Targeted Genetics \$8.0 million, which included up-front prepaid research and development funding of \$3.0 million, upon initiation of the collaboration. Biogen will also provide Targeted Genetics with a minimum of \$3.0 million of additional research and development funding over three years, at a rate of \$1.0 million per year. Under the terms of the collaborative agreement, Targeted Genetics granted Biogen an exclusive worldwide license to sell products developed in the collaboration and assumed responsibility for manufacturing and supplying bulk vector supplies to Biogen to support product development, clinical trials and product commercialization.

Under a related funding agreement, Biogen also agreed to provide Targeted Genetics with loans of up to \$10.0 million and to purchase up to \$10.0 million of Targeted Genetics common stock, each at Targeted Genetics' discretion. Targeted Genetics may make up to five draws against the \$10.0 million loan amount, with any draws bearing interest at market rates. Any draws against the loan, all of which must be made before September 2005, mature after five years but no later than September 2006. Until September 2003, Targeted Genetics can elect to have Biogen purchase the \$10.0 million of common stock in one or more tranches, at a price per share equal to the average of the daily closing prices of a share of Targeted Genetics common stock for a specified period of time before and after the applicable exercise date. As of December 31, 2000, Targeted Genetics had neither drawn any proceeds on this loan nor exercised its right to have Biogen purchase shares of its common stock.

Assuming successful commercialization of products under the Biogen collaboration, Targeted Genetics could receive an aggregate of up to \$125 million in license fees, development funding, milestone payments, loan proceeds and equity investments connected to the Biogen agreements. Targeted Genetics will receive royalties based upon any sales of products that result from the collaborative product development efforts or, alternatively, will sell product to Biogen at transfer prices that include sales-based and cost-based components.

The research and development funding agreement is effective to September 30, 2003, with an option to extend the term if both parties agree. The product manufacturing and supply provisions of the agreement are effective for the term of the patents covering the Targeted Genetics technology. Although Biogen may terminate the development and commercialization agreement at any time following the first anniversary of the agreement, Biogen's obligation under the related funding agreement to pay the minimum annual project funding (totaling \$3.0 million over three years) would continue.

Targeted Genetics is amortizing the \$5.0 million up-front fee paid by Biogen over the initial three-year research and development performance period. Targeted Genetics will recognize revenue on the remaining \$3.0 million of up-front payment and the \$1.0 million minimum annual project funding as it performs research and development efforts. Targeted Genetics performed no research and development efforts attributable to the Biogen collaboration agreements in 2000.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Genetics Institute Agreement

In November 2000, Targeted Genetics entered into a collaboration to develop gene therapy products for the treatment of hemophilia with Genetics Institute, the biotechnology research division of Wyeth-Ayerst, a division of American Home Products Corporation. Under terms of the research and development funding agreement, Genetics Institute paid Targeted Genetics \$5 million in nonrefundable up-front payments and \$500,000 in reimbursements for research performed before the collaboration and will pay up to \$15 million for developing a hemophilia A candidate product over a three-year research and development collaboration. Subject to the achievement of specified objectives, Genetics Institute could pay additional product development and commercialization milestones payments of up to \$60 million. In addition, Targeted Genetics also granted Genetics Institute an option to collaborate on the development of a hemophilia B product candidate, which, if developed, would trigger additional payments to Targeted Genetics. Genetics Institute also agreed, upon the occurrence of specified events, to enter into an agreement to loan Targeted Genetics up to \$10 million to finance manufacturing facility expansions. Under a related supply agreement, Genetics Institute agreed to pay Targeted Genetics to manufacture product for clinical trials and, upon approval, for commercial use according to a sales-based formula. In addition, Genetics Institute agreed to manage and fund the costs of clinical trials and related regulatory filings required for product approval and marketing. Genetics Institute will retain global marketing rights for any products resulting from the alliance.

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, to be extended should regulatory agencies approve a product for commercial use. Genetics Institute has the right to terminate both agreements at will, with 180 days' notice. Should Genetics Institute exercise this right to terminate, all rights that Targeted Genetics granted or otherwise extended to Genetics Institute related to the hemophilia technology would return to Targeted Genetics.

