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D GENETICS 1995

Progress Report

Annual Report

1995 FINANCIAL HIGHLIGHTS

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Year Ended December 31, 1995 1994 1993 1992 1991

Results of Operations

Revenues	\$ 842,460	\$ 448,822	\$ 412,076	\$ 548,549	\$ —
Expenses	10,764,744	8,848,167	5,477,588	1,943,011	1,383,154
Net loss	(9,922,284)	(8,399,345)	(5,065,512)	(1,394,462)	(1,383,154)
Net loss per share	(.94)	(1.40)	(3.73)	(1.25)	N.M. ⁽²⁾
Pro forma net loss per share ⁽¹⁾	(.94)	(1.03)	(0.73)	(0.27)	N.M. ⁽²⁾

Financial Condition

Cash, cash equivalents and securities available for sale	\$ 14,442,562	\$ 11,474,787	\$ 6,797,182	\$ 15,266,485	\$ —
Total assets	19,960,460	17,045,881	12,115,184	15,876,914	—
Long-term obligations, including current portion	3,286,508	2,837,370	1,184,706	14,659	—
Shareholders' equity	15,772,836	13,242,145	12,115,184	15,296,537	—

⁽¹⁾ Pro forma net loss per share reflects the assumed conversion of all shares of preferred stock into common stock.

⁽²⁾ N.M.—Not meaningful, as Targeted Genetics was a wholly owned subsidiary of Immunex Corporation until February 1992.

ted four important clinical trials, continued vital research and development
successfully completed a self-managed secondary offering that raised \$12.5
der we're calling this, our second annual report, a Progress Report. In these
I about the important work we did in 1995 and learn how this work fits
mission and objectives. Clearly, there is much work to be done before we
commercial product. Yet we're pleased to report that the progress we made
considerably closer to that goal.

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1995: A year of significant progress.

Progress is defined as "a forward or onward movement to an objective or goal." Nothing could better describe 1995, our first full year as a public company.

The work we did this year addressed the challenges we described in our 1994 annual report: to make clinical progress and expedite early Phase I studies, to scale up manufacturing processes and cell processing capabilities, and to raise additional capital.

Progress on three fronts.

In response to these challenges, our progress in 1995 came in three main areas: clinical development programs, research programs, and business development. You'll find more details about our progress in all three areas later in this report. Here are the highlights.

Clinical development programs. In last year's annual report, we said that we had filed investigational new drug (IND) applications in three areas: for treating cystic fibrosis with an *in vivo* gene therapy delivered using AAV vectors; for treating malignant melanoma with an *ex vivo* IL-7-based tumor vaccine delivered using retroviral vectors; and for treating Gaucher disease with an *ex vivo* stem cell gene therapy delivered using retroviral vectors. In 1995, all of these projects entered their first human clinical trials.

Research programs. Over the past year, our research efforts were focused on improving gene delivery systems based on AAV vectors and retroviral vectors, and on optimizing our proprietary CTL immunotherapy technology. We also continued development of a novel recombinant protein-based non-viral gene delivery (NVGD) system.

Business development. Showing strong support from both new and existing investors, we completed a self-managed public offering that raised \$12.2 million net of expenses. These proceeds provide us with the funds to cover operating costs through 1996. We also substantially improved our AAV manufacturing process, bringing us closer to the large-scale production necessary to supply the expanded clinical trials we are expecting in the near future. In addition, we successfully demonstrated the ability of our Rapid Expansion Method (REM) technology to rapidly expand CTL clones specific for cancer cells. This technology, which is currently being applied to our CTL immunotherapy program for HIV, represents an improvement of at least a hundred-fold over standard methods for T cell clone expansion. Finally, believing it is vital to protect our intellectual properties, we have aggressively filed patents relating to our key technologies.

Our mission is to develop and commercialize proprietary gene and cell therapy products for the treatment of acquired and inherited diseases.

Key point of difference: multiple delivery systems

every	AAV vectors are suitable for diseases in which genes must be delivered to non-dividing or slowly dividing cells, such as cells lining the lungs and arteries.
delivery	Retroviral vectors are suitable for diseases in which target cells are rapidly dividing, such as cancer or AIDS.
delivery	Non-viral vectors may provide greater flexibility related to the size and sequence of transferred genes, and may also allow targeted <i>in vivo</i> delivery.

Differentiate

Differentiation is critical to developing therapies that are both effective and safe. This is the key to successful products. During the year, we differentiated our company in several ways.

Gene therapy platform in gene delivery. Our multiple gene delivery platform allows us to apply our technology to a variety of disease states, providing maximum opportunity for commercial success.

