
**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, 1999

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 10, 2000: \$487,060,066

Indicate the number of shares outstanding of each of the Registrant's classes of common stock as of March 10, 2000:

| <u>Title of Class</u> | <u>Number of shares</u> |
|-------------------------------|-------------------------|
| Common Stock, \$.01 par value | 36,344,346 |

DOCUMENTS INCORPORATED BY REFERENCE

(1) Portions of the Proxy Statement for the Annual Meeting of Shareholders to be held on May 16, 2000, 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 the treatment of 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 the treatment of cystic fibrosis and cancer. 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 is based on the following five key principles:

Multiple gene delivery systems. 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. Therefore, our strategy has been to develop multiple gene delivery systems. Our systems are based on three different vector technologies: adeno-associated viral (AAV), synthetic and retroviral. We believe these systems will give us the flexibility to develop gene therapies for a broader range of diseases than we could develop using a single gene delivery system.

Emphasis on product development infrastructure. We believe that an abundance of basic research is being conducted in the area of gene therapy, and that those who are capable of translating that research into products will derive significant value. A great deal of discovery research has been focused on gene therapy techniques, but much less effort has been focused on the creation of the product development infrastructure necessary to move concepts through preclinical studies and clinical trials into the commercial realm. Therefore, we have focused the overwhelming 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 product development focus will increase the probability of our reaching the market with products before our competitors.

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. Although most experts believe that gene therapy will be a powerful approach to treating diseases in the future, many believe that this is a long-term proposition. We believe that we have two lead products with significant potential to demonstrate clinical proof of concept in the near term: tgAAV-CF for cystic fibrosis and tgDCC-E1A for cancer. We expect both of

these products to be in Phase II clinical trials in 2000, with the possibility of entering pivotal clinical trials in 2001. We believe that proof of concept in cystic fibrosis and cancer will serve to demonstrate the value not only of our two lead product candidates but of our AAV and synthetic gene delivery technologies as well.

Pipeline development. 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 should, over time, support 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 to our future products under development. We believe that we can derive significant future value by leveraging our infrastructure, knowledge and expertise with additional pipeline products. Currently, we have ongoing preclinical product development activities in the areas of hemophilia, rheumatoid arthritis, cardiovascular disease and HIV vaccines.

Long-term value retention. We believe that our products under development have significant long-term potential. Therefore, it is important to us that we retain a substantial financial interest in the sales of commercial products that result from our work. For products based on our AAV delivery system, we intend to retain, at a minimum, manufacturing rights to all products that 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 | Research | Preclinical | Phase I | Phase II | Phase III |
|----------------------------------|----------|-------------|---------|----------|-----------|
| AAV Vectors: | | | | | |
| Cystic Fibrosis (tgAAV-CF) | XXXXXX | XXXXXX | XXXXXX | | |
| Hemophilia A | XXXXXX | XXXXXX | | | |
| Rheumatoid Arthritis | XXXXXX | XXXXXX | | | |
| Cardiovascular Disease | XXXXXX | XXXXXX | | | |
| HIV Vaccine | XXXXXX | XXXXXX | | | |
| Synthetic Vectors: | | | | | |
| Head and Neck Cancer (tgDCC-E1A) | XXXXXX | XXXXXX | XXXXXX | XXXXXX | |
| Ovarian Cancer (tgDCC-E1A) | XXXXXX | XXXXXX | XXXXXX | | |
| Metastatic Cancer | XXXXXX | XXXXXX | | | |

In addition to our gene therapy technologies, we have patents and expertise in cell therapy that may prove to be extremely valuable. Our expertise enables us to isolate potent disease-specific cytotoxic T lymphocytes (CTLs) from small samples of patient blood and to efficiently multiply them 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.

Clinical Product Development Programs

tgAAV-CF

Cystic fibrosis is the most common single-gene deficiency affecting the Caucasian population, afflicting approximately 24,000 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.

Based on our research and development to date, we believe that tgAAV-CF may be superior to other gene therapy approaches for the treatment of cystic fibrosis, due to the duration of its effect and lack of toxicity. In preclinical studies in rabbits, we were able to detect expression of the CFTR gene in the lung for periods of up to six months with no side effects. These results were supported in similar studies in rhesus monkeys, in which gene transfer occurred in up to 50% of targeted airway cells and gene expression persisted for up to six months. Based on these preclinical data, we began our clinical program in late 1995 to evaluate the safety and feasibility of using tgAAV-CF as a treatment for cystic fibrosis lung disease. tgAAV-CF has been granted orphan drug status by the United States Food and Drug Administration (FDA).

Our first clinical trial, which began in late 1995, was a Phase I open-label, single-dose clinical trial at Johns Hopkins University and the University of Florida. In this trial, we administered tgAAV-CF to eight cohorts of adult cystic fibrosis patients at increasing dosage levels. We administered a liquid form of tgAAV-CF to the right lower lobe of the lung, using a bronchoscope, and to one nostril of each of 18 patients. The results of the trial indicated that the product was safe with no apparent side effects. We recently reopened this trial to treat patients at higher dosages.

Our second clinical trial began in late 1995 at Stanford University. We designed this trial as a Phase I/II trial, in which tgAAV-CF was administered to the maxillary sinuses of cystic fibrosis patients with chronic sinusitis. We completed the Phase I part of this trial, designed as a dose escalation study, in 1996. A total of ten patients were enrolled and 15 sinuses were treated, in five cohorts with increasing doses. The results of the trial indicated that tgAAV-CF was safe and well tolerated with no resulting inflammatory response or other side effects, even after repeated delivery. Administration of tgAAV-CF, furthermore, resulted in consistent gene transfer and persistence of the gene for at least 70 days after treatment. In addition, the dose level was established for the Phase II part of the trial, in which 23 patients received tgAAV-CF in one sinus and a placebo in the other. The Phase II part of the trial was completed in mid-1998. The results of the trial indicated that the drug was safe and well-tolerated in all patients treated, and that markers of inflammation were reduced in the treated sinuses.

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. We are compiling and analyzing data from this study and expect to present the results in the first half of 2000. We plan to begin a Phase II clinical trial, in which patients will receive multiple doses of tgAAV-CF, in mid-2000.

In November 1998, we entered into a license and collaboration agreement related to tgAAV-CF with Medeva Pharmaceuticals, Inc., a subsidiary of Medeva PLC (Medeva). Under this agreement, Medeva received exclusive worldwide marketing rights to tgAAV-CF in exchange for agreeing to provide significant funding to Targeted Genetics. The section below entitled "Research and Development Collaborations" provides a detailed description of this relationship.

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-Chol, 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 cold virus. Dr. Mien Chie Hung and his colleagues at University of Texas M.D. Anderson Cancer Center (M.D. Anderson) 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. Preclinical mouse studies indicate that tgDCC-E1A inhibits expression of the HER-2/*neu* oncogene, inhibits growth and metastasis of cancer cells and increases significantly the long-term survival of the mice. We have worldwide rights, under patents filed by Dr. Hung, to the use of the E1A gene as a tumor inhibitor.

Other research, conducted by Dr. Steven Frisch and his colleagues at the Burnham Institute, has indicated that E1A has other anti-tumor effects unrelated to the inhibition of HER-2/*neu* expression. *In vitro* experiments have shown that E1A, when introduced to a variety of tumor cells, can alter tumor cells so that they appear to revert to normal cells and lose their malignant characteristics. Furthermore, *in vivo* studies in mice involving tumor cells not overexpressing HER-2/*neu* indicated that administration of E1A reduced tumor growth rates. In pre-clinical studies we also found that E1A make tumor cells susceptible to being killed by certain chemotherapeutic agents. We have worldwide rights to patents filed by Dr. Frisch that are complementary to those filed by Dr. Hung.

Our first Phase I clinical trial of tgDCC-E1A began in 1996 at M.D. Anderson, Rush Presbyterian Medical Center in Chicago (Rush) and Virginia Mason Medical Center in Seattle. In this trial, patients with ovarian or breast cancer received weekly doses of tgDCC-E1A for up to six months. We conducted the trial as an interpatient escalating dose study delivering doses of tgDCC-E1A into the peritoneal cavity (intestines) of the ovarian cancer patients and into the pleural cavity (lungs) of the breast cancer patients. We designed this trial to assess safety, levels of gene transfer and expression and tumor response. We treated a total of 18 patients through the trial's completion in early 1998. The results indicated that clinicians can 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.

Our second Phase I clinical trial began in early 1997 at M.D. Anderson, Rush and Wayne State University in Detroit. In this trial, we administered to patients with inoperable primary head or neck tumors or metastatic breast or lung tumors up to ten weekly doses of tgDCC-E1A, injected directly into the tumor. We conducted the trial as an interpatient escalating dose study with four dose levels and treated a total of 18 patients through the trial's completion in early 1998. The objectives of the trial were to assess safety, levels of gene transfer and expression and tumor response. The results indicated that the drug was safe and that the E1A gene was present and active in tumor cells. Additionally, in a majority of the patients, tumor growth was inhibited or treated tumors shrank in size, or both.

Based on the data obtained from the two Phase I clinical trials described above, we began a Phase II clinical trial of tgDCC-E1A for head and neck cancer in October 1998. We completed this trial, which we conducted at five cancer centers, in the fall of 1999, treating a total of 23 patients. We are compiling and analyzing the data from the study and expect to present the results in the first half of 2000.

In late 1999, we began the first in a series of clinical trials testing tgDCC-E1A administered in combination with chemotherapeutic drugs. In this Phase I clinical trial, we will treat ovarian cancer patients with advanced stage disease with a combination of tgDCC-E1A, Taxol and Cisplatin at increasing dosage levels. We anticipate enrolling up to 21 patients in this study, which is ongoing at the University of Arizona and M.D. Anderson. We expect to complete patient enrollment in this clinical trial by the end of 2000. Also in 2000, we plan to begin additional clinical trials of tgDCC-E1A in combination with chemotherapeutic drugs in head and neck cancer and, potentially, other cancers.

Preclinical Product Development Programs

Hemophilia A

Hemophilia A is a hereditary disorder caused by the absence or severe deficiency of Factor VIII, a blood protein essential for proper coagulation. According to the National Hemophilia Foundation, approximately 14,000 people in the United States live with hemophilia A. 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 can result. In addition, both recombinant and naturally-derived Factor VIII protein is expensive, and the naturally-derived protein from human serum may carry blood-borne pathogens, such as HIV, EBV (Epstein Barr Virus) and hepatitis C.

We believe that there is strong rationale for the development of a gene therapy product that could be administered prophylactically to hemophilia A patients in order 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 stop 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 the treatment of hemophilia A. The characteristics of AAV vectors, including the demonstrated safety profile and their ability to persist in cells and express genes for extended periods of time, should provide important advantages compared to competing gene delivery methods. Additionally, AAV vectors have been shown to express genes efficiently in liver cells, the site from which Factor VIII protein is normally produced in the human body. We have invested in significant infrastructure to support the development of tgAAV-CF, which we believe can be efficiently adapted also to the development of 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 its native form, the Factor VIII gene is too large to fit into an AAV vector. Dr. Christopher Walsh of

UNC developed a vector that contains a smaller version of the Factor VIII gene, one that is missing a portion of the gene called the “B-domain.” In the human body, when clotting activity is required, a natural process removes the B-domain to create an active Factor VIII protein. Dr. Walsh’s vector has been shown to produce active Factor VIII protein in a mouse model. Furthermore, in the same model, Dr. Walsh has shown that when the gene is transferred to liver cells, the gene expression persists for at least 12 months and the level of Factor VIII released into the bloodstream reached up to 27 percent of normal levels. Based on these encouraging data, we are collaborating with Dr. Walsh to move his AAV-Factor VIII vector into clinical trials as quickly as possible. We expect to begin a Phase I clinical trial in 2001. We intend to design this clinical trial to establish safety and measure Factor VIII protein levels that result from the administration of various dosage levels of the product.

Metastatic Cancer

Based on our clinical testing of tgDCC-E1A, we believe that we have demonstrated the potential of E1A as a tumor inhibitor. Therefore, we 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 that was developed in collaboration with Dr. Leaf Huang of the University of Pittsburgh. The LPD formulation, which contains lipid, polycation and DNA, results in the formation of small, stable particles encapsulated in a lipid shell. In 1999, we conducted tests of tgLPD-E1A in a mouse model of human breast cancer tumors. In this study, conducted in collaboration with Dr. Mien Chie Hung of M.D. Anderson, 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. 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 preparing to begin a Phase I clinical trial of tgLPD-E1A by 2001.