Targeted Genetics is amortizing the \$5.0 million up-front fee and the up-front \$500,000 research reimbursement from the Genetics Institute collaboration over the initial three-year research and development performance period.

Genzyme Agreement

When Targeted Genetics acquired Genovo, it assumed a three-year Development and License Agreement with Genzyme Corporation under which Genovo was committed to perform, at its own cost, up to \$2.9 million per year of research and development activities. Under the terms of this agreement, should Targeted Genetics achieve specified regulatory milestones, Genzyme would be required to make milestone payments and pay royalties to Targeted Genetics on sales of any products developed under the agreement. In November 2000, Targeted Genetics amended the development agreement to expand the collaboration's technological scope and financial terms and establish a development plan for the second year of the three-year collaborative effort. This agreement is effective from August 1999 to August 2002, with an option to extend the term if both parties agree.

Targeted Genetics also assumed a separate agreement that granted Genzyme an option to purchase up to \$11.4 million of Genovo equity, of which \$3.4 million had been purchased as of the Genovo acquisition date. After the November 2000 amendment to the development agreement, Genzyme exercised its option to purchase 311,295

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

shares of Targeted Genetics' common stock, at a purchase price of \$12.8495 per share, providing \$4.0 million of proceeds to Targeted Genetics.

International AIDS Vaccine Initiative Agreement

In February 2000, Targeted Genetics entered into a collaboration to develop a vaccine to prevent AIDS with the International AIDS Vaccine Initiative (IAVI) and Children's Research Institute on the campus of Children's Hospital in Columbus, Ohio. Under the terms of the collaboration, IAVI will fund development, preclinical and Phase I studies. IAVI expects to invest up to \$6 million in research funding during the first three years of the agreement, provided that specified milestones are achieved.

Under the terms of the IAVI agreement, Targeted Genetics has rights to manufacture any vaccine developed under the collaboration and will retain worldwide exclusive commercialization rights to any product that may stem from the collaboration. If Targeted Genetics declines to produce the vaccine for developing countries in reasonable quantity at a reasonable price, as determined in accordance with a variety of factors specified in the agreement, IAVI will have rights to obtain licenses from Targeted Genetics 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, Targeted Genetics will have exclusive rights to commercialize in industrialized countries any successful vaccine developed under the collaboration.

10. Alkermes License

In June 1999, Targeted Genetics entered into an agreement with Alkermes, Inc. to acquire the exclusive rights to sublicense a patent and other pending patent applications for manufacturing AAV vectors. The license to this technology, first developed by Children's Hospital in Columbus, Ohio, covers the use of cell lines for the manufacture of AAV vectors and expands a previously acquired limited field license to these rights. Targeted Genetics issued to Alkermes 500,000 shares of its common stock and warrants to purchase a total of up to 2.0 million additional shares in exchange for this technology license. Under the terms of the license, Targeted Genetics must attempt to commercialize the technology. Additionally, Targeted Genetics is obligated to make milestone payments if any product candidates using this technology reach clinical trial and regulatory milestones and to pay royalties upon the sale of any AAV products using the licensed technology or the sublicensing of the Alkermes technology.

Targeted Genetics recorded a \$3.2 million noncash charge with respect to the Alkermes license in its 1999 operating results, because the underlying technology is not complete and Targeted Genetics will have to invest significant resources to develop and prove its commercial feasibility. This charge was computed based on the value of the warrants and shares of common stock issued to Alkermes. Targeted Genetics computed the value of the warrants issued to Alkermes using the Black-Scholes valuation method.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

11. Lease Commitments

Targeted Genetics leases its research and office facilities in Seattle, Washington under two noncancellable operating leases that expire on March 31, 2004 and leases its manufacturing facilities in Bothell, Washington under a noncancellable operating lease that expires on October 1, 2015. The research and office facility leases may be extended under two additional five-year renewal options at the then-prevailing fair market value rental rate. The manufacturing facility lease may be extended for an additional five-year period. Targeted Genetics also leases research and office facilities in Sharon Hill, Pennsylvania, under a noncancellable operating lease that expires in November 30, 2005. This lease may be extended for two additional five-year periods and has an early termination option allowing for termination of the lease on November 30, 2001, with advance notice.