AAV development. We have tremendous promise as a company with distinct advantages in developing delivery systems. In the first clinical trials of AAV, we co-own or have licensed important AAV vector technologies for use in gene therapy applications, plus non-viral delivery, under two patents.

Clinical trials. We have clinical trials in progress for cystic fibrosis, HIV infection, and cancer.

Only company developing cloned, antigen-specific CTLs that target disease-causing cells.

We believe this approach will produce more effective treatments with fewer side effects than therapies currently being tested. Our proprietary cell expansion technology makes this approach commercially feasible.

Alliance with collaborators strengthens our technology base. We maintain active relationships with a number of academic institutions and other collaborators, giving us access to proprietary gene and cell therapy technology. We also have rights to use certain Immunex Corporation technology in the field of gene therapy.

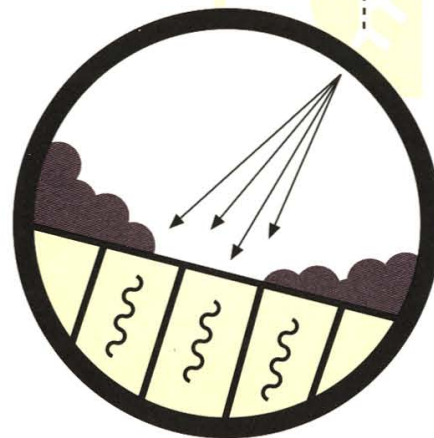
Experienced management team. We have staffed our management team with biotechnology veterans, assembled a multi-disciplinary research team that represents both molecular- and cellular-based sciences, and put together a collaborative network that optimizes our technology base.

Going forward, these strengths position Targeted Genetics well to handle the challenges of successfully bringing gene therapy products to market.

Trial design

Patients in our trial at Johns Hopkins have CF and mild lung disease. They receive a single dose of AAV-CFTR to one side of the nose and placebo to the opposite side. They also receive a single dose of AAV-CFTR administered to one lobe of the right lung.

Cystic fibrosis results from a lack of a functional CFTR gene, which results in build-up of mucus in the lungs, infections and early death. A gene therapy for cystic fibrosis may be possible by delivering the CFTR gene directly to cells on the surface of the lungs. We believe that AAV vectors will be useful for the long-term correction of the cystic fibrosis gene defect.



First human trial of AAV vector in new gene therapy for cystic fibrosis

Johns Hopkins Children's Center Pediatric Clinical Research Unit, Baltimore, Maryland

Objective

Evaluate the safety of the AAV-CFTR vector as part of our overall AAV development goal of correcting the defect in CF respiratory tract cells by producing normal functioning CFTR protein.

Number of patients

This trial is enrolling 12 adult patients. Two patients are treated at each of six escalating dose levels.

Major endpoints

1. Safety.
2. Assessment of *in vivo* gene transfer of the AAV-CFTR vector.
3. Physiologic measurements of CFTR function.

	Research	Preclinical	Phase I	Phase II	Phase III
therapy					
or disease					
nity					
rapy					
or vaccine					
therapy					
se					

5

A second CF trial.

In December 1995, we initiated a second AAV clinical trial. This Phase I/II trial tests our AAV-CFTR vector as a potential gene therapy for chronic sinusitis in patients with cystic fibrosis, the vast majority of whom develop chronic sinus disease. The trial, being conducted at Stanford University, is designed to evaluate the safety of AAV-CFTR and its potential to relieve symptoms of sinusitis.

Significance of trials.

Our two CF trials are significant not only because they are the first human clinical trials of their kind, but also because the information we expect to gather from them will enhance our overall efforts in AAV development. We will be able to apply the knowledge we gain testing AAV in the lung and sinus to other diseases.

Perhaps more importantly, performing two clinical trials simultaneously—at Johns Hopkins and at Stanford—targeting different sites within the respiratory system should allow more rapid clinical development of AAV-CFTR.

Both trials give us an excellent opportunity to rapidly test our AAV vector delivery system because it is relatively straightforward to deliver the vector to the target organs. Also,

the trials give us the opportunity to address, early on, important manufacturing and regulatory issues, and allow us to demonstrate the strengths of our multi-disciplinary approach. All told, our cystic fibrosis trials involve Targeted Genetics researchers and collaborators in the areas of genetics, molecular biology, electrophysiology, immunology, and respiratory physiology.

Evaluating new applications for AAV vector technology.