Rheumatoid Arthritis

Our interest in developing a gene therapy product for the treatment of 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. The TNF receptor (TNFR) gene, which is the basis for Immunex’s Enbrel product for the treatment of rheumatoid arthritis, was included in that license. We believe that the characteristics of AAV vectors make them well suited for delivery of genes to joints. We are in the process of conducting preclinical experiments designed to demonstrate the potential of delivering the TNFR gene to joints using AAV vectors to provide sustained, localized production of the TNFR protein. We envision an AAV-TNFR product as an attractive alternative to systemic TNFR protein therapy in patients susceptible to infection or with disease symptoms limited to one or several joints.

Cardiovascular Disease

We are collaborating with Collateral Therapeutics, Inc. to assess the feasibility of an AAV-based product for the delivery of therapeutic genes to the heart. Collateral has rights to a gene known as AC6, which it believes may be useful in the treatment of congestive heart failure. Collateral is testing AAV vectors in animal models to determine the feasibility of delivering AC6 with an AAV vector. If these preclinical tests are successful, we may collaborate with Collateral to develop an AAV-AC6 gene therapy product.

Acquired Immune Deficiency Syndrome (AIDS)

We are collaborating with the International AIDS Vaccine Initiative and Children's Hospital in Columbus, Ohio to develop a vaccine to prevent AIDS. The vaccine will utilize our AAV vectors to deliver HIV genes with the goal of eliciting a protective immune response against the virus. The collaboration will extend for a period of up to three years, beginning in March 2000, and will include development, preclinical and Phase I clinical studies. We have the right to commercialize in industrialized countries any vaccine product that may result from this development collaboration. We also have the option to manufacture the vaccine for non-industrialized nations.

Core Technologies

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 the three different vector technologies on which our systems are based, AAV, synthetic and retroviral, 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.

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 absence of, specific genes causes certain diseases, 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, whereby 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 then 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 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;
- complexing 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. Together with our scientific collaborators, we have developed significant expertise in the design and use of AAV vectors in gene therapy. We believe that AAV vectors are particularly well suited for the treatment of a number of diseases because:

- AAV has never been associated with causing any 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 of 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 in cells of the cardiovascular system, joints 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.

Synthetic Vectors. We have exclusive rights to a significant body of synthetic gene delivery technology based on cationic lipids. These synthetic vectors 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 and they can be used *in vivo* as well as *ex vivo*. We believe that synthetic vectors have several characteristics that make them particularly well suited for the treatment of 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 with Dr. Leaf Huang of the University of Pittsburgh to develop a series of synthetic delivery systems based on his discoveries. Dr. Huang's original DC-Chol system is used in our potential tgDCC-E1A cancer product. We have an exclusive license to an issued U.S. patent on DC-Chol for the treatment of cancer and certain other diseases. Also, we have obtained from the University of Pittsburgh broad licenses to a series of Dr. Huang's more recent discoveries in this area. In one of these discoveries, which we call LPD, DNA

is condensed and 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 a joint venture with Elan, Emerald Gene Systems, Ltd., to focus on combining our AAV and synthetic gene delivery technologies with Elan's drug delivery technologies. Elan's contributed technologies include targeting ligands, permeation enhancers 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.

Retroviral Vectors. We believe that retroviral vectors may be well suited for *ex vivo* genetic modification of rapidly dividing cells, such as T cells and stem cells. We have a strong position in retroviral gene delivery technology through our relationship with Dr. A. Dusty Miller, a leader in the development of packaging cell lines for retroviral vectors. One of Dr. Miller's inventions in this area is an improved retroviral vector packaging cell line called PG13, which we have licensed exclusively from the Fred Hutchinson Cancer Research Center. Our research has shown that vectors produced in this cell line have improved efficiency for *ex vivo* transfer of genes to human T cells and stem cells.

Cell Therapy

Overview. The immune system is the body's major defense mechanism against disease. It functions through a complex interplay of components that allow the body to detect foreign agents and defend against infections and diseases. The immune system recognizes parts of proteins called antigens that are present on the surface of diseased cells but are not present on normal cells. The immune response to an antigen involves the integrated action of various classes of white blood cells, including lymphocytes. There are two major classes of lymphocytes, B cells and T cells.

T cells direct cell-mediated immunity by recognizing antigens on diseased cells. The two main classes of T cells are CD4 cells and CD8 cells. In general, CD8 cells are CTLs that recognize, contact and kill the diseased cells. CD4 cells are primarily helper cells that coordinate the function of other immune cells, including CTLs, by secreting growth factors known as cytokines. CTLs are disease-specific: they individually recognize and bind only to a single, specific antigen. Only in the presence of CD4 helper cells, furthermore, do these specific CTLs proliferate to produce the large population of antigen-specific CTLs required to elicit an effective immune response.

In some diseases, the immune system fails to mount or maintain an effective immune response. For infectious diseases and cancer, it is believed that this failure may be associated with an inadequate CTL response. For example, HIV infects and kills CD4 cells, which leads to subsequent loss of CTL function and therefore to destruction of the immune system by the virus.

Targeted CTLs. We have developed a highly targeted form of cell therapy, with which we intend to produce a disease-specific immune response through the infusion of large numbers of antigen-specific CTLs. In our Targeted CTL program, antigen-specific CTLs are isolated from a small sample of the patient's blood, multiplied to large numbers *ex vivo* and then reinfused into the patient. In essence, these Targeted CTLs are intended to amplify the natural disease-fighting function of the immune system relating to specific infected or cancerous cells.

We believe that our Targeted CTL program represents an improvement over other approaches to immunotherapy because:

- it is based on highly potent, cloned, antigen-specific CTLs;
- virtually all of the reinfused CTLs target the specific diseased cells; and
- side effects may be reduced due to the uniformity and consistency of the reinfused cells.

Our focus on Targeted CTLs originated from research conducted by Drs. Philip Greenberg and Stanley Riddell, collaborators at the Fred Hutchinson Cancer Research Center. These researchers conducted a Phase I clinical trial to evaluate the use of cytomegalovirus (CMV) -specific CTLs to provide an immune response against CMV in bone marrow transplant patients. This trial represented the first use of cloned, antigen-specific CTLs. None of the 14 patients receiving the CTLs developed CMV viremia or disease. Dr. Riddell is now conducting a Phase II clinical trial to follow up on the promising results observed in Phase I. Other work by Drs. Greenberg and Riddell has shown, moreover, that Targeted CTLs may be useful in treating HIV infection.

In 1998, we completed a preclinical study in which we administered Targeted CTLs to chimpanzees chronically infected with hepatitis B virus (HBV). The objective of the study was to establish safety of the therapy and, potentially, obtain proof of concept that HBV-specific Targeted CTLs could be promising as a treatment for humans infected with HBV. The preliminary results of the study, which we presented in August 1998, indicated that the therapy was safe and that there were trends toward efficacy, evidenced by a temporary drop in viral burden, increased levels of liver enzymes and improvement in liver condition. This study has given us additional reason to believe that Targeted CTLs have potential to treat viral diseases.

Rapid Expansion Method. The Targeted CTL program is made possible by our proprietary Rapid Expansion Method, or REM, which we use to rapidly grow CTLs for infusion into the patient. We believe that REM represents a significant improvement over other methods of growing T cell clones. Using REM, CTL clones can be multiplied over a thousand-fold in less than two weeks. We can grow billions of CTLs from individual cloned cells over several weeks, while preserving the cells' disease-fighting capabilities. We have seen consistent results from REM both with CD8 and CD4 T cells. Furthermore, we have shown that REM is effective for growing Targeted CTLs for a number of viral diseases and cancers, such as HIV, CMV, HBV, malignant melanoma and prostate tumor peptides. We have filed patent applications relating to the original REM process and to subsequent process improvements on a worldwide basis. Since 1998 we have received one U.S. patent in this area.

Research and Development Collaborations

Celltech Group plc/Medeva PLC

In November 1998, we entered into agreements with Medeva Pharmaceuticals, Inc. (Medeva), a subsidiary of Medeva PLC to develop and commercialize tgAAV-CF, our potential gene therapy product 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 development and clinical support, Medeva agreed to pay the costs of Phase II and subsequent clinical trials of the product. While we may manage Phase II clinical trials in the United States, Medeva was assigned the responsibility for conducting all other trials and securing worldwide registration of tgAAV-CF. Under the terms of the tgAAV-CF agreements, we granted Medeva an exclusive worldwide license

to sell tgAAV-CF, but we 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 certain conditions, up to an additional \$10 million toward building a GMP manufacturing facility for higher-volume production of tgAAV-CF.

In January 2000, Medeva merged with Celltech/Chiroscience to become part of the Celltech Group plc. Celltech has assumed Medeva's rights and responsibilities under our agreements.

Assuming successful commercialization of the 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 Medeva/Celltech tgAAV-CF agreements. Under a long term supply agreement we would also receive proceeds from sales of tgAAV-CF, assuming successful commercialization, based upon a pricing formula intended to provide us with a significant percentage of Celltech's net revenue from product sales. The research and development funding agreement is effective through October 1, 2001, with options 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. and Elan Corporation, plc

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. The joint venture is based in Bermuda and is owned 80.1% by Targeted Genetics and 19.9% by Elan. 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. Emerald's research and development program will be Elan's exclusive effort in the field of gene delivery and our exclusive effort in the combination of our technologies with drug delivery technologies. Generally, Emerald's research and development will be conducted under contract by Elan and Targeted Genetics and Emerald will reimburse each company for the costs of the research and development plus a profit percentage. Elan and Targeted Genetics will fund the expenses of Emerald in proportion to their ownership interests.

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

- a \$5 million purchase of our common stock at the signing of the agreements; 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;

Elan has also agreed to provide additional funding as follows:

- an additional \$5 million purchase of our common stock one year from the date of our agreements;
- a \$12 million line of credit under a convertible note to fund our ongoing investment in Emerald.

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

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.

We believe that the issued patent broadly covers a manufacturing method that is key to making AAV-based products in a commercially viable, cost-effective manner. 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 to market price at the time of the transaction. Alkermes will also receive milestone payments and royalties on products manufactured using the licensed patents

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, which were converted into 1,920,000 shares of common stock at the time of our initial public offering, Immunex granted us a worldwide, exclusive field-of-use license for certain 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, to these improvements. Immunex currently owns approximately 7% 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 the development of 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 107 patent applications relating to our product and technology development programs with the United States Patent and Trademark Office (USPTO), as well as foreign counterparts of some of these applications in Europe, Japan and certain other countries. Of these patent applications, 29 patents have been issued or allowed by the USPTO.

In addition to the intellectual property that we own or have exclusively licensed, we have licensed several issued and pending patents on a nonexclusive basis. Among these are the two key patents that relate to the use of AAV vectors for gene therapy 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, we do not know whether any patent applications will result in the issuance of patents or, if any patents are issued, whether the patents will be subjected to further proceedings limiting their scope, whether they will provide significant proprietary protection or whether they will 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 or any licensor were the first creator of

inventions covered by pending patent applications or that we or the licensor were 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 relating to the nonexclusively licensed CFTR gene delivered in our tgAAV-CF product candidate. As a nonexclusive licensee of the CFTR gene, we do not expect to directly participate in the CFTR gene interference proceeding. If the eventual outcome of the CFTR interference proceeding is unfavorable to our licensor, we may have to obtain a license from the prevailing party in order to proceed with development of tgAAV-CF. Costs associated with obtaining a license may be substantial and could include ongoing royalties in excess of those we currently pay under our existing CFTR gene license. Any license required in this circumstance may not be available to us on acceptable terms, if at all. Although we do not foresee material expenditures related to interference proceedings, these proceedings could result in substantial financial costs to us, even if the eventual outcome were favorable to us. Our patents, if issued, may not be held valid or enforceable by a court and a competitor's technology or product may not be found to infringe these patents. Litigation, which could result in substantial cost to us, may be necessary to enforce our patents or to determine the scope and validity of other parties' proprietary rights. If the outcome of litigation were adverse, our business could be adversely affected. We are unable to predict how courts will resolve any future issues relating to the validity and scope of our patents, should they be challenged.

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 might be able to obtain 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. 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 any potential liability for damages, we could be required to obtain a license to continue to manufacture or market the affected product or use the affected process. Costs associated with any required license could be substantial and could include ongoing royalties. Any license required under any infringed patent may not be available to us on acceptable terms, if at all.

In addition to patent protection, we rely upon trade secret protection for our confidential and proprietary information. Other parties may independently develop substantially equivalent proprietary information and techniques or gain access to our trade secrets or disclose our technology. 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, the agreements also provide that all inventions resulting from work performed by them while employed by Targeted Genetics 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 information.