Future minimum payments under noncancelable leases at December 31, 2000 were as follows:

	Operating	Capital
Year Ending December 31:		
2001	\$2,168,081	\$ 901,264
2002	2,198,077	658,231
2003	2,214,815	293,105
2004	1,665,468	40,962
2005	1,537,725	8,976
Thereafter	14,650,186	-
Total minimum lease payments	\$24,434,352	1,902,538
Less amount representing interest		(170,975)
Present value of minimum capitalized lease payments		\$1,731,563

Rent expense under operating leases for the years ended December 31, 2000, 1999 and 1998 was \$1.1 million, \$587,000 and \$533,000, respectively.

12. Employee Retirement Plan

Targeted Genetics sponsors an employee retirement plan under Section 401(k) of the Internal Revenue Code. All employees of Targeted Genetics and its subsidiaries who are 21 years old or older are eligible to participate in the plan. Contributions made into the 401(k) plan by Targeted Genetics are made at the discretion of the board of directors. Targeted Genetics incurred \$144,000, \$90,000 and \$0 of expense in 2000, 1999 and 1998, respectively, related to contributions to the plan.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

13. Income Taxes

At December 31, 2000, Targeted Genetics had net operating loss carryforwards of \$80.7 million and research and experimental credit carryforwards of \$3.1 million. The carryforwards, which are available to offset future federal income taxes, begin to expire in 2008. Targeted Genetics has provided a valuation allowance to offset the excess of deferred tax assets over the deferred tax liabilities, due to the uncertainty of realizing the benefits of the net deferred tax asset. The valuation allowance increased by \$10.8 million in 2000 and \$3.9 million in 1999.

Significant components of Targeted Genetics' deferred tax assets and liabilities were as follows:

	December 31,	
	2000	1999
Deferred tax assets:		
Net operating loss carryforwards	\$ 27,453,000	\$ 23,828,000
Deferred revenue	5,548,000	1,815,000
Research and experimental credit carryforwards	3,094,000	-
Depreciation	954,000	842,000
Other	384,000	185,000
Total deferred tax assets	\$ 37,433,000	\$ 26,670,000
Valuation allowance for deferred tax assets	\$ 37,433,000	\$ 26,670,000

Utilization of federal income tax carryforwards is subject to limitation under Section 382 of the Internal Revenue Code. Targeted Genetics' past sales and issuances of common stock have resulted in "ownership changes," as defined under Section 382, that may result in limitations on the future use of some portion of the net operating loss carryforwards.

14. Joint Venture

When Targeted Genetics and Elan formed the Emerald joint venture in July 1999, Elan purchased \$12.0 million of Targeted Genetics' Series B convertible exchangeable preferred stock. The preferred stock is convertible, at Elan's option, into Targeted Genetics common stock or into shares representing a 30.1% interest in Emerald, which would increase Elan's ownership in Emerald to 50%. Targeted Genetics used the proceeds of the convertible exchangeable preferred stock sale to purchase its 80.1% interest in Emerald. Emerald used these proceeds to pay \$15.0 million to Elan for a license giving Emerald exclusive rights to use Elan drug delivery technologies within the gene delivery field.

At its formation, Emerald issued preferred and common stock valued at \$15.0 million to Targeted Genetics and Elan. Targeted Genetics currently owns an 80.1% interest in Emerald common stock and Elan owns a 19.9% nonvoting interest, in preferred shares. Although Targeted Genetics owns 100% of the voting common shares, 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 Targeted Genetics from exercising control over Emerald,

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Targeted Genetics does not consolidate the financial statements of Emerald but instead accounts for its investment in Emerald under the equity method of accounting.