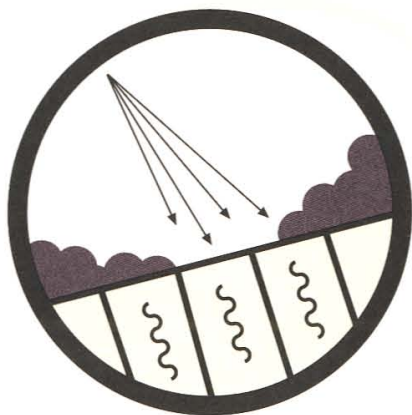
Clinical trials were just one part of our work with adeno-associated virus vectors in 1995. Last year we also initiated several research programs aimed at evaluating new applications for this technology.

One of these programs is focused on using AAV vectors for mucosal delivery of genes via the gastrointestinal tract. A second program, being conducted in collaboration with scientists at North Carolina's Bowman Gray Medical Center, indicates that AAV vectors may be useful for the delivery of genes to certain vascular cell types.

In 1996, we will continue our work in these areas while also exploring opportunities to address other diseases and maximize the value of this delivery system as a platform technology.

We believe that the work we are doing helps move the entire field of gene therapy forward.

The vast majority of patients with cystic fibrosis develop chronic sinus disease, which is caused by thick, sticky mucus clogging the sinuses, rendering them susceptible to sinus infections.



Trial design

Two-part trial. Part one is a Phase I dose escalation trial that evaluates the safety of AAV-CFTR and allows selection of the ideal therapeutic dose for the Phase II component. Part two is a Phase II randomized, double-blind placebo controlled trial in which patients will have AAV-CFTR administered to one sinus and placebo administered to the other sinus.

Making strides in CTL immunotherapy.

In 1995, we completed a Phase I clinical trial of antigen-specific cytotoxic T lymphocytes (CTLs) in patients with human immunodeficiency virus (HIV) infection. While none of the six patients treated in this trial showed any serious adverse events associated with the CTL infusions, persistence of the CTLs was shorter than observed in a trial for cytomegalovirus (CMV) previously performed by one of our collaborators. This shorter persistence was due at least in part to an unexpected immune response to the HyTK safety gene we administered.

Despite shorter persistence, our 1995 trial did provide us with important information. We observed no toxicities; showed we are able to generate HIV-specific CTLs from HIV patients; proved we can grow large numbers of antigen-specific CTLs rapidly using our proprietary Rapid Expansion Method (REM); and demonstrated that a significant proportion of the cloned HIV-specific CTLs do engraft when reinfused into patients. We used this data to design a second Phase I trial, again in patients with HIV.

Second HIV trial.

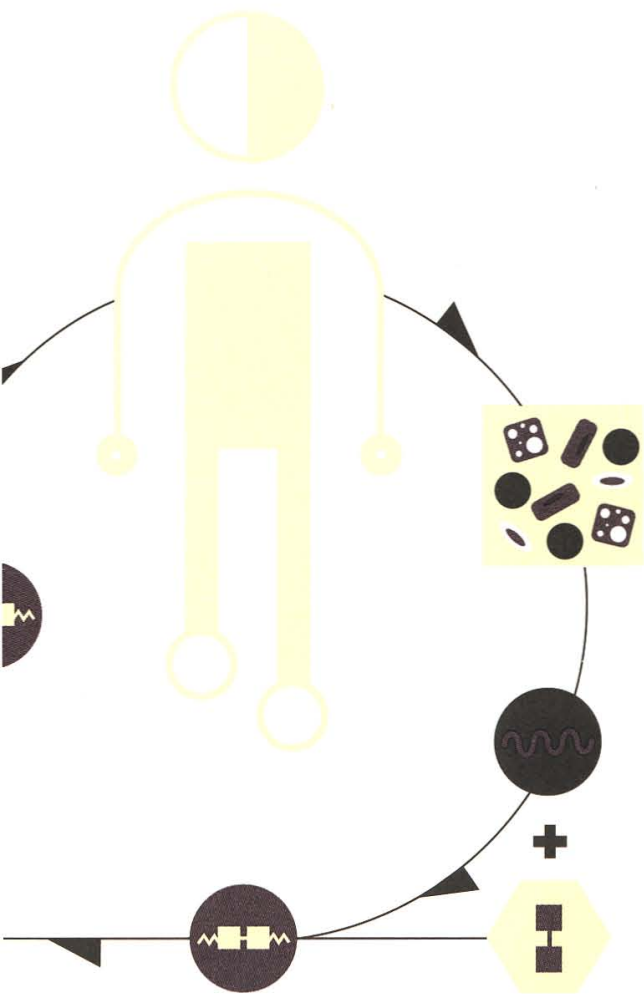
Our second HIV trial will be initiated in the first half of 1996. In this trial, we will administer both unmodified cells and cells marked with a gene which is not known to cause an immune reaction, instead of modifying the CTLs with the HyTK gene. Patients in this second trial will be monitored for safety, *in vivo* persistence, antiviral activity, and generation of an immune response.