Competition

We are aware of a number of companies and institutions that are developing or considering the development of potential gene therapy and cell therapy treatments. These include other gene therapy 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 that are based on established technologies. 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, in obtaining FDA and other regulatory approvals, and in manufacturing, marketing and distributing products. We also compete with others to acquire products or technology from research institutions or universities. 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. 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 develop new technologies and products that are available for sale before our potential products or that may be more effective than our potential products. In addition, 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. and foreign governmental agencies before commercialization in the applicable countries. Human therapeutic products are subject to rigorous preclinical and clinical testing and other premarket approval procedures administered by the FDA and similar authorities in foreign countries. 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 regulators. In some cases, state requirements may also apply.

Gene therapy and cell therapy are relatively new technologies and have not been extensively tested in humans. The regulatory requirements governing gene and cell therapy products and related clinical procedures are uncertain and are subject to change. Obtaining approval from the FDA and other regulatory authorities for a new therapeutic product is likely to take several years, if approval is ever obtained, and could involve substantial expenditures. Moreover, ongoing compliance with applicable requirements may also require the expenditure of substantial resources. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or prevent the marketing of our products.

The activities required before a new therapeutic agent may be marketed in the United States begin with preclinical testing. Preclinical tests include laboratory evaluation and may require animal studies to assess the product's potential safety and effectiveness. Animal safety studies must be conducted in accordance with the FDA's Good Laboratory Practice regulations. The results of these studies must be submitted to the FDA as part of an Investigational New Drug application, which must be reviewed and cleared by the FDA before proposed clinical testing can begin. Clinical trials must be conducted in accordance with the FDA's Good Clinical Practices regulations under protocols that detail the objectives of the trial, the parameters to be used to monitor safety and the efficacy criteria to be evaluated. Each protocol must be submitted to the FDA as part of the application. The FDA's review or approval of a study protocol does not necessarily mean that a trial successfully demonstrating safety or efficacy will result. Further, each clinical trial must be approved by and conducted under the auspices of an independent institutional review board at the institution at which the trial will be conducted. This board will consider, among other things, ethical factors, the safety of human subjects and the possible

liability of the institution. This review board is also responsible for continuing oversight of the approved protocols in active trials. A review board may require changes in a protocol, and the review board may not permit any given trial to be initiated or completed.

Clinical trials are typically conducted in three sequential phases, although the phases may overlap. In Phase I, gene therapy clinical trials generally involve a small number of patients, who may or may not be afflicted with a specific disease, to determine the preliminary safety profile. In Phase II, clinical trials are conducted with larger groups of patients afflicted with a specific 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 others for market approval. The FDA receives reports on the progress of each phase of clinical testing, and it may require the modification, suspension or termination of clinical trials if patient risk is too high. Because gene therapy products are a new category of therapeutics, we cannot be certain of the length of the clinical trial period or the number of patients the FDA will require to be enrolled in a particular clinical trial in order to establish to its satisfaction the safety and effectiveness of the products.

After completion of clinical trials of a product candidate, we are required to obtain FDA approval to market the product in the U.S. The FDA's legal authority is defined in the Federal Food, Drug and Cosmetics Act. Our products are regulated by the Center for Biologics Evaluation and Research. While we expect this regulatory structure to continue, we also expect the FDA's regulatory approach to evolve as it increases its scientific knowledge and experience in gene therapy. Current FDA regulations relating to biologic therapeutics require us to submit a Biologics License Application to the FDA before the FDA will permit commercial marketing. This application includes product development activities, results of preclinical studies and clinical trials, and detailed manufacturing information. Unless the FDA gives expedited review status, this stage of the review process takes at least one year. The FDA may refuse to accept a Biologics License Application if it fails to meet predetermined requirements.

The FDA is an agency focused on public health, reviewing all products for safety and efficacy. Both standards must be met before the FDA grants product approval. Should the FDA have concerns with respect to product safety and efficacy, it may delay product review or request additional data. The FDA may ultimately decide that our license application 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.

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.

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 on a continuing basis in production, record keeping and quality control. Our manufacturing facilities are subject to periodic inspections by the FDA to ensure compliance. Failure to pass these inspections could subject us to possible FDA action, such as the suspension of manufacturing, seizure of product, withdrawal of approval or other regulatory sanctions. The FDA could also require us to recall a product.

In addition to regulations enforced by the FDA, 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. Our research and development activities involve the controlled use of hazardous materials, chemicals, biological materials and radioactive compounds. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by state and federal laws and regulations, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, we could be held liable for any resulting damages, and any resulting liability could exceed our financial resources.

Human Resources

At December 31, 1999, we had 92 full-time-equivalent employees, 72 of which are directly involved in research and development. Of these employees, 16 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.

Executive Officers

The following table lists the executive officers of Targeted Genetics who will serve in the capacities noted until their successors are duly appointed and qualified.

| <u>Name</u> | <u>Age</u> | <u>Position</u> |
|-------------------------|------------|---|
| H. Stewart Parker | 44 | President, Chief Executive Officer and Director |
| Barrie J. Carter, Ph.D. | 55 | Executive Vice President and Director of Research and Development |
| James A. Johnson | 43 | Senior Vice President, Finance and Administration, Chief Financial Officer, Treasurer and Secretary |

H. STEWART PARKER managed the formation of Targeted Genetics as a wholly owned subsidiary of Immunex and has served as president, chief executive officer and director since our inception in 1989. She served in various capacities at Immunex from August 1981 through December 1991, most recently as vice president, corporate development. From 1991 to January 1993, Ms. Parker also served as president and a director of Receptech Corporation, a company formed by Immunex in 1989 to accelerate the development of soluble cytokine receptor products. Ms. Parker is a member of the executive committee and the board of directors of BIO, the primary trade organization for the biotechnology industry. She received her B.A. and M.B.A. from the University of Washington.

BARRIE J. CARTER has served as executive vice president and director of research and development since August 1992. For the previous 22 years he was employed by the National Institutes of Health (NIH) in Bethesda, Maryland, and from 1982 to 1992 was chief of the laboratory of molecular and cellular biology at the National Institute for Diabetes and Digestive and Kidney Diseases. Dr. Carter received his B.Sc. (Honors) from the University of Otago, Dunedin, New Zealand and his Ph.D. in the Biochemistry Department of the University of Otago Medical School. Before joining the NIH, he spent a period of postdoctoral training at the Imperial Cancer Research Fund Laboratories in London, England. His long-term research interests are in the molecular biology of viruses, development of AAV vectors and gene therapy. Dr. Carter serves on the editorial boards of *Human Gene Therapy*, as a section editor of *Current Opinion in Molecular Therapeutics* and as an associate editor of

Virology. Since 1995, he has been an affiliate professor of medicine at the University of Washington Medical School.

JAMES A. JOHNSON serves as senior vice president, finance and administration, chief financial officer, treasurer and secretary. He joined Targeted Genetics in March 1994 as vice president, finance, chief financial officer, treasurer and secretary and was promoted to his current position in January 1999. He was employed by Immunex from January 1988 to February 1994, initially as director of finance, and then as vice president, finance beginning February 1990. While at Immunex, Mr. Johnson served as treasurer of Targeted Genetics from our inception in 1989. From November 1989 to January 1993, he also served as treasurer and assistant secretary of Receptech. He received his B.A. from the University of Washington.

ITEM 2. PROPERTIES

We currently occupy approximately 41,000 square feet of laboratory and office space in two adjoining buildings in Seattle, Washington. The lease on our primary facility, for approximately 36,000 square feet, extends to April 1, 2004 and has two five-year extension options. The average annual rent payment for our main facility is approximately \$550,000 during the current five-year lease term. The lease on our adjoining office space, for approximately 5,000 square feet, expires on March 31, 2004 and has two additional five-year extension options. The average annual rent payment for our adjoining office space is approximately \$95,000 during the current term of the lease. In order to continue to grow our AAV vector manufacturing capability, we expect that we will need to expand our manufacturing operations to a separate facility. In 1999, we began the process of identifying alternatives for this expansion. Otherwise, we believe that our current facilities, together with approximately 2,000 square feet of expansion space remaining in our primary facility and additional expansion space available in the adjoining office complex, will be adequate to meet our projected needs for the next several years. Within that time frame, however, we could be required to locate alternative facilities, depending on the extent of our company's growth and development.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any 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 the year ended December 31, 1999.

PART II

ITEM 5. MARKET PRICE OF THE REGISTRANT'S COMMON STOCK AND RELATED SHAREHOLDER MATTERS

Our common stock trades on The Nasdaq National Market under the symbol TGEN. At March 1, 2000, we had approximately 200 shareholders of record and approximately 15,300 total 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 Medeva 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 |
|-------------|-------------|------------|
| 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 |
| 1998 | | |
| 4th Quarter | \$ 2.31 | \$ 1.31 |
| 3rd Quarter | 1.75 | 0.88 |
| 2nd Quarter | 4.25 | 1.31 |
| 1st Quarter | 3.13 | 0.97 |

On June 6, 1999, we issued 500,000 unregistered shares of common stock to Alkermes, Inc. at an aggregate offering price of \$812,500, along with warrants to purchase an additional 2,000,000 shares of common stock. The warrants are divided into two tranches: a warrant to purchase 1,000,000 shares of common stock at a price of \$2.50 expiring June 9, 2007 and a warrant to purchase 1,000,000 shares of common stock at a price of \$4.16 expiring June 9, 2009. On July 22, 1999, we issued 2,148,899 unregistered shares of common stock to Elan at an aggregate offering price of \$5 million. On August 9, 1999 we issued 677,392 unregistered shares of common stock to Medeva at an aggregate offering price of \$1.5 million. Each of these transactions did not involve a public offering and therefore was exempt from registration under Section 4(2) of the Securities Act of 1933.

ITEM 6. SELECTED FINANCIAL DATA

| | Year Ended December 31, | | | | |
|---|--------------------------------|---------------|--------------|---------------|---------------|
| | 1999 (1) | 1998 | 1997 | 1996 | 1995 |
| Results of Operations | | | | | |
| Revenue | \$ 6,847,993 | \$ 7,510,252 | \$ 1,327,585 | \$ 1,330,458 | \$ 174,625 |
| Expenses | 21,084,502 | 16,372,987 | 15,828,094 | 27,894,811 | 10,462,429 |
| Loss from operations | (14,236,509) | (8,862,735) | (14,500,509) | (26,564,353) | (10,287,804) |
| Net loss applicable to common stock | (27,030,648) | (8,687,049)d | (14,187,774) | (26,038,042) | (9,922,284) |
| Basic and diluted net loss per share from operations | (0.84) | (0.33) | (0.70) | (1.59) | (0.94) |
| Shares used in computing basic and diluted net loss per share | 32,173,756 | 26,637,823 | 20,196,325 | 16,407,928 | 10,532,950 |
| Financial Condition | | | | | |
| Cash, cash equivalents and securities available for sale | \$ 7,153,269 | \$ 11,956,796 | \$ 5,037,821 | \$ 19,051,070 | \$ 14,442,562 |
| Total assets | 13,692,478 | 16,204,083 | 9,767,084 | 25,139,052 | 19,960,460 |
| Long-term obligations, including current portion | 3,267,071 | 2,072,044 | 2,547,324 | 3,378,420 | 3,286,508 |
| Shareholders' equity | 6,965,514 | 11,981,759 | 5,591,587 | 19,507,788 | 15,772,836 |

(1) Expenses increased in 1999 due to the Alkermes license fee write off described in further detail in Item 7 of “Management’s Discussion and Analysis” in the subsection entitled “Operating Expenses”. Net loss increased in 1999 due to our 80.1% share of Emerald’s losses, as described in Item 7 in the subsection entitled “Other Income and Expense,” and due to the Alkermes license fee write off.

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

Overview

We were incorporated in March 1989 as a wholly owned subsidiary of Immunex Corporation and began operations as an independent company in 1992. Our goal, both then and now, is to research and develop gene and cell therapy products to treat acquired and inherited diseases. We now have two lead products in clinical trials, tgAAV-CF for treating cystic fibrosis and tgDCC-E1A for treating cancer, and several additional product candidates in preclinical development. Since our founding, we have focused our efforts on technology and product development, which we have funded primarily through the sale of equity securities. In addition, we have endeavored to enter into product collaborations with other companies as a means to obtain outside funding for our programs and to broaden the application of our technology platform. We have completed three collaborations to date that provide ongoing funding of our research and development programs:

- a tgAAV-CF product development collaboration established, with Medeva PLC in November 1998;
- a gene delivery technology development joint venture with Elan Corporation plc, Emerald Gene Systems, Ltd. (Emerald), in July 1999; and
- an AAV-based AIDS vaccine development program with the International Aids Vaccine Initiative (IAVI), established in February 2000.