The condensed financial statements of Emerald as of December 31, 2000 and 1999 and for the year ended December 31, 2000 and the period from July 21, 1999 (date of inception) through December 31, 1999 are as follows:

	December 31, 2000	December 31, 1999
Current assets	\$ 6,114	\$ 2,250
Total assets	\$ 6,114	\$ 2,250
Current liabilities	331,143	744,696
Total shareholders' equity	(325,029)	(742,446)
Total liabilities and shareholders' equity	\$ 6,114	\$ 2,250
	Year ended December 31, 2000	Period from July 21, 1999 (date of inception) through December 31, 1999
Revenue	\$ -	\$ -
Technology access fee	-	15,000,000
Operating expenses	3,087,091	742,446
Net loss	\$ (3,087,091)	\$ (15,742,446)

Included in Targeted Genetics' December 31, 2000 and 1999 balance sheets are \$177,000 and \$446,000, respectively, of receivables from Emerald for services performed by Targeted Genetics for Emerald. The balance sheets also include accounts payable to Emerald of \$262,000 for 2000 and \$595,000 for 1999, for Targeted Genetics' 80.1% share of Emerald's funding requirements as of each date. Targeted Genetics expects to advance Emerald its share of the required funding and collect the \$177,000 Emerald account receivable for 2000 during the first quarter of 2001. Targeted Genetics is required to provide additional funding to Emerald as needed in relation to its ownership interest in Emerald. Targeted Genetics provided \$2.8 million of funding to Emerald in 2000 and no funding to Emerald in 1999.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

15. Condensed Quarterly Financial Information (unaudited)

The following table presents the quarterly results for 2000 and 1999. The results for the three months ended March 31, 2000, June 30, 2000 and September 30, 2000 have been restated from those presented in the quarterly reports on Form 10-Q for these periods as a result of the adoption of the new accounting policy with respect to revenue recognition.

	Q1	Q2	Q3	Q4
2000	<i>(Restated)</i>	<i>(Restated)</i>	<i>(Restated)</i>	
Revenue	\$2,699,886	\$2,277,496	\$1,193,620	\$4,511,698
Loss before cumulative effect of change in accounting principle.....	(2,537,182)	(3,560,548)	(32,004,465)	(5,871,809)
Cumulative effect of change in accounting principle.....	(3,681,687)	-	-	-
Net loss.....	(6,218,869)	(3,560,548)	(32,004,465)	(5,871,809)
Basic and diluted loss per share before cumulative effect of change in accounting principle.....	(0.08)	(0.10)	(0.86)	(0.14)
Basic and diluted net loss per common share.....	(0.18)	(0.10)	(0.86)	(0.14)
	Q1	Q2	Q3	Q4
2000 amounts as previously reported				
Revenue	2,174,958	1,752,568	6,342,782	
Net loss	(3,062,110)	(4,085,476)	(27,575,303)	
Basic and diluted loss per common share	(0.09)	(0.12)	(0.75)	
1999				
Revenue.....	1,204,725	1,418,392	1,364,545	2,860,331
Net loss	(2,684,246)	(5,878,489)	(15,188,537)	(2,903,863)
Basic and diluted loss per common share	(0.09)	(0.19)	(0.46)	(0.09)

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

TARGETED GENETICS CORPORATION

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF REGISTRANT

(a) The information required by this item with respect to our directors is incorporated by reference to the section captioned "Election of Directors" in the proxy statement for our annual meeting of shareholders to be held on May 8, 2001. We will file the proxy statement within 120 days of December 31, 2000, our fiscal year end.

(b) The information required by this item with respect to our executive officers is incorporated by reference to the section captioned "Executive Officers" in the proxy statement for our annual meeting of shareholders to be held on May 8, 2001.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item with respect to executive compensation is incorporated by reference to the section captioned "Executive Compensation" in the proxy statement for our annual meeting of shareholders to be held on May 8, 2001.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this item with respect to beneficial ownership is incorporated by reference from the section captioned "Principal Shareholders" in the proxy statement for our annual meeting of shareholders to be held on May 8, 2001.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

None.