Ultimately, data generated from both HIV trials will provide us with information essential for effectively designing follow-on clinical trials.

We believe that the choices we have made as to which diseases to address make sense from both technological and market perspectives.

CTLs play an important role in how the body defends itself against viral pathogens and cancer. By using REM we can rapidly expand CTL clones specific for viral targets such as HIV and CMV, and certain cancers such as malignant melanoma.

CTLs are isolated from the patient's blood, genetically modified to allow tracking of the CTLs in vivo, expanded using Targeted Genetics' proprietary Rapid Expansion Method (REM), and reinfused into the patient.



Objective

Evaluate the safety of IL-7–producing melanoma cells in patients, and evaluate the potential of these cells to enhance tumor-specific immunity.

Number of patients

Up to nine patients are being evaluated. The IL-7 transduced tumor cells are given to patients in three biweekly subcutaneous injections.

Major endpoints

1. Safety.
2. Generation of tumor-specific immunity.
3. Clinical response.

Human clinical trial of interleukin-7 in gene therapy for metastatic malignant melanoma

UCLA Medical Center,
Los Angeles, California

Successes in CTL research.

There were a number of exciting developments in our CTL research last year that have led us to expand our CTL immunotherapy program beyond its original focus on HIV. With REM, our CTL technology becomes a platform for treating a great number of infections and cancers.

We generated data demonstrating that REM can be used to expand CTL clones specific for infected and cancerous cells by more than a thousandfold in less than two weeks. This represents an improvement of at least a hundredfold over standard methods for T cell clone expansion. It's also key to making CTL immunotherapy commercially feasible. To date, we have shown that by using REM we can rapidly expand CTL clones specific for viral targets, such as HIV and CMV, and certain cancers such as malignant melanoma.

Trial design

Patients' melanoma cells are removed and mixed with a melanoma cell line that has been genetically modified with Targeted Genetics' IL-7/HyTK retroviral vector to produce IL-7. The mixture of IL-7–producing cells and patient tumor cells are treated with radiation to prevent growth, then injected back into patients to stimulate the body's anti-tumor immune response.

IL-7 to treat

iated a Phase I trial at the Center, designed to test an IL-7)-based melanoma vaccine with metastatic malignant cancer). IL-7 is a cytokine of the immune system, and is a stimulator of T cells, which plays a role in the elimination of such as cancers or virally induced diseases in animal models have shown that cells genetically modified to produce IL-7 can stimulate an effective immune response against tumors.

human melanoma cell line was infected with IL-7, which is then fused with the patient's own tumor cells to produce a vaccine along with the antigens from the tumor cells. We plan to start the trial later this year.

Expanding CTL immunotherapy.

The importance of this clinical trial is twofold. First, we will investigate the potential of this IL-7 vaccine as a therapeutic product. Second, and even more important to our product development strategy, we will study the immunological activity that is stimulated by the administration of the IL-7 vaccine. Using tumor and blood samples from each patient, we will perform laboratory experiments that may help us identify and characterize CTLs specific for malignant melanoma tumor cells. This is the first step toward expanding our CTL immunotherapy program beyond viral infections into the area of oncology.

At the same time, we are proceeding with additional preclinical research in breast and colon cancers. Using tumor and blood samples from patients treated surgically for these types of cancer, we will be working to isolate CTLs specific to these tumors, expanding them with our REM process, and examining their effects *in vitro* in killing tumor cells. By late 1996, we hope to have generated the data we need to support the move into clinical trials in 1997 using CTL immunotherapy to treat metastatic cancer.