Although our technology appears promising, we do not know whether any commercially viable products will result from our research and development efforts. We do not anticipate that we will have any commercial product revenues for at least the next several years. Through December 31, 1999 our accumulated losses total approximately \$103.5 million. 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 collaborations, complete collaborations, enter into licensing agreements and recognize varying amounts of revenue from our research and development activity. We had revenue of \$6.8 million for the year ended December 31, 1999. Of this amount, \$6.4 million was generated from our tgAAV-CF collaboration agreements with Medeva. We earned the remainder from a collaborative agreement with our affiliate, Emerald Gene Systems, for research and development services in the fourth quarter of the year. Although our 1998 revenue of \$7.5 million was greater than our 1999 revenue, we believe that this does not reflect a meaningful trend because revenue for 1998 included \$6.0 million in fees earned up-front when we established the Medeva collaboration. Revenue for 1998 also included approximately \$1.2 million earned from Medeva for product development efforts in the fourth quarter of the year.

We had revenue of \$1.3 million for the year ended December 31, 1997. This amount included a \$1.0 million product milestone payment related to our tgDCC-E1A cancer product, which we received under a European development collaboration that has since been terminated. Other revenue in 1997 consisted of grant funding earned from research grants awarded by the National Institutes of Health.

We expect our collaborative agreement revenue to increase in 2000. We expect to realize significant revenue from our Medeva tgAAV-CF collaboration, including research and development funding, revenue from the supply of tgAAV-CF product for clinical trials and, potentially, payments upon the achievement of important product development milestones. We also expect to receive increased research and development funding from Emerald. In addition, our IAVI collaboration should provide a new source of research and development funding.

Operating Expenses

Research and Development

Research and development expenses increased to \$14.3 million for 1999 from \$13.3 million for 1998. The increase for 1999 compared to 1998 reflects increased expenses related to the tgAAV-CF collaboration and, to a lesser extent, costs incurred to support the Emerald joint venture. These increases were partially offset by decreases in tgDCC-E1A development expenses. In 1998, we had higher expenses related to the development of manufacturing methods for tgDCC-E1A and paid a \$1.0 million milestone payment in common stock at the start of Phase II clinical trials. Additionally, 1998 results included severance expenses we incurred when we downsized our operations early that year.

Research and development expenses for 1998 remained approximately the same as research and development expenses for 1997. The tgDCC-E1A manufacturing and milestone expenses and severance expenses we incurred in 1998 generally offset higher personnel and patent costs in 1997. We expect research and development expenses to increase for year 2000 due to increases in staffing in the second half of 1999 and early 2000 to support the Medeva and Emerald projects and projected increases in external expenses necessary to support tgDCC-E1A product development in 2000.

Technology License Fee

We incurred a noncash expense of \$3.2 million in 1999 to acquire a technology license from Alkermes, Inc. We acquired this license by issuing to Alkermes 500,000 shares of our common stock and warrants to purchase up to 2,000,000 additional shares. We received from Alkermes an exclusive sub-license to a patent related to the manufacture of AAV vectors, which we use in our tgAAV-CF cystic fibrosis program, among others. 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. We expensed the entire value assigned to the license. While the technology we acquired under the exclusive license has promise, we expensed the value of the securities 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 1998 or 1997.

General and Administrative

General and administrative expenses increased to \$3.6 million for 1999 from \$3.0 million for 1998. This increase was primarily attributable to increases in personnel costs, increased business development activity and investor communications costs related to the formation of the Emerald joint venture. General and administrative expenses increased to \$3.0 million 1998 from \$2.8 million for 1997. The increase was attributable to legal fees incurred related to the Medeva transaction and increased investor and public relations costs. These increases were partially offset by decreases in operating expenses achieved through our February 1998 reduction in staff.

Other Income and Expense

Equity in Loss of Joint Venture

We recognized a \$12.6 million loss in 1999 for our 80.1% equity share in the loss of the Emerald joint venture. Emerald's losses for the year ended December 31, 1999 included a \$15.0 million noncash charge for an exclusive license to Elan's drug delivery technology and \$742,000 in losses attributable to Emerald's research and development activities, which began in the fourth quarter of the year. We expect to record additional equity in losses of Emerald in 2000 and for the foreseeable future.

Investment Income

Income from marketable securities decreased to \$426,000 for 1999, from \$440,000 for 1998 and \$651,000 for 1997. The decreases in 1999 and 1998 resulted from lower average balances of cash available for investment.

Interest Expense

Interest expense has decreased over the last three years to \$235,000 for 1999 from \$265,000 for 1998 and \$338,000 for 1997, because of declining principal balances on our capital leases and installment loans. This expense related to obligations under capital leases and installment loans we use to finance purchases of laboratory and computer equipment, furniture and leasehold improvements. We do not expect decreases in interest expense to continue, since we plan to continue to finance our asset purchases under leases or loans. We borrowed \$1.0 million under a loan agreement with Medeva in late 1999, and we may elect to borrow additional amounts from Medeva or Elan in the future under existing loan commitments.

Year 2000 Issue

As of December 31, 1999 we completed our Year 2000 readiness evaluation and compliance efforts. Since December 31, 1999 we have not encountered any Year 2000 compliance problems. Nonetheless, some problems related to Year 2000 risks may not appear until several months after January 1, 2000. Year 2000 issues could include problems with third-party products or services that we use or with which our information systems exchange data. Any problems that are not identified and corrected successfully and completely could adversely affect our business. We expect that the cost to fix any Year 2000 problems that may be identified, however, will involve internal labor-hours and will not be material. The costs of our Year 2000 readiness efforts to date are less than \$100,000.

Impact of New Accounting Pronouncements

In June 1998, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities*. This new statement, 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. Statement No. 133 requires companies to recognize all derivatives as either assets or liabilities on the balance sheet and measure those instruments at fair value. Gains or losses resulting from changes in the values of those derivatives would be accounted for depending on the use of the derivative and whether it qualifies for hedge accounting under the standard. The impact of Statement No. 133 on Targeted Genetics' financial position and results of operations is not expected to be material.

In December 1999, the Securities Exchange Commission issued Staff Accounting Bulletin 101 “*Revenue Recognition in Financial Statements*” which provides the SEC’s views on applying generally accepted accounting principles to revenue recognition issues. The Company is currently evaluating its revenue recognition policies and has not yet determined the financial statement impact of this bulletin.

Liquidity and Capital Resources

Since our inception, we have financed our capital requirements through the issuance of equity securities, revenue from collaborations and grants and proceeds from leases and loans. As of December 31, 1999, we had cash, cash equivalents and securities available for sale totaling \$7.2 million, compared to \$12.0 million as of December 31, 1998. The decrease is attributable to our use of cash to fund our operating losses and capital expenditures. Capital expenditures of \$1.9 million for 1999 reflected construction of equipment for a 100-liter scale AAV vector manufacturing facility within our corporate headquarters. Our cash outflows were partially offset by cash inflows when we:

- issued 2,148,899 shares of our common stock to Elan in connection with the Emerald joint venture, providing total proceeds of \$5.0 million;
- issued 677,392 shares of our common stock to Medeva in connection with our tgAAV-CF collaboration, providing total proceeds of \$1.5 million; and
- received loan proceeds of \$1.0 million from Medeva in October 1999, 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.

Although we expect our expenses to continue to increase in 2000, we expect revenue from Medeva, Emerald and IAVI to increase as well, substantially offsetting expense increases. We also have contractual commitments for the following cash resources:

- a \$5.0 million equity investment by Elan,
- funds available under a \$12.0 million convertible loan from Elan; and
- an additional \$1.0 million of proceeds under our loan agreement with Medeva.

In March 2000, we entered into a definitive agreement to sell 2,164,286 shares of newly issued common in a private placement. This transaction added approximately \$28 million to our cash position.

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 not be successful in establishing any additional collaborative relationships or in maintaining our existing ones. 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, financial condition or operating results 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 we cannot expect internally generated cash flow to 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:

- technology partnerships;
- technology sales;
- technology licenses;
- issuing debt; or
- equity arrangements.

If we cannot obtain additional financing when needed or on acceptable terms, we will be unable to fund continuing operations. In addition, if we raise additional funds by issuing equity securities, our shareholders will likely experience significant dilution of their ownership interest.

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, 1999, we have incurred losses totaling \$103.5 million. We expect to continue to incur substantial additional losses in the future, due primarily to the following factors:

- all of our products are in a testing phase and have not received regulatory approval; and
- we will likely 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 clinical trials are unsuccessful or we do not receive regulatory approval for our products, which are in the early stage of product development, we may be unable to generate sufficient revenues to maintain our business.

We do not yet have products in the commercial markets. All of our potential products, including tgAAV-CF, our cystic fibrosis product candidate, and tgDCC-E1A, our cancer product candidate, 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. Our clinical trials may not demonstrate the safety and efficacy of our potential products, and we may encounter unacceptable side effects or other problems in the clinical trials. Should this occur, we may have to delay or discontinue development of the potential product that causes the problem. After a successful clinical trial, we cannot market products in the United States until we receive regulatory approval. If we are unable to gain regulatory approval of our products after successful clinical trials and then commercialize and sell those products, we may be unable to introduce and sell a quantity of products sufficient to maintain our business or secure additional financing to fund our operations.

Delays or unexpected costs in obtaining approval of our products or complying with governmental regulatory requirements could decrease our ability to generate revenue and make funding our operations more difficult.

The regulatory process in the gene and cell therapy industry is costly, time consuming and subject to unpredictable delays. Accordingly, we cannot predict with any certainty 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 revenue and make it more difficult to obtain additional financing necessary to fund our operations. In addition, all manufacturing operations are subject on an ongoing basis to the current Good Manufacturing Practices requirement of the Food and Drug Administration. While we currently anticipate that we will be able to manufacture product that meets this requirement, we may be unable to attain or maintain compliance with current or future Good Manufacturing Practices requirements. If we discover previously unknown problems after we receive regulatory approval of a potential product or fail to comply with applicable regulatory 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 decrease our ability to generate revenue.

Failure to recruit patients could delay or prevent clinical trials of our potential products, which could cause a delay or inability to introduce products to market and a resulting decrease in our ability to generate revenue.

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 usefulness of our technology or termination of the clinical trials altogether. If we are unable to timely introduce potential products to market after successful clinical trials, our ability to generate revenue may decrease and we may be unable to secure additional financing.

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 have licenses to patents on a number of genes, processes, practices and techniques critical to our present and potential products. If we fail to obtain and maintain patent protection for our technology, our competitors may market competing products that threaten our market position. The failure of our licensors to obtain and maintain patent protection for technology they license to us could similarly harm our business. 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. Even if we secure a patent, the patent may not afford adequate protection against our competitors.

We also rely on unpatented proprietary technology. Because this technology does not benefit from the protection of patents, we may be unable to meaningfully protect this proprietary technology from unauthorized use or misappropriation by a third party.

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

As the biotechnology industry expands, the risk increases that other companies may claim that our processes and potential products infringe on their patents. Defending these claims 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 or obtain a license in order to continue

manufacturing or marketing the affected product or using the affected process. We may be unable to obtain a license on acceptable terms.

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. While we do not expect to directly participate in the CFTR gene interference proceedings, we have an interest in the outcome. If the eventual outcome does not favor our licensor, we would have to secure a license to the CFTR gene from the prevailing party to continue with development of tgAAV-CF. The costs of licensing the CFTR gene could be substantial and could include royalties greater than those we currently pay. If we cannot secure this license on acceptable terms and on a timely basis, 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.

If we or our business partners are unable to successfully market and distribute our products, our business will fail.

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. Furthermore, our present or future collaborators may pursue the development or marketing of competing products. 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 fail.

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

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

- Research and development;
- Clinical trials;
- Obtaining FDA and other regulatory approvals;
- Manufacturing; and
- Marketing and distribution.

Consequently, our competitors may be able to commercialize 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 the failure of our products to achieve market acceptance.

In addition, gene and cell therapy are new and rapidly evolving fields and are expected to continue to undergo significant and rapid technological change. Rapid technological development by our competitors 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 and scientific collaborators, we will be unable to successfully and timely develop our potential products and may be unable to generate sufficient revenue to maintain our business.