PART IV

ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

(a) 1. Financial Statements

The following financial statements are submitted in Item 8 of this report:

	<u>Page(s) in 10-K</u>
Targeted Genetics Corporation Report of Ernst and Young LLP, Independent Auditors	37
Targeted Genetics Corporation Balance Sheets at December 31, 2000 and 1999	38
Targeted Genetics Corporation Statements of Operations for the years ended December 31, 2000, 1999 and 1998	39
Targeted Genetics Corporation Statements of Shareholders' Equity for the period from December 31, 1997 through December 31, 2000	40
Targeted Genetics Corporation Statements of Cash Flows for the years ended December 31, 2000, 1999 and 1998	41
Targeted Genetics Corporation Notes to Financial Statements	42-61

2. Financial Statement Schedules

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

3. Exhibits

3.1	Restated Articles of Incorporation (Exhibit 3.1)	(M)
3.2	Amended and Restated Bylaws (Exhibit 3.2)	(D)
4.1	Rights Agreement, dated as of October 17, 1996, between Targeted Genetics and ChaseMellon Shareholder Services (Exhibit 2.1)	(C)
4.2	First Amendment of Rights Agreement, dated July 21, 1999, between Targeted Genetics and ChaseMellon Shareholder Services(Exhibit 1.9)	(K)
10.1	Form of Indemnification Agreement between the registrant and its officers and directors (Exhibit 10.1)	(L)
10.2	Form of Senior Management Employment Agreement between the registrant and its executive officers (Exhibit 10.2)	(D)
10.3	Gene Transfer Technology License Agreement, dated as of February 18, 1992, between Immunex Corporation and Targeted Genetics* (Exhibit 10.3)	(L)
10.4	PHS Patent License Agreement-Non-Exclusive, dated as of July 13, 1993, between National Institutes of Health Centers for Disease Control and Targeted Genetics* (Exhibit 10.4)	(L)
10.5	Patent License Agreement, dated as of December 25, 1993, between The University of Florida Research Foundation, Inc. and Targeted Genetics* (Exhibit 10.5)	(L)
10.6	Research and Exclusive License Agreement, dated as of January 1, 1994, between Targeted Genetics and the Fred Hutchinson Cancer Research Center* (Exhibit	(E)