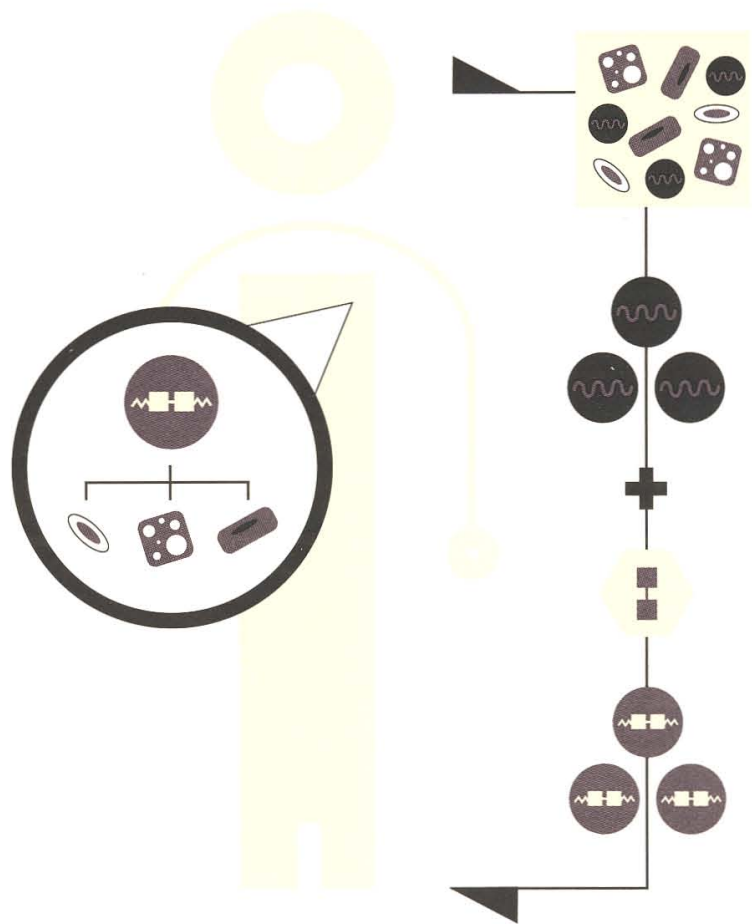
Annual Report

ways believed that one of our greatest strengths is our broad base.

Gaucher disease is one of many inherited diseases affecting blood cells that may be cured using stem cell gene therapy.

Trial design

Peripheral blood cells are collected from patients at the Fred Hutchinson Cancer Research Center, and stem cells—cells from which all blood cells are derived—are purified to enhance transduction using CellPro's CEPRATE® SC Stem Cell Concentration System. Our retroviral vector carrying the glucocerebrosidase (GC) gene and packaged using the PG13 cell line is used to transduce, or transfer, the gene to the purified stem cells in the laboratory. These cells are then reinfused into patients.



Gene therapy trial for Gaucher disease in collaboration with the Fred Hutchinson Cancer Research Center

Fred Hutchinson Cancer Research Center, Seattle, Washington

Objective

Determine the safety of introducing a GC gene into patients' stem cells, and ascertain the extent to which the GC gene persists in the body.

Number of patients

This trial is enrolling five patients.

Major endpoints

1. Safety.
2. Long-term persistence of transduced cells.

ances in stem cell

initiated a Phase I clinical trial of potential stem cell gene therapy for Gaucher disease.

Gaucher disease affects approximately 1 in 500 Americans in varying degrees. The disease is caused by a missing enzyme responsible for producing an enzyme called glucocerebrosidase (GC), and a buildup of lipids in bones and organs. The lipid buildup can cause bone pain, bone damage, enlarged spleen and liver, and—in a small number of cases—lead to death. There is no cure for Gaucher disease.

A Phase I Gaucher disease trial is being conducted by the Fred Hutchinson Cancer Research Center. The purpose of the trial is to determine whether transfer of a normal copy of the gene to patients' peripheral blood stem cells from which all blood cells are derived—is safe, and the extent to which the gene persists in the body.

For the gene transfer, the normal GC gene is packaged inside a proprietary retrovirus produced in a novel packaging cell line called PG13, and then delivered to

blood stem cells. The PG13 retroviral cell line is a cell line that packages high-efficiency vectors for the transduction of human cells, especially blood cells.

Research proves PG13 increases transduction efficiency.

We have achieved significant improvements in transduction efficiencies of human CTL clones using PG13. For stem cells, we achieved an eightfold improvement in transduction frequency compared to that reported by other groups, when genes were delivered using PG13 and a proprietary method for transferring genes to stem cells.

The United States Patent and Trademark Office has issued a patent on PG13, and the cell line has been exclusively licensed to Targeted Genetics. The PG13 technology was developed by Dr. A. Dusty Miller at the Fred Hutchinson Cancer Research Center. Dr. Miller is a recognized leader in the development of viral vectors for use in gene therapy. He is an exclusive collaborator with Targeted Genetics and a member of our scientific advisory board.

Progress in NVGD.

We have always believed that one of our greatest strengths is our broad technology base. In order to continue strengthening this technology base, we have built a significant in-house research effort dedicated to developing our novel recombinant protein-based non-viral gene delivery (NVGD) system. This program is focused on developing a targetable, injectable system that will provide highly efficient transient or stable gene expression, depending upon the disease target.