Our future success depends in part on our ability to attract and retain key employees. We have programs in place to retain personnel, including programs to create a positive work environment and competitive compensation packages. Because competition for employees in our field is intense, however, we may be unable to retain our existing personnel or attract additional qualified employees. If we experience turnover or difficulties recruiting new employees, our research and development could be delayed and we could experience difficulties in generating sufficient revenue to maintain our business.

Our success also depends on the continued availability of outside scientific collaborators to perform research and develop processes to advance and augment our internal research efforts. Competition for collaborators in gene and cell therapy is intense. If we are unsuccessful in recruiting or maintaining our relationships with scientific collaborators, we could experience delays in our research and development or loss of access to important enabling technology.

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 may be unable to obtain or develop the necessary manufacturing capabilities. If we cannot, we will be unable to introduce sufficient product to sustain our business.

Our use of hazardous materials to develop our 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. 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 revenues and make it more difficult to fund our operations.

The costs of product liability claims and product recalls could exceed the amount of our insurance, which could significantly harm our results of operations or our reputation and result in a decline in the value of our stock.

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 product liability insurance, and the amounts of claims against us may exceed our insurance coverage. Product liability insurance is expensive and may not continue to be available on acceptable terms. A product liability claim not covered by insurance or in excess of our insurance or a product recall could significantly harm our financial results or our reputation. Either of these could result in a decrease in our stock price, and you could lose all or part of your investment.

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 the market price of our common stock to decline.

ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK

This item discusses our exposure to market risk related to changes in interest rates, equity prices and foreign currency exchange rates.

Interest Rate Sensitivity

Short-Term Investments

As of December 31, 1999, we had short-term investments of \$3.1 million. These short-term investments consisted of highly liquid investments with original maturities at the date of purchase of between 18 months and two years, with an average maturity of less than one year. These investments are subject to interest rate risk and will decrease in value if market interest rates increase.

We performed a sensitivity analysis on our investment portfolio as of December 31, 1999. This analysis was based on a modeling technique that measures the hypothetical market value change that would result from an increase in market interest rates of 100 or 200 basis points over a six-month and twelve-month time horizon. The market value changes resulting from a 100 or 200 basis-point increase in short-term treasury security yields were not material because all of our investments held as of December 31, 1999 mature in 2000.

Because we expect to hold most of these investments until maturity, we do not expect the realized value of these investments to be affected to any significant degree by the effect of a sudden change in market interest rates. Declines in interest rates over time, however, would reduce our interest income.

Long Term Obligations

As of December 31, 1999, we had outstanding long term obligations, primarily related to capital equipment leases, leasehold improvements and our loan agreement with Medeva of \$3.3 million, at fixed interest rates of up to 14.62%. Because the interest rates on our long term obligations are fixed, a hypothetical 10 percent decrease in interest rates would not have a material impact on our financial position. Increases in interest rates could, however, increase the interest expense associated with any future borrowings. We do not hedge against interest rate increases.

Market and Credit Risk

We do not use derivative financial instruments in our investment portfolio to manage interest rate risk. We do, however, limit our exposure to interest rate and credit risk by establishing and strictly monitoring clear policies and guidelines for our fixed income portfolios. At the present time we limit to one year the maximum average maturity period of securities in our investment portfolio. Our guidelines also establish credit quality standards, limits on exposure to duration and credit risk criteria. We do not expect our exposure to market and

credit risk to be material. As of December 31, 1999, we had a concentration of accounts receivable with one of our collaborators.

Equity Price Risk

Our equity price risk is limited to the risk inherent in our ownership of 80.1% of Emerald, our joint venture with Elan, and an immaterial equity interest we have in another biotechnology company. Accordingly, we do not hedge against equity price changes.

Foreign Currency Exchange Rate Risk

We realize all of our revenue in dollars and receive substantially all of our cash from Medeva's U. S.-based operations and Emerald's Bermuda-based operations. Therefore, we do not believe that we have any significant direct foreign currency exchange rate risk and we do not hedge against foreign currency exchange rate changes.

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 balance sheets of Targeted Genetics Corporation as of December 31, 1999 and 1998, and the related statements of operations, shareholders' equity, and cash flows for each of the three years in the period ended December 31, 1999. 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 financial position of Targeted Genetics Corporation at December 31, 1999 and 1998, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1999 in conformity with accounting principles generally accepted in the United States.

ERNST & YOUNG LLP

Seattle, Washington
March 1, 2000

TARGETED GENETICS CORPORATION

BALANCE SHEETS

ASSETS

| | December 31, | |
|------------------------------------|--------------|--------------|
| | 1999 | 1998 |
| Current assets: | | |
| Cash and cash equivalents | \$ 4,100,798 | \$ 1,870,841 |
| Securities available for sale | 3,052,471 | 10,085,955 |
| Accounts receivable | 1,391,339 | 102,359 |
| Receivable from joint venture | 445,818 | - |
| Prepaid expenses and other | 269,864 | 387,408 |
| Total current assets | 9,260,345 | 12,446,563 |
| Property, plant and equipment, net | 4,021,466 | 3,299,253 |
| Other assets | 410,667 | 458,267 |
| | \$13,692,478 | \$16,204,083 |

LIABILITIES AND SHAREHOLDERS' EQUITY

| | | |
|--|---------------|---------------|
| Current liabilities: | | |
| Accounts payable | \$ 2,278,338 | \$ 1,664,074 |
| Payable to joint venture | 594,699 | - |
| Accrued payroll and other liabilities | 586,856 | 486,206 |
| Current portion of long-term obligations | 1,160,174 | 1,171,836 |
| Total current liabilities | 4,620,067 | 3,322,116 |
| Long-term obligations | 2,106,897 | 900,208 |
| Shareholders' equity: | | |
| Preferred stock, 6,000,000 shares authorized | | |
| Series A preferred stock, \$.01 par value, 400,000 shares authorized, none issued and outstanding at December 31, 1999 and 1998 | | |
| Series B preferred stock, \$.001 par value, 12,015 shares authorized, issued and outstanding at December 31, 1999, none authorized at December 31, 1998 | -- | -- |
| | 12,390,513 | -- |
| Common stock, \$.01 par value, 80,000,000 shares authorized, 34,019,175 and 30,652,375 shares issued and outstanding at December 31, 1999 and 1998, respectively | 98,122,922 | 88,455,138 |
| Accumulated deficit | (103,532,432) | (76,501,784) |
| Accumulated other comprehensive income | (15,489) | 28,405 |
| Total shareholders' equity | 6,965,514 | 11,981,759 |
| | \$13,692,478 | \$ 16,204,083 |

See accompanying notes to the financial statements.

TARGETED GENETICS CORPORATION

STATEMENTS OF OPERATIONS

| | Year Ended December 31, | | |
|---|--------------------------------|-----------------------|------------------------|
| | 1999 | 1998 | 1997 |
| Revenue: | | | |
| Collaborative agreements | \$ 6,402,175 | \$ 7,192,048 | \$ 888,335 |
| Collaborative agreements with affiliates | 445,818 | - | - |
| Other | - | 318,204 | 439,250 |
| Total revenue | <u>6,847,993</u> | <u>7,510,252</u> | <u>1,327,585</u> |
| Operating expenses: | | | |
| Research and development | 14,291,066 | 13,327,152 | 13,043,288 |
| Technology license fee | 3,200,000 | - | - |
| General and administrative | 3,593,436 | 3,045,835 | 2,784,806 |
| Total operating expenses | <u>21,084,502</u> | <u>16,372,987</u> | <u>15,828,094</u> |
| Loss from operations | (14,236,509) | (8,862,735) | (14,500,509) |
| Equity in loss of joint venture | (12,609,699) | - | - |
| Investment income | 425,726 | 440,478 | 650,892 |
| Interest expense | <u>(234,653)</u> | <u>(264,792)</u> | <u>(338,157)</u> |
| Net loss | \$ (26,655,135) | \$ (8,687,049) | \$ (14,187,774) |
| Accretion of dividend on preferred stock | <u>(375,513)</u> | <u>-</u> | <u>-</u> |
| Net loss applicable to common stock | <u>\$ (27,030,648)</u> | <u>\$ (8,687,049)</u> | <u>\$ (14,187,774)</u> |
| Basic and diluted net loss per share | <u>\$ (0.84)</u> | <u>\$ (0.33)</u> | <u>\$ (0.70)</u> |
| Shares used in computation of basic and diluted net loss per share | <u>32,173,756</u> | <u>26,637,823</u> | <u>20,196,325</u> |

See accompanying notes to the financial statements.

TARGETED GENETICS CORPORATION
STATEMENTS OF SHAREHOLDERS' EQUITY

| | <u>Preferred Stock Shares</u> | <u>Preferred Stock Amount</u> | <u>Common Stock Shares</u> | <u>Common Stock Amount</u> | <u>Accumulated Deficit</u> | <u>Accumulated Other Comprehensive Income</u> | <u>Total Shareholders' Equity</u> |
|--|---------------------------------------|---------------------------------------|------------------------------------|------------------------------------|--------------------------------|---|---|
| Balance at December 31, 1996 | - | - | 20,136,468 | \$73,115,362 | \$ (53,626,961) | \$ 19,387 | \$ 19,507,788 |
| Net loss - 1997 | - | - | - | - | (14,187,774) | - | (14,187,774) |
| Unrealized losses on securities available for sale | - | - | - | - | - | (14,206) | (14,206) |
| Comprehensive loss | | | | | | | (14,201,980) |
| Exercise of stock options | - | - | 15,380 | 8,414 | - | - | 8,414 |
| Exercise of warrants | - | - | 59,266 | 277,365 | - | - | 277,365 |
| Balance at December 31, 1997 | - | - | 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 | - | - | - | - | (27,030,648) | - | (27,030,648) |
| Unrealized losses on securities available for sale | - | - | - | - | - | (43,894) | (43,894) |
| Comprehensive loss | | | | | | | (27,042,542) |
| Issuance of Series B Convertible Exchangeable Preferred stock | 12,015 | 12,015,000 | - | - | - | - | 12,015,000 |
| Accretion on 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 | <u>12,015</u> | <u>\$12,390,513</u> | <u>34,019,175</u> | <u>98,122,922</u> | <u>\$(103,532,432)</u> | <u>\$ (15,489)</u> | <u>\$6,965,514</u> |

See accompanying notes to the financial statements.

TARGETED GENETICS CORPORATION

STATEMENTS OF CASH FLOWS

| | Year Ended December 31, | | |
|--|--------------------------------|---------------------|---------------------|
| | 1999 | 1998 | 1997 |
| Operating activities: | | | |
| Net loss | \$ (27,030,648) | \$ (8,687,049) | \$(14,187,774) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Equity in loss of joint venture | 12,609,699 | - | - |
| Expenses paid with common stock | 3,200,000 | 1,000,000 | - |
| Depreciation and amortization | 1,614,019 | 1,635,797 | 1,641,151 |
| Increase in accounts receivable | (1,289,035) | (59,198) | (3,528) |
| Increase in accounts receivable from joint venture | (445,818) | - | - |
| Increase (decrease) in current liabilities | 586,193 | 485,259 | (190,996) |
| Decrease (increase) in prepaid expenses and other | 62,347 | (143,769) | 42,317 |
| Decrease (increase) in accrued interest on securities available for sale | 79,608 | (65,746) | 162,497 |
| Net cash used in operating activities | <u>(10,613,635)</u> | <u>(5,834,706)</u> | <u>(12,536,333)</u> |
| Investing activities: | | | |
| Purchases of property, plant and equipment | (1,856,199) | (238,623) | (704,896) |
| Purchases of securities available for sale | (483,014) | (17,664,960) | (814,251) |
| Maturities and sales of securities available for sale | 7,392,996 | 11,693,951 | 12,130,074 |
| Increase in other assets | - | (15,000) | (50,000) |
| Net cash provided by (used in) investing activities | <u>5,053,783</u> | <u>(6,224,632)</u> | <u>10,560,927</u> |
| Financing activities: | | | |
| Net proceeds from sale of capital stock | 6,467,784 | 14,053,997 | 285,779 |
| Proceeds from equipment financing transactions | 1,294,389 | 176,289 | 468,363 |
| Loan proceeds from collaborative partner | 1,000,000 | - | - |
| Payments under capital leases and loans | (1,347,877) | (1,311,952) | (1,299,459) |
| Accretion on preferred stock | 375,513 | -- | -- |
| Net cash provided by (used in) financing activities | <u>7,789,809</u> | <u>12,918,334</u> | <u>(545,317)</u> |
| Net increase (decrease) in cash and cash equivalents | 2,229,957 | 858,996 | (2,520,723) |
| Cash and cash equivalents, beginning of year | 1,870,841 | 1,011,845 | 3,532,568 |
| Cash and cash equivalents, end of year | <u>\$ 4,100,798</u> | <u>\$ 1,870,841</u> | <u>\$ 1,011,845</u> |
| Cash paid during the year for interest | \$202,883 | \$264,702 | \$338,157 |
| Supplemental disclosure of non-cash investing and financing activity: | | | |
| Preferred stock issuance in exchange for interest in joint venture | 12,015,000 | - | - |
| Equipment financed through renewal of capital lease | -- | 594,983 | -- |

See accompanying notes to the financial statements

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS

1. Nature of Operations

Targeted Genetics Corporation (“Targeted Genetics” or the “Company”) is developing gene therapy products for the treatment of certain acquired and inherited diseases. Targeted Genetics was incorporated in the state of Washington in March 1989. The Company’s operations constitute one business segment.