- 10.9)
- 10.7 PHS Patent License Agreement- Exclusive, dated as of March 10, 1994, between National Institutes of Health Centers for Disease Control and Targeted Genetics* (Exhibit 10.10) (E)
- 10.8 License Agreement, dated as of March 28, 1994, between Targeted Genetics and the University of Michigan* (Exhibit 10.13) (E)
- 10.9 Patent and Technology License Agreement, effective as of March 1, 1994, between the Board of Regents of the University of Texas M.D. Anderson Cancer Center and RGene Therapeutics, Inc.* (Exhibit 10.29) (A)
- 10.10 First Amended and Restated License Agreement, effective as of October 12, 1995, between The University of Tennessee Research Corporation and Rgene Therapeutics, Inc.* (Exhibit 10.30) (A)
- 10.11 Amendment to First Amended and Restated License Agreement, dated as of June 19, 1996, between The University of Tennessee Research Corporation and RGene Therapeutics, Inc.* (Exhibit 10.1) (B)
- 10.12 Second Amendment to First Amended and Restated License Agreement, dated as of April 17, 1998, between The University of Tennessee Research Corporation and RGene Therapeutics, Inc.* (G)
- 10.13 Revised License Agreement, effective as of October 1, 1996, between the University of Pittsburgh of the Commonwealth System of Higher Education and Targeted Genetics* (Exhibit 10.21) (D)
- 10.14 License Agreement, dated as of March 15, 1997, between the Burnham Institute and Targeted Genetics* (Exhibit 10.23) (E)
- 10.15 Exclusive Sublicensing Agreement, dated June 9, 1999, between Targeted Genetics and Alkermes, Inc. (Exhibit 10.36) (J)
- 10.16 License Agreement, dated as of August 31, 1999, between Targeted Genetics and the University of North Carolina Research Center* (Exhibit 10.17) (L)
- 10.17 Master Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.1) (H)
- 10.18 License and Collaboration Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.2) (H)
- 10.19 Supply Agreement, dated as of November 23, 1998, between Targeted Genetics and Medeva Pharmaceuticals, Inc.* (Exhibit 1.3) (H)
- 10.20 Credit Agreement, dated as of November 23, 1998, between Targeted Genetics, Medeva Pharmaceuticals, Inc. and Medeva PLC* (Exhibit 1.5) (H)
- 10.21 Funding Agreement, dated as of July 21, 1999, among Targeted Genetics, Elan International Services, Ltd., and Elan Corporation, plc (Exhibit 1.3) (K)
- 10.22 Subscription, Joint Development and Operating Agreement, dated as of July 21, 1999, among Elan Corporation, plc, Elan International Services, Ltd., Targeted Genetics and Targeted Genetics Newco, Ltd. * (Exhibit 1.4) (K)
- 10.23 Convertible Promissory Note, dated July 21, 1999, issued by Targeted Genetics to Elan International Services, Ltd. (Exhibit 1.5) (K)
- 10.24 License Agreement dated July 21, 1999, between Targeted Genetics Newco, Ltd. and Targeted Genetics * (Exhibit 1.6) (K)
- 10.25 License Agreement, dated July 21, 1999, between Targeted Genetics Newco, Ltd. and Elan Pharmaceutical Technologies, a division of Elan Corporation, plc * (Exhibit 1.7) (K)
- 10.26 Olive Way Building Lease to Olive Way Building, dated as of November 20, 1993, as amended between Targeted Genetics and Ironwood Apartments, Inc. (successor in interest to Metropolitan Federal Savings and Loan Association) (Exhibit 10.29) (L)
- 10.27 Office Lease, dated as of October 7, 1996, between Benaroya Capital Company, (D)

	LLC and Targeted Genetics (Exhibit 10.26)	
10.28	1992 Restated Stock Option Plan (Exhibit 99.1)	(F)
10.29	Stock Option Plan for Nonemployee Directors (Exhibit 10.34)	(E)
10.30	1999 Stock Option Plan (Exhibit 99.1)	(I)
10.31	2000 Genovo Inc. Roll-Over Stock Option Plan (Exhibit 99.1)	(P)
10.32	Canyon Park Building Lease, dated as of June 30, 2000, between Targeted Genetics and CarrAmerica Corporation	(M)
10.33	Agreement and Plan of Merger dated as of August 8, 2000, among Targeted Genetics, Genovo, Inc., TGC Acquisition Corporation and Biogen,* (Exhibit 2.1)	(N)
10.34	Product Development and Marketing Agreement dated as of August 8, 2000, between Targeted Genetics and Biogen, Inc.* (Exhibit 10.1)	(O)
10.35	Funding Agreement dated as of August 8, 2000, between Targeted Genetics and Biogen, Inc. (Exhibit 10.2)	(O)
10.36	Product Development and Marketing Agreement, dated as of November 9, 2000, between Targeted Genetics and Genetics Institute, Inc. **	(Q)
10.37	Supply Agreement, dated as of November 9, 2000, between Targeted Genetics and Genetics Institute, Inc.**	(Q)
21.1	Subsidiaries	
23.1	Consent of Ernst & Young LLP	

*Portions of these exhibits have been omitted based on a grant of confidential treatment from the Securities and Exchange Commission. The omitted portions of these exhibits have been filed separately with the SEC.

**Portions of these exhibits have been omitted based on a request of confidential treatment filed with the SEC. The omitted portions of these exhibits have been filed separately with the SEC.

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

(B) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q for the period ended June 30, 1996, filed on August 12, 1996.

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

(D) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K for the year ended December 31, 1996, filed on March 12, 1997.

(E) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K for the year ended December 31, 1997, filed on March 31, 1998.

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

(G) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K for the year ended December 31, 1998, filed on March 10, 1999.