We are supplementing this effort through academic collaborations and by in-licensing technology. In 1995, we initiated our first NVGD-based research collaboration with scientists at the Fox Chase Cancer Center in Philadelphia.

Moving the business ahead.

Our management is keenly aware of the need to make progress in our business efforts, not just in research and development. In 1995, this progress came in a number of forms.

Self-managed public offering.

In July, we completed a self-managed public offering that raised \$12.2 million, net of expenses, through the sale of 830,598 units at a price of \$15 per unit. Each unit comprised four shares of common stock and a warrant to purchase one additional share of common stock. Our goal was to raise \$10 million from this offering. However, strong investor demand enabled us to increase the size of the offering. The offering brings the total number of outstanding shares of common stock to 12.3 million.

Partnering efforts advanced.

Although we have been successful in raising capital to date, we recognize the value that larger companies can bring to our programs. Corporate partnering can provide not only important financial resources, but also the expertise and infrastructure that will enhance our product commercialization efforts. We are working to establish a major collaboration to develop and commercialize CTL immunotherapy products for infectious diseases and cancer. We're also pursuing partnerships to develop broad-based gene delivery systems to exploit near- and long-term market opportunities for gene therapy products.

We believe that it is possible to combine fiscal responsibility with clinical productivity.

V manufacturing process.

Phase I Small Business
arch (SBIR) grant from the
tes of Health, we have made
rovements in our AAV
technology. Our goal is to
scale manufacturing process
ntly producing commercial
V vectors for the treatment
and other diseases. Efforts
ld pay off significantly over
y lowering the cost of pro-
g the size of manufacturing
tting the amount of capital
edicated to manufacturing

Looking to the future.

We believe the progress we made as
a company in 1995 validates our philosophy
and direction:

That our employees are our biggest advan-
tage and greatest differentiating factor.

That a single delivery system is inadequate
for delivering genes to all cellular targets.

That the work we are doing helps move the
entire field of gene therapy forward.

That the choices we have made as to which
diseases to address make sense from both
technological and market perspectives.

That it is possible to combine fiscal respon-
sibility with clinical productivity.

And above all, that our broad array of
proprietary technologies, strong science
foundation, and long-term perspective
make us uniquely qualified to meet the
challenges that lie ahead.



course, moving ahead.

field of gene therapy right now?" That's a question all of us at Targeted Genetics
e days. It's not surprising. There's a great deal of confusion about gene therapy,
and its promise. Yet I believe our recent work provides a clear answer to

all about progress. Not breakthrough progress, but solid incremental progress
ult of sound decisions and thorough research. This is the kind of well-founded
es to advance gene therapy products from the laboratory to the marketplace, for
n which it does not pay to rush.

e, the progress we made in 1995 is impressive for a company of our size and age.
lved in initiating three different types of clinical trials applying multiple technolo-
better prepared than ever before to move ahead; to take science and put it in
o design better delivery systems and products.

ost important progress we made in 1995 was demonstrating our ability to move
a series of fronts at once. Not only did we address the challenges inherent in
trials, but we also handled a number of manufacturing and regulatory issues—
ing a wide range of research programs.

to point out the long and careful preclinical work we completed before entering
that are described elsewhere in this report. For instance, we did not move ahead
c fibrosis trials until we were convinced that our preclinical data had demon-
potential as a therapeutic product. Similarly, we waited to begin our stem cell gene
Gaucher disease until we were sure we had the best available vector. It's all part
at making important advancements in the business of gene therapy means using
echnology responsibly.

At the same time, we recognize that beginning the clinical phase of research is more critical in gene and cell therapy than in many other fields of drug development because animal models are, in many cases, inadequate for obtaining the kind of information we need to move forward. At some point, we simply need to get in and find out how useful our therapies are in humans; these clinical trials are vital to setting the future direction of our efforts.

As with any Phase I trial, safety is the primary goal of the trials we initiated in 1995. We'll be attempting to show that the treatments do not cause undesirable side effects. We also hope to establish the effectiveness of our vectors at doing what they are designed to do: introduce into target cells genes that persist for an adequate length of time.

Clinical trials are now underway in each of our product development programs: *in vivo* AAV gene therapy, CTL immunotherapy, and stem cell gene therapy. In each case, in addition to addressing a specific disease, we are generating valuable new information about our basic gene and cell therapy technology. This will help us to better focus resources toward programs that have the most promise.