2. Summary of Significant Accounting Policies

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 market, consist principally of money market accounts and short-term government obligations. 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, all of which mature within one year. Targeted Genetics currently classifies its entire investment portfolio as securities available for sale. Such securities are stated at market value, with the 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 judged to be other than temporary on securities available for sale 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, investments, accounts receivable and accounts payable reasonably approximate fair value because of the short-term nature of these items. The Company believes the carrying amounts of the note payable and capital leases obligations approximate fair value because the interest rates on these instruments change with, or approximate, market interest rates.

Property, Plant and Equipment

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.

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

Stock Compensation

As permitted by the provisions of Financial Accounting Standards Board Statement No. 123, *Accounting for Stock-Based Compensation*, the Company 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 apply the disclosure-only provisions to account for its stock option plans. The Company does not recognize any compensation expense related to the plans since 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 123 and are subject to periodic revaluation over their vesting terms.

Revenue under Collaborative Agreements

Revenue under collaborative agreements is recognized according to the terms of the collaborative agreements. Nonrefundable product license fees that are not dependent on future performance are recognized as revenue when received. Up-front signing or licensing fees that are dependent on future performance are recognized ratably over the period in which the related work is performed. Milestone revenue is recognized upon the achievement of the related milestone and when collection is probable. Revenue earned from the performance of research and development is recognized over the period in which the related work is performed. Advance payments received in excess of amounts earned are classified as deferred revenue.

Net Loss Per Share

Basic net loss per share is computed based upon the weighted average number of common shares outstanding during the period. The Company's 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.

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.

New Accounting Pronouncements

In June 1998, the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, *Accounting for Derivative Instruments and Hedging Activities*. This new statement, 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. Statement No. 133 requires

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

companies to recognize all derivatives as either assets or liabilities on the balance sheet and measure those instruments at fair value. Gains or losses resulting from changes in the values of those derivatives would be accounted for depending on the use of the derivative and whether it qualifies for hedge accounting under the standard. The impact of Statement No. 133 on Targeted Genetics' financial position and results of operations is not expected to be material.

In December 1999, the Securities Exchange Commission issued Staff Accounting Bulletin 101 *Revenue Recognition in Financial Statements* which provides the SEC's views on applying generally accepted accounting principles to revenue recognition issues. The Company is currently evaluating its revenue recognition policies and has not yet determined the financial statement impact of this bulletin.

3. Significant Concentrations

The Company's collaborative agreement with Medeva PLC, provided 87%, 88% and 0% of revenue in fiscal years ending December 31, 1999, 1998 and 1997, respectively. See note 8. At December 31, 1999 and 1998, amounts receivable from Medeva represented 76% and 100%, respectively, of the Company's accounts receivable balance. The Company 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.

4. Securities Available for Sale

All securities available for sale at December 31, 1999 mature within one year. 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 |
| December 31, 1998: | | | | |
| U.S. Treasury securities and obligations of U.S. government agencies | 6,184,441 | 6,106 | - | 6,190,547 |
| U.S. corporate securities | 3,873,109 | 22,370 | (71) | 3,895,408 |
| | <u>\$10,057,550</u> | <u>\$ 28,476</u> | <u>\$ (71)</u> | <u>\$10,085,955</u> |

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

Unrealized gains and losses on securities available for sale consisted of the following:

| | Year Ended December 31, | | |
|-------------------------------------|-------------------------|------------------|--------------------|
| | 1999 | 1998 | 1997 |
| All gains (losses) | \$ (39,336) | \$ 37,909 | \$ (15,564) |
| Less reclassifications to net loss: | | | |
| Gross realized gains | (8,059) | (19,940) | (4,448) |
| Gross realized losses | 3,501 | 5,255 | 5,806 |
| Unrealized gains (losses) | <u>\$ (43,894)</u> | <u>\$ 23,224</u> | <u>\$ (14,206)</u> |

5. Property, Plant and Equipment

Property, plant and equipment consisted of the following:

| | December 31, | |
|--|---------------------|---------------------|
| | 1999 | 1998 |
| Furniture and equipment | \$ 5,522,248 | \$ 4,240,248 |
| Leasehold improvements | 5,567,091 | 4,625,027 |
| | <u>11,089,339</u> | <u>8,865,275</u> |
| Less accumulated depreciation and amortization | 7,067,873 | 5,566,022 |
| | <u>\$ 4,021,466</u> | <u>\$ 3,299,253</u> |

Depreciation expense totaled \$1,531,420 in 1999, \$1,491,702 in 1998, and \$1,492,406 in 1997.

The Company has leased 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, 1999 and 1998 was \$3,784,055 and \$2,857,915, respectively, with related accumulated amortization of \$2,489,772 and \$1,553,880 at December 31, 1999 and 1998, respectively.

6. Long-Term Obligations

Long-term obligations consisted of the following:

| | December 31, | |
|-------------------------------|---------------------|-------------------|
| | 1999 | 1998 |
| Capitalized lease obligations | \$ 2,055,062 | \$ 1,705,375 |
| Note payable to collaborator | 1,018,689 | - |
| Deferred state sales tax | 193,320 | 308,609 |
| Other | - | 58,060 |
| | <u>3,267,071</u> | <u>2,072,044</u> |
| Less current portion | 1,160,174 | 1,171,836 |
| | <u>\$ 2,106,897</u> | <u>\$ 900,208</u> |

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

Future aggregate principal payments related to long-term obligations are \$1,141,485 in 2000, \$606,346 in 2001, \$419,129 in 2002, \$77,115 in 2003, and \$1,004,307 in 2004.

The Company has an agreement with Medeva/Celltech under which, subject to certain circumstances, Medeva/Celltech will loan the Company 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, 1999, the Company has borrowed \$1.0 million under the agreement. No amount was borrowed at December 31, 1998. Interest on borrowings is payable annually in arrears at a rate that is 150 basis points over the one-month LIBOR rate, but not less than 5% nor more than 7% per year. The Company recognized \$18,689 of interest expense in 1999. Principal is due and payable in November 2003, or earlier if the cumulative net product sales of the Company's cystic fibrosis product equal or exceed \$60.0 million. The loan agreement contains financial covenants including limits on the Company's ability to declare or pay dividends. The Company can at its option, and with Medeva'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 twenty-day period preceding the repayment date.

7. Shareholders' Equity

Series B Preferred Stock

In July 1999, Elan International Services, Ltd. purchased \$12,015,000 of the Company's Series B preferred stock in conjunction with the formation of the Emerald Gene Systems Ltd. ("Emerald") joint venture. See note 13. This preferred stock bears an annual dividend of 7%, accrued semi-annually and added to principal. The Series B preferred stock is convertible until July 2005, at Elan's option, into the Company's common stock at a price of \$3.32 per share. As of December 31, 1999 the Company had accrued dividends of \$376,000. Elan's holdings of the Series B preferred stock were convertible into 3,732,106 shares of the common stock as of December 31, 1999. The Company would issue 5,740,548 shares of its common stock if Elan were to elect to convert its preferred stock to 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 certain transactions involving a change of control of the Company.

Should the Company liquidate or wind-down its operations, the agreement gives Series B 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 par value. The Company has redemption rights to these shares only in certain instances involving 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.

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

Warrants

In June 1999, the Company 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 are priced at \$2.50 and \$4.16 per share, respectively. See note 9.

In 1998, the Company 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.

The Company has outstanding warrants to purchase a total of 126,016 shares related to equipment financing, consulting and license agreements. These warrants have a weighted average price of \$4.42 per share and expire between May 2001 and March 2004.

At December 31, 1999, 6,459,349 shares of common stock were reserved for all outstanding warrants.

Shareholder Rights Plan

The Company 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 certain persons or groups that attempt to acquire the Company on terms not approved by the Company's Board of Directors.

Stock Options

The Company has three stock option plans. Beginning in 1999 the Company began granting all options from the 1999 Stock Option Plan (the "1999" Plan), and discontinued grants from the other two plans. 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 the Company and consultants, agents, advisors and independent contractors who provide services to the Company. 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, 1999, options to purchase 1,175,125 shares were available for future grant under the 1999 Plan. The following table summarizes activity related to the Company's stock option plans:

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

| | Shares | Weighted Average Exercise Price |
|----------------------------|------------------|--|
| Balance, December 31, 1996 | 1,214,414 | \$3.57 |
| Granted | 571,728 | 3.75 |
| Exercised | (15,380) | 0.55 |
| Canceled | (74,060) | 4.42 |
| Balance, December 31, 1997 | 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 | <u>2,441,342</u> | 2.26 |

During 1999, options were exercised at prices ranging from \$0.55 to \$2.25 per share. Options for 1,094,420, 628,785 and 611,465 shares were exercisable at December 31, 1999, 1998 and 1997, respectively. In 1998, the Company 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 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, 25% upon the date six months after the grant date, 25% upon the date twelve months after the grant date and 6.25% at the end of each three-month period thereafter.

The following table summarizes information for outstanding and exercisable options at December 31, 1999:

| Range of Exercise Prices | Outstanding | | | Exercisable | |
|-----------------------------|------------------|--|---|------------------|--|
| | Shares | Weighted Average Exercise Price | Weighted Average Remaining Contractual Life | Shares | Weighted Average Exercise Price |
| \$0.50 - \$1.22 | 647,890 | \$1.07 | 7.38 | 426,476 | \$1.03 |
| 1.38 - 1.72 | 624,125 | 1.63 | 8.98 | 111,216 | 1.68 |
| 1.94 - 2.25 | 577,717 | 2.13 | 8.69 | 110,934 | 2.13 |
| 2.50 - 6.25 | 591,610 | 4.29 | 5.64 | 445,794 | 4.31 |
| 0.50 - 6.25 | <u>2,441,342</u> | \$2.54 | 7.68 | <u>1,094,420</u> | 2.54 |

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

In conformity with the provisions of Statement No. 123, *Accounting for Stock-Based Compensation*, the Company has elected to follow the intrinsic value method allowed under that statement for its stock option plans and present pro forma disclosures using the fair value accounting approach. Had compensation costs been recorded, the following amounts would have been reported:

| | 1999 | 1998 | 1997 |
|---|----------------|----------------|-----------------|
| Net loss -- as reported | \$(27,030,648) | \$ (8,687,049) | \$ (14,187,774) |
| Net loss -- pro forma | (27,985,273) | (9,512,398) | (15,068,834) |
| Basic net loss per share -- as reported | (0.84) | (0.33) | (0.70) |
| Basic net loss per share -- pro forma | (0.87) | (0.36) | (0.75) |

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:

| | 1999 | 1998 | 1997 |
|---|---------|---------|---------|
| Expected dividend rate | Nil | Nil | Nil |
| Expected stock price volatility | 0.908 | .814 | .696 |
| Risk-free interest rate | 5.05% | 5.38% | 6.53% |
| Expected life of options from vest date | 3 years | 3 years | 3 years |

The weighted average fair value of options granted during 1999, 1998 and 1997 was \$1.94, \$1.11 and \$2.51, 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

As of December 31, 1999, the Company had reserved a total of 13,807,922 shares of common stock for issuance pursuant to conversion of preferred stock and stock options.