(H) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K, filed on January 6, 1999.

(I) Incorporated by reference to the designated exhibit included with Targeted Genetics' Registration Statement on Form S-8 (No. 333-78523), filed on May 14, 1999.

(J) Incorporated by reference to the designated exhibit included with Targeted Genetics' Quarterly Report on Form 10-Q for the period ended June 30, 1999, filed on August 5, 1999.

K Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K, filed August 4, 1999.

(L) Incorporated by reference to the designated exhibit included with Targeted Genetics' Annual Report on Form 10-K for the year ended December 31, 1999, filed on March 23, 2000.

(M) Incorporated by reference to Targeted Genetics' Quarterly Report on Form 10-Q for the period ending June 30, 2000, filed on August 11, 2000.

(N) Incorporated by reference to the designated exhibit included with Targeted Genetics' Current Report on Form 8-K, filed on August 23, 2000.

(O) Incorporated by reference to the designated exhibit included with Targeted Genetics Current Report on Form 8-K, filed on September 13, 2000.

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

(Q) Incorporated by reference to the designated exhibit included with Targeted Genetics Current Report on Form 8-K, filed on February 21, 2001.

(b) Reports on Form 8-K

On October 2, 2000 Targeted Genetics filed a current report on Form 8-K reporting our September 19, 2000 acquisition of Genovo, Inc.

On November 9, 2000 Targeted Genetics filed an amended current report on Form 8-K to provide the financial statements of Genovo, Inc. required by Item 7(a) of Form 8-K and the pro forma financial statements required by Item 7(b) of Form 8-K.

SIGNATURES

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

TARGETED GENETICS CORPORATION

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

Date: March 14, 2001

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ H. Stewart Parker</u> H. Stewart Parker	President and Chief Executive Officer (Principal Executive Officer)	<u>March 14, 2001</u>
<u>/s/ David J. Poston</u> David J. Poston	Senior Director, Finance; Assistant Secretary (Interim Principal Financial and Accounting Officer)	<u>March 14, 2001</u>
<u>/s/ Jeremy L. Curnock Cook</u> Jeremy L. Curnock Cook	Chairman of the Board	<u>March 14, 2001</u>
<u>/s/ Jack L. Bowman</u> Jack L. Bowman	Director	<u>March 14, 2001</u>
<u>/s/ Joseph M. Davie, Ph.D., M.D.</u> Joseph M. Davie, Ph.D., M.D.	Director	<u>March 14, 2001</u>
<u>/s/ James D. Grant</u> James D. Grant	Director	<u>March 14, 2001</u>
<u>/s/ Louis P. Lacasse</u> Louis P. Lacasse	Director	<u>March 14, 2001</u>
<u>/s/ Nelson L. Levy, Ph.D., M.D.</u> Nelson L. Levy, Ph.D., M.D.	Director	<u>March 14, 2001</u>
<u>/s/ Mark Richmond, Ph.D.</u> Mark Richmond, Ph.D.	Director	<u>March 14, 2001</u>

EXHIBIT 21.1

Subsidiaries of Targeted Genetics Corporation

The Company has four subsidiaries as of December 31, 1999 as follows:

Name of Subsidiary	Jurisdiction of Organization
CellExSys	Washington
Emerald Gene Systems	Bermuda
Genovo, Inc.	Delaware
TGCF Manufacturing, Inc.	Washington

EXHIBIT 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements (Form S-8 Nos. 33-83064, 333-03889, 333-28151, 333-58907, 333-78523 and 333-48220 and Form S-3 Nos. 333-51625 333-86509, 333-50214 and 333-33192) pertaining to Targeted Genetics Corporation's 1992 Restated Stock Option Plan, Stock Option Plan for Nonemployee Directors, 1999 Stock Option Plan and Genovo Roll-Over Stock Option Plan, of our report dated February 12, 2001, with respect to the financial statements of Targeted Genetics Corporation included in the Annual Report (Form 10-K) for the year ended December 31, 2000.

Ernst & Young LLP

Seattle, Washington
March 13, 2001