I believe that our broad technology base represented by these trials will prove to be essential to successfully building our business. In the case of gene therapy, our multiple gene delivery system approach will provide us with the tools for delivering genetic material to many different cell types. Our company is proud of the fact that in the four clinical trials we started in 1995, we used three different gene delivery systems. This is particularly impressive considering that only two other types of viral gene delivery systems had been used in some 150 gene therapy clinical trials up to that point. In the case of cell therapy, our CTL immunotherapy program provides a platform for addressing a wide array of infectious diseases and cancers.

I also believe that our broad technology base gives us a better perspective on overall issues involved with gene therapy and cell therapy. These are fields in which success depends on the involvement of an enormous array of disciplines, a fact that is reflected in the multi-disciplinary nature of our internal research team and our scientific advisory board.

Research is at the very heart of what we do as a company. In addition to providing the thorough groundwork that led to our clinical trials, our researchers furthered their science in a number of ways. For

g 1995, we made significant improvements to our stem cell transduction process, effectively percentage of cells we can genetically modify.

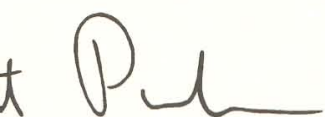
ated data demonstrating that our proprietary Rapid Expansion Method (REM) can be used clones specific for infected and cancerous cells by greater than a thousandfold in less than is represents a tremendous improvement over standard methods for expansion of T cell Furthermore, is the key to making disease-specific T cell therapy commercially feasible.

Also made important progress in the areas of vector manufacturing and development, which ability to provide the quantities of vectors required for expanded gene therapy clinical completed the buildout and startup of a new manufacturing process development laboratory ate headquarters. We are working on a clinical cell processing facility and quality control will allow us to aggressively expand our CTL immunotherapy program.

ult market, we successfully completed a \$12.5 million equity offering, which was 25 percent d. This wholly self-managed offering not only provided capital to help fund our company's ough the end of 1996, but also broadened our shareholder base.

o look at gene therapy and cell therapy as long-term propositions. At the same time, we optimistic about our ability to develop treatments for diseases for which there are no Our dedicated team of employees, our broad technology base, and our developing ability ds for gene and cell therapy clinical trials make us well-prepared to move our products zation.

come in 1996. But the progress we made in 1995 makes us more confident than ever that



ker

Chief Executive Officer

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL
CONDITION AND RESULTS OF OPERATIONS

Overview

Targeted Genetics Corporation, a development stage company, was incorporated in March 1989 as a wholly owned subsidiary of Immunex Corporation. The Company's activities were carried out as a project within Immunex through December 31, 1991. In 1992, the Company began to operate independently from Immunex and raised \$16.6 million, net of expenses, in a private placement of preferred stock. The Company subsequently raised an additional \$23.8 million in two public offerings of common stock. Currently, the Company has no significant revenue sources other than interest income earned on investments, and it has generated an accumulated deficit of \$27.6 million through December 31, 1995. It is not anticipated that the Company will have any product-related revenues for a number of years. Accordingly, the Company expects to generate substantial additional losses in the future attributable to the continuation of preclinical and clinical research programs, development of manufacturing capabilities and the preparation for commercialization of its products under development.

Results of Operations

Investment and other income increased significantly for the year ended December 31, 1995, over the amount reported for 1994. The increase was attributable to a higher average investment balance during the year and higher rates of return on those balances. In 1995, the Company earned other income of \$174,625 from R&D arrangements.

Research and development expenses increased significantly for the year ended December 31, 1994, compared with 1993. For the two years ended December 31, 1994, the increase in research and development expense was largely due to the emphasis on supporting the advancement of clinical, manufacturing process development and regulatory programs. The increase in research and development expenses in 1995 was largely attributable to continued expansion of manufacturing process development expertise and other nominal increases in research, clinical and regulatory expenses, including staffing. Research and development expenses will continue to increase in the future, especially as related to clinical trials. Continued growth, however, is dependent on the availability of capital.

General and administrative expenses also increased significantly for the year ended December 31, 1994, compared with 1993. The Company added crucial administrative staff in the areas of business development, finance, human resources and facility management to support research and development activities. During 1994, the Company also experienced an increase in expenses associated with being a publicly traded company. For the year ended December 31, 1995, the Company experienced modest growth in general and administrative expenses compared with 1994. The growth was related to an increase in corporate development activities and, to a lesser extent, additional administrative staffing. Over the three years presented, the increase in general and administrative expenses has roughly tracked the rate of increase in research and development spending. The Company expects this relationship to continue in future years.

egan incurring interest expense in 1994 related to equipment financing transactions. The sub- for the year ended December 31, 1995, versus 1994, is due to an increased level of equip- It is expected that the Company will continue to finance equipment purchases if favorable ble.