8. Collaborative Agreements

Celltech Group plc Agreement

In 1998 Targeted Genetics entered into a series of agreements (the "CF Agreements") with Medeva. In January 2000, Medeva merged with Celltech/Chiroscience to become part of Celltech Group plc. Celltech has assumed Medeva's rights and responsibilities under our agreements. Targeted Genetics and Medeva are collaborating to develop on a worldwide basis the Company's tgAAV-CF gene therapy product for the treatment of cystic fibrosis. Upon signing the CF Agreements, Targeted Genetics received a license and technology access fee of \$5.0 million 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. Medeva agreed to pay up to \$5.0 million per year for three years to fund the Company's tgAAV-CF research and development activities and certain Phase I clinical trial expenses. In addition, Medeva agreed to pay the costs of Phase II and subsequent clinical trials of the product. 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, the Company will manufacture and supply bulk product to Celltech under a pricing formula constructed to compensate with a fixed percentage of Celltech's net product

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

sales. The research and development funding agreement is effective from October 1998 to October 2001, with options to extend the term if both parties agree. The long-term supply agreement is effective for the term of the patents covering the Company's tgAAV-CF technology. Celltech has the option to terminate the CF Agreements at will with 180 days notice. Should Celltech exercise this right to terminate the CF Agreements, all rights related to tgAAV-CF technology would return to the Company. The Company recognized \$6.4 million and \$7.0 million of revenue under the CF Agreements in 1999 and 1998.

Under separate agreements, Medeva agreed to purchase \$3.0 million of Company common stock and, subject to certain provisions, to loan the Company up to \$12.0 million. Medeva purchased \$3.0 million of common stock in two tranches: 750,000 shares of common stock for \$1.5 million upon signing of the stock purchase agreement in 1998 and 677,392 shares of common stock for \$1.5 million in 1999. Subject to certain conditions, the Company can draw up to \$2.0 million to partially fund construction of facilities to support Phase III trials and initial commercialization. At December 31, 1999, the Company has drawn \$1.0 million. See note 6. Under certain conditions, Medeva agreed to loan us up to an additional \$10 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 the \$10.0 million commitment.

Elan Corporation plc

In July 1999, the Company and Elan formed Emerald, a joint venture to develop enhanced gene delivery technology and products.

Elan has agreed to loan the Company up to \$12.0 million under a convertible promissory note agreement to support its share of the joint venture's research and development costs. The note has a six-year term, accrues interest at 12% per year. The note and related accrued interest are convertible into the Company's common stock at conversion prices set at 150% of the average closing price of the Company's common stock for the 60 trading days ending two business days before the time the Company draws loan proceeds. The note agreement includes provisions allowing the Company to convert the debt into the Company's common stock at the lesser of the current market price or the conversion price, at its option. As of December 31, 1999, the Company has not drawn on the note.

The Company also entered into an agreement with Elan that requires Elan to purchase up to \$10.0 million of the Company's common stock at a premium to market price. Elan purchased \$5.0 million of Targeted Genetics' common stock in connection with closing of the joint venture transaction, or 2,148,899 shares. At the Company's option, Elan will purchase an additional \$5.0 million of Targeted Genetics common stock in July 2000 at 120% of the market price at that time.

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

9. Alkermes License

On June 9, 1999, the Company entered into an agreement with Alkermes, Inc. to acquire the exclusive rights to a patent for the manufacture of 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. The Company issued 500,000 shares of its common stock and warrants to purchase a total of up to 2,000,000 additional shares in exchange for this technology license. See note 7. Under the terms of the license, the Company is responsible for endeavoring to commercialize the technology. Additionally, the Company is obligated to make milestone payments as products using this technology reach clinical trial and regulatory milestones. The Company is also obligated to pay royalties upon the sale of AAV products or sub-licensing of the licensed technology. The Company recorded a \$3.2 million non-cash charge with respect to the Alkermes license in its 1999 operating results, because the underlying technology is not complete and the Company will have to invest significant resources to develop and prove its commercial feasibility.

10. Lease Commitments

The Company leases its research and office facilities under two noncancellable operating leases that expire March 31, 2004. The leases may be extended under two additional five-year renewal options at the then-prevailing fair market value rental rate.

Future minimum payments under noncancellable leases at December 31, 1999 were as follows:

| | <u>Operating</u> | <u>Capital</u> |
|---|---------------------|---------------------|
| Year Ending December 31: | | |
| 2000 | \$ 617,713 | \$ 1,147,974 |
| 2001 | 634,451 | 655,783 |
| 2002 | 664,447 | 408,263 |
| 2003 | 681,185 | 81,321 |
| 2004 | 177,810 | 5,115 |
| Thereafter | - | - |
| Total minimum lease payments | <u>\$ 2,775,606</u> | 2,298,456 |
| Less amount representing interest | | 243,394 |
| Present value of minimum capitalized lease payments | | <u>\$ 2,055,062</u> |

Rent expense under operating leases for the years ended December 31, 1999, 1998 and 1997 was \$587,000, \$533,000 and \$533,000, respectively.

11. Employee Retirement Plan

The Company sponsors an employee retirement plan in accordance with Section 401(k) of the Internal Revenue Code. All employees 21 years old or older are eligible to participate in the plan. Contributions made into the plan are at the discretion of the board of directors. The Company incurred \$90,181, \$0, and \$99,426 of expense in 1999, 1998 and 1997, respectively, related to contributions to the plan.

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

12. Income Taxes

At December 31, 1999, the Company had net operating loss carryforwards of \$70.1 million and research and experimental credit carryforwards of \$1.8 million. The carryforwards are available to offset future federal income taxes and begin to expire in 2008. The Company 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 \$3.9 million in 1999 and \$2.8 million during 1998.

Significant components of the Company's deferred tax assets and liabilities were as follows:

| | December 31, | |
|--|----------------------|----------------------|
| | 1999 | 1998 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | \$ 23,828,000 | \$ 20,354,000 |
| Research and experimental credit carryforwards | 1,815,000 | 1,628,000 |
| Depreciation | 842,000 | 721,000 |
| Other | 185,000 | 97,000 |
| Total deferred tax assets | <u>\$ 26,670,000</u> | <u>\$ 22,800,000</u> |
| Valuation allowance for deferred tax assets | <u>\$ 26,670,000</u> | <u>\$ 22,800,000</u> |

Utilization of federal income tax carry-forwards is subject to certain limitations under Section 382 of the Internal Revenue Code of 1986. The Company's 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.

13. Joint Venture

In July 1999, the Company and Elan formed Emerald, a joint venture to develop enhanced gene delivery technology and products. At the time the joint venture was formed, Elan purchased \$12,015,000 of the Company's Series B convertible exchangeable preferred stock. See note 7. The preferred stock is convertible, at Elan's option, into Targeted Genetics common stock or into shares representing a 30.1% interest in Emerald, increasing 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.

The Company formed Emerald by issuing Emerald preferred and common stock valued at \$15,000,000 to Targeted Genetics and Elan. The Company currently owns an 80.1% interest in Emerald and Elan owns 19.9% (non-voting) preferred shares while Targeted Genetics owns 100% of the voting common shares, Elan and its subsidiaries have retained significant minority investor rights that are considered "participating rights" as defined

TARGETED GENETICS CORPORATION

NOTES TO FINANCIAL STATEMENTS (Continued)

in the Financial Accounting Standards Board'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*. Elan's participating rights prevent the Company from exercising control over Emerald. Accordingly, the Company 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 information of Emerald as of December 31, 1999 and for the period from July 21, 1999 (date of inception) through December 31, 1999 is as follows:

| | |
|--|-----------------------|
| Current assets | \$ 2,250 |
| Total assets | <u>2,250</u> |
| Current liabilities | 744,696 |
| Total shareholders' equity | <u>(742,446)</u> |
| Total liabilities and shareholders' equity | <u>2,250</u> |
| Revenue | \$ - |
| Technology access fee | 15,000,000 |
| Operating expenses | <u>742,446</u> |
| Net loss | <u>\$(15,742,446)</u> |

Included in the Company's December 31, 1999 balance sheet are a \$445,818 receivable from Emerald for services performed by the Company for Emerald and a payable to Emerald of \$594,699 for the Company's 80.1% share of Emerald's funding requirements as of December 31, 1999. The Company expects to advance Emerald its share of the required funding and collect the \$445,818 Emerald account receivable during the first quarter of 2000. The Company is required to provide additional funding to Emerald as needed in relation to its ownership interest in Emerald.

14. Subsequent Events

On March 1, 2000 Targeted Genetics announced that it had entered into a definitive agreement for the placement of 2,164,286 shares of newly issued common stock that resulted in gross proceeds to the Company of \$30.3 million.

AUDITORS' REPORT

To the Shareholders of

Emerald Gene Systems, Ltd.

We have audited the balance sheet of Emerald Gene Systems, Ltd. as at December 31, 1999 and the statement of loss shareholders' deficit and cash flow for the 166 day period then ended. 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 audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform an audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

In our opinion, these financial statements present fairly, in all material respects, the financial position of the company as at December 31, 1999 and the results of its operations for the 166 day period then ended in accordance with accounting principles generally accepted in the United States.

February 29, 2000
Hamilton, Bermuda

ERNST & YOUNG
Chartered Accountants

EMERALD GENE SYSTEMS, LTD.
(Incorporated in Bermuda)
BALANCE SHEET

DECEMBER 31, 1999

(expressed in United States dollars)

1999

ASSETS

Current assets

Prepaid expenses \$ 2,250

LIABILITIES

Current liabilities

Accounts payable and accrued expenses \$ 6,350
Due to related party (Note 3) 277,502
Due to shareholders (Note 3) 460,844
744,696

SHAREHOLDERS' EQUITY

Share capital (Note 5) 12,000
Contributed surplus (Note 6) 14,988,000
Deficit (15,742,446)
(742,446)
\$ 2,250

See accompanying notes.

EMERALD GENE SYSTEMS, LTD.
(Incorporated in Bermuda)

STATEMENT OF LOSS
FOR THE 166 DAY PERIOD ENDED DECEMBER 31, 1999
(expressed in United States dollars)

1999

| | | |
|-------------------------------------|----|----------------------------|
| Revenue | \$ | - |
| Expenses | | |
| License fee (Note 4) | | 15,000,000 |
| Research and development (Note 3) | | 723,320 |
| General and administrative expenses | | <u>19,126</u> |
| Net loss | \$ | <u><u>(15,742,446)</u></u> |

See accompanying notes.

EMERALD GENE SYSTEMS, LTD.
(Incorporated in Bermuda)

STATEMENTS OF SHAREHOLDERS' DEFICIT

FOR THE 166 DAY PERIOD ENDED DECEMBER 31, 1999
(expressed in United States dollars)

| | <u>Preferred Stock Shares</u> | <u>Preferred Stock Amount</u> | <u>Common Stock Shares</u> | <u>Common Stock Amount</u> | <u>Contributed Surplus</u> | <u>Accumulated Deficit</u> | <u>Total Shareholders' Equity</u> |
|------------------------------|---------------------------------------|---------------------------------------|------------------------------------|------------------------------------|--------------------------------|--------------------------------|---|
| Balance at July 19, 1999 | - | \$ - | - | \$ - | \$ - | \$ - | \$ - |
| Issuance of common shares | - | - | 7,491 | 7,491 | 1,199,478 | - | 1,206,969 |
| Issuance of preferred shares | 4,509 | 4,509 | - | - | 13,788,522 | - | 13,793,031 |
| Net loss - 1999 | - | - | - | - | - | (15,742,446) | (15,742,446) |
| Balance at December 31, 1999 | <u>4,509</u> | <u>\$4,509</u> | <u>7,491</u> | <u>\$ 7,491</u> | <u>\$14,988,000</u> | <u>\$(15,742,446)</u> | <u>\$ 6,965,514</u> |

See accompanying notes to the financial statements.

EMERALD GENE SYSTEMS, LTD.
(Incorporated in Bermuda)

STATEMENT OF CASH FLOWS
FOR THE 166 DAY PERIOD ENDED DECEMBER 31, 1999
(expressed in United States dollars)

1999

| | | |
|--|----|-------------------|
| Operating activities | \$ | - |
| Net Loss | | \$(15,742,446) |
| Adjustment to convert to a cash basis | | |
| Prepaid expenses | | (2,250) |
| Accounts payable and accrued expenses | | 6,350 |
| Due to related party | | 277,502 |
| Due to shareholders | | <u>460,844</u> |
| Financing activities | | |
| Proceeds from issuance of common shares | | 7,491 |
| Proceeds from issuance of common shares | | 4,509 |
| Increase in contributed surplus | | <u>14,988,000</u> |
| Changes in cash, and cash at end of period | \$ | - |

See accompanying notes.

EMERALD GENE SYSTEMS, LTD.

NOTES TO THE FINANCIAL STATEMENTS

DECEMBER 31, 1999

(expressed in United States dollars)

1. Operations

The company was incorporated July 19, 1999 in Bermuda. The company is owned by Elan International Services Ltd. ("EIS"), a wholly-owned subsidiary of Elan Corporation plc, and Targeted Genetics Corporation ("TGC"), holding 19.9% and 80.1% of the shares respectively. The primary objective of the company is to carry on the business of the development, testing, registration, manufacturing, commercialization, and licensing of "Products" (as defined in the Subscription, Joint Development and Operating Agreement ("JDOA") dated July 21, 1999 between EIS, TGC and others.) The focus of the collaborative venture will be to develop the "Products" using the Elan Intellectual Property, the TGC Intellectual Property and the Emerald Technology pursuant to the JDOA.

2. Significant accounting policy

The company follows accounting principles generally accepted in the United States. Significant accounting policies are as follows:

(a) Research and development costs

Research costs are charged as an expense of the period in which they are incurred. Development costs are deferred to future periods if certain criteria relating to future benefits are satisfied and if the costs do not exceed the expected future benefits.

(b) Use of estimates

The preparation of financial statements in accordance with GAAP requires management to make estimates and assumptions that affect the reported amount of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amount of revenues and expenses during the reporting period. Actual results could differ significantly from those estimates.

3. Related party transactions

The following table summarizes the company's related party transactions for the period:

| | 1999 |
|---|------------|
| Research and development costs | |
| To companies related through common ownership | \$ 277,502 |
| To shareholders | 445,818 |

EMERALD GENE SYSTEMS, LTD.

NOTES TO THE FINANCIAL STATEMENTS

DECEMBER 31, 1999
(expressed in United States dollars)

These transactions are in the normal course of operations and are measured at the exchange amount, which is the amount of consideration established and agreed to by the related parties.

At the end of the period, the amounts due to related entities are as follows:

| | | |
|---|----|---------|
| Due to shareholders | \$ | 460,844 |
| Due to companies related through common ownership | \$ | 277,502 |

These balances are unsecured, and interest free with no set terms of repayment.

4. License Fee

During 1999, the company paid a license fee to Elan Corporation plc in the amount of \$15,000,000 to acquire certain rights to Elan intellectual property.

5. Share capital

| | 1999 |
|---|-----------|
| Authorised, issued and fully paid: | |
| 6,000 voting common shares, of par value \$1.00 per share | \$ 6,000 |
| 1,491 non-voting common shares (with option to convert into voting common shares after July 21, 2001), par value \$1.00 per share | 1,491 |
| 3,612 non-voting preferred shares, of par value \$1.00 per share | 3,612 |
| 897 non-voting preferred shares (with option to convert into voting common shares upon exercise of Exchange Right) | 897 |
| | \$ 12,000 |

6. Contributed surplus

Contributed surplus represents share premium on amounts contributed by shareholders in addition to their subscription to the issued share capital.

7. Year 2000 Issue (unaudited)

The Year 2000 Issue arises because many computerized systems use two digits rather than four to identify a year. Date-sensitive systems may recognize the year 2000 as 1900 or some other date, resulting in errors when information using Year 2000 dates is processed. In addition, similar problems may arise in some systems which use certain dates in 1999 to represent something other than a date.

EMERALD GENE SYSTEMS, LTD.

NOTES TO THE FINANCIAL STATEMENTS

DECEMBER 31, 1999

(expressed in United States dollars)

7. Year 2000 Issue (unaudited), cont'd.

Although the change in date has occurred, it is not possible to conclude that all aspects of the Year 2000 Issue that may effect the entity, including those related to customers, suppliers, or other third parties, have been fully resolved.

8. Taxes

Under current Bermuda law the company is not required to pay any taxes in Bermuda on either income or capital gains. The company has received an undertaking from the Minister of Finance in Bermuda that in the event of such taxes being imposed, the company will be exempted from taxation until the year 2016.

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

None.

PART III

ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF REGISTRANT

(a) The information required by this item concerning our directors is incorporated by reference to the sections captioned "Election of Directors" in the proxy statement for our annual meeting of shareholders to be held on May 12, 2000. We will file the proxy statement within 120 days of December 31, 1999, our fiscal year end.

(b) The information required by this item concerning our executive officers is provided in Part I of this annual report.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item 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 12, 2000.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The information required by this item is incorporated by reference from the section captioned "Principal Shareholders" in the proxy statement for our annual meeting shareholders to be held on May 12, 2000.

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 | 31 |
| Targeted Genetics Corporation Balance Sheets at December 31, 1999 and 1998 | 32 |
| Targeted Genetics Corporation Statement of Operations for the years ended December 31, 1999, 1998 and 1997 | 33 |
| Targeted Genetics Corporation Statements of Shareholders' Equity for the period from December 31, 1996 through December 31, 1999 | 34 |
| Targeted Genetics Corporation Statement of Cash Flows for the years ended December 31, 1999, 1998 and 1997 | 35 |
| Targeted Genetics Corporation Notes to Financial Statements | 37-48 |
| Emerald Gene Systems, Ltd. Report of Ernst and Young Chartered Accountants, Independent Auditors | 49 |
| Emerald Gene Systems, Ltd. Balance Sheet at December 31, 1999 | 50 |
| Emerald Gene Systems, Ltd. Statements of Operations for the 166 day period ended December 31, 1999 | 51 |
| Emerald Gene Systems, Ltd. Statements of Shareholders' Equity for the 166 day period ended 1999 | 52 |
| Emerald Gene Systems, Ltd. Statement of Cash Flows for the 166 day period ended 1999 | 53 |
| Emerald Gene Systems, Ltd. Notes to Financial Statements | 54-56 |

2. Financial Statement Schedules

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

3. Exhibits

| | | |
|------|--|-----|
| 3.1 | Amended and Restated Articles of Incorporation (Exhibit 3.1) | (D) |
| 3.2 | Amended and Restated Bylaws (Exhibit 3.2) | (D) |
| 3.3 | Articles of Amendment of the Company, filed with the State of Washington on July 21, 1999 (Exhibit 1.8) | (K) |
| 4.1 | Rights Agreement, dated as of October 17, 1996, between the Company and ChaseMellon Shareholder Services (Exhibit 2.1) | (C) |
| 4.2 | Registration Rights Agreement, dated as of July 21, 1999, by and among the Company and Elan International Services, Ltd. (Exhibit 1.2) | (K) |
| 4.3 | First Amendment of Rights Agreement, dated July 21, 1999, between the Company and ChaseMellon Shareholder Services(Exhibit 1.9) | (K) |
| 4.4 | Warrant to purchase 2,000,000 shares of common stock of the Company, issued to Alkermes, Inc. on June 9, 1999. (Exhibit 10.38) | (J) |
| 10.1 | Form of Indemnification Agreement between the registrant and its officers and directors | |
| 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 the Company* | |

- 10.4 PHS Patent License Agreement-Non-Exclusive, dated as of July 13, 1993, between National Institutes of Health Centers for Disease Control and the Company*
- 10.5 Patent License Agreement, dated as of December 25, 1993, between The University of Florida Research Foundation, Inc. and the Company*
- 10.6 Research and Exclusive License Agreement, dated as of January 1, 1994, between the Company and the Fred Hutchinson Cancer Research Center* (Exhibit 10.9) (E)
- 10.7 PHS Patent License Agreement- Exclusive, dated as of March 10, 1994, between National Institutes of Health Centers for Disease Control and the Company* (Exhibit 10.10) (E)
- 10.8 License Agreement, dated as of March 28, 1994, between the Company 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 the Company* (Exhibit 10.21) (D)
- 10.14 License Agreement, dated as of March 15, 1997, between the Burnham Institute and the Company* (Exhibit 10.23) (E)
- 10.15 Exclusive Sublicensing Agreement, dated June 9, 1999, between the Company and Alkermes, Inc. (Exhibit 10.36) (J)
- 10.16 Common Stock Purchase Agreement, dated June 9, 1999, between the Company and Alkermes, Inc. (Exhibit 10.37) (J)
- 10.17 License Agreement, dated as of August 31, 1999, between the Company and the University of North Carolina Research Center**
- 10.18 Master Agreement, dated as of November 23, 1998, between the Company and Medeva Pharmaceuticals, Inc.* (Exhibit 1.1) (H)
- 10.19 License and Collaboration Agreement, dated as of November 23, 1998, between the Company and Medeva Pharmaceuticals, Inc.* (Exhibit 1.2) (H)
- 10.20 Supply Agreement, dated as of November 23, 1998, between the Company and Medeva Pharmaceuticals, Inc.* (Exhibit 1.3) (H)
- 10.21 Common Stock Purchase Agreement, dated as of November 23, 1998, between the Company, Medeva Pharmaceuticals, Inc. and Medeva PLC* (Exhibit 1.4) (H)
- 10.22 Credit Agreement, dated as of November 23, 1998, between the Company, Medeva Pharmaceuticals, Inc. and Medeva PLC* (Exhibit 1.5) (H)
- 10.23 Securities Purchase Agreement, dated as of July 21, 1999, between the Company, Elan Corporation and Elan International Services, Ltd., a wholly owned subsidiary of Elan Corporation (Exhibit 1.1) (K)
- 10.24 Funding Agreement, dated as of July 21, 1999, among the Company, Elan International Services, Ltd., and Elan Corporation, plc (Exhibit 1.3) (K)
- 10.25 Subscription, Joint Development and Operating Agreement, dated as of July 21, (K)

| | | |
|-------|--|-----|
| | 1999, among Elan Corporation, plc, Elan International Services, Ltd., the Company and Targeted Genetics Newco, Ltd. * (Exhibit 1.4) | |
| 10.26 | Convertible Promissory Note, dated July 21, 1999, issued by the Company to Elan International Services, Ltd. (Exhibit 1.5) | (K) |
| 10.27 | License Agreement dated July 21, 1999, between Targeted Genetics Newco, Ltd. and the Company * (Exhibit 1.6) | (K) |
| 10.28 | 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) |
| 10.29 | Olive Way Building Lease to Olive Way Building, dated as of November 20, 1993, as amended between the Company and Ironwood Apartments, Inc. (successor in interest to Metropolitan Federal Savings and Loan Association) | |
| 10.30 | Office Lease, dated as of October 7, 1996, between Benaroya Capital Company, LLC and the Company (Exhibit 10.26) | (D) |
| 10.31 | 1992 Restated Stock Option Plan (Exhibit 99.1) | (F) |
| 10.32 | Stock Option Plan for Nonemployee Directors (Exhibit 10.34) | (E) |
| 10.33 | 1999 Stock Option Plan (Exhibit 99.1) | (I) |
| 21.1 | Subsidiaries | |
| 23.1 | Consent of Ernst & Young LLP | |
| 27.1 | Financial Data Schedule | |

*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 Securities and Exchange Commission. The omitted portions of these exhibits have been filed separately with the SEC.

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

(D) Incorporated by reference to the Company's Registration Statement on Form 8-A, filed October 22, 1996.

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

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

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

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

(K) Incorporated by reference to the designated exhibit included with the Company's Current Report on Form 8-K, filed August 4, 1999.

(b) Reports on Form 8-K

We filed a Form 8-K on December 15, 1999 to revise the factors included under "Risk Factors" in Amendment No. 3 to the Company's Registration Statement on Form S-3 (No. 333-86509) and in Post-Effective Amendment No. 2 to the Company's Registration Statement on Form S-3 (No. 333-51625) to comply with the SEC's plain English requirements.

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 24, 2000

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, Director (Principal Executive Officer) | <u>March 24, 2000</u> |
| <u>/s/ James A. Johnson</u> James A. Johnson | Senior Vice President, Finance and Administration, Chief Financial Officer, Treasurer and Secretary (Principal Financial and Accounting Officer) | <u>March 24, 2000</u> |
| <u>/s/ Jeremy L. Curnock Cook</u> Jeremy L. Curnock Cook | Chairman of the Board, Director | <u>March 24, 2000</u> |
| <u>/s/ Jack L. Bowman</u> Jack L. Bowman | Director | <u>March 24, 2000</u> |
| <u>/s/ James D. Grant</u> James D. Grant | Director | <u>March 24, 2000</u> |
| <u>/s/ Louis P. Lacasse</u> Louis P. Lacasse | Director | <u>March 24, 2000</u> |
| <u>/s/ Nelson L. Levy, Ph.D., M.D.</u> Nelson L. Levy, Ph.D., M.D. | Director | <u>March 24, 2000</u> |
| <u>/s/ Mark Richmond, Ph.D.</u> Mark Richmond, Ph.D. | Director | <u>March 24, 2000</u> |