Capital Resources

1, 1995, the Company had cash, cash equivalents and securities available for sale totaling \$14.4 ed to \$11.5 million at December 31, 1994. The increase was primarily attributable to the com- -managed stock and warrant offering, which resulted in net proceeds of \$12.2 million in July pany also completed equipment financing transactions totaling \$1.1 million during 1995. increases, the Company used \$8.5 million to fund its operations, \$1.4 million for purchases boratory expansion and acquisition of technology and patent rights and \$0.7 million for pay- uipment leases and notes.

expects that its cash needs will continue to increase in future periods due to expansion l development programs, increased clinical trial activity, growth of administrative staff and facilities to accommodate increased numbers of employees. Accordingly, the Company will bstantial additional funds to continue development and commercialization of its products. The re cash requirements will be affected by results of research and development, preclinical stud- rials; acquisition of products or technology, if any; relationships with corporate collaborators, tion of the Company's research and development programs; competing technological and ments; the time and costs of manufacturing scale-up and commercialization activities; and

estimates that, at its current rate of spending, its existing cash, cash equivalents and securities e will be sufficient to meet capital requirements through the end of 1996. In order to strength- tion, the Company is aggressively pursuing agreements with corporate partners that would h and development funding and equity investment. Also, up to approximately \$4.0 million of l would be provided if warrant holders were to exercise outstanding warrants. Depending on ns, the Company may also seek additional sources of public or private equity capital. There ance, however, that adequate funds will be available when needed or will be available on terms Company.

BALANCE SHEETS

December 31,	1995	1994
Assets		
Current assets:		
Cash and cash equivalents	\$ 2,154,814	\$ 2,306,979
Securities available for sale	12,287,748	9,167,808
Deposits, prepaid expenses and other	196,150	254,225
Total current assets	14,638,712	11,729,012
Property, plant and equipment, net	4,959,502	5,038,812
Other assets	362,246	278,057
	<u>\$ 19,960,460</u>	<u>\$ 17,045,881</u>
Liabilities and Shareholders' Equity		
Current liabilities:		
Accounts payable	\$ 564,403	\$ 704,804
Accrued payroll and other liabilities	336,713	261,562
Current portion of long-term obligations	881,210	584,371
Total current liabilities	1,782,326	1,550,737
Long-term obligations	2,405,298	2,252,999
Commitments		
Shareholders' equity:		
Preferred stock, \$.01 par value, 6,000,000 shares authorized, none outstanding	—	—
Common stock, \$.01 par value, 40,000,000 shares authorized, 12,317,183 and 8,958,831 outstanding at December 31, 1995 and 1994, respectively	43,295,436	31,024,884
Unrealized gains (losses) on securities available for sale	66,319	(116,104)
Deficit accumulated during development stage	(27,588,919)	(17,666,635)
Total shareholders' equity	15,772,836	13,242,145
	<u>\$ 19,960,460</u>	<u>\$ 17,045,881</u>

See accompanying notes to financial statements.

S OF OPERATIONS

	1995	1994	1993	Period from 3-9-89 (date of inception) through 12-31-95
Income	\$ 667,835	\$ 448,822	\$ 412,076	\$ 2,077,282
	174,625	—	—	174,625
Expenses	842,460	448,822	412,076	2,251,907
Research and development	8,194,913	6,763,549	4,261,154	22,771,120
Administrative	2,267,516	1,891,947	1,216,434	6,574,720
	302,315	192,671	—	494,986
Other expenses	10,764,744	8,848,167	5,477,588	29,840,826
	\$ (9,922,284)	\$ (8,399,345)	\$ (5,065,512)	\$ (27,588,919)
Net income (loss)	\$ (0.94)	\$ (1.40)	\$ (3.73)	
Weighted average number of shares outstanding	10,532,950	6,005,141	1,359,840	
Weighted average number of shares outstanding, assuming conversion of convertible preferred stock to common stock:				
Basic	\$ (0.94)	\$ (1.03)	\$ (0.73)	
Diluted	10,532,950	8,151,547	6,955,826	

See notes to financial statements.

STATEMENTS OF SHAREHOLDERS' EQUITY

Period from March 9, 1989 (date of inception) through December 31, 1995	Preferred stock	Common stock	Advances from Immunex	Unrealized gains (losses) on securities available for sale	Deficit accumulated during development stage	Total shareholders' equity
Net loss from March 9, 1989 (date of inception) through December 31, 1991	\$ —	\$ —	\$ 2,807,316	\$ —	\$ (2,807,316)	\$ —
Sale of 1,080,000 shares of common stock	—	27,600	—	—	—	27,600
Issuance of 1,920,000 shares of Series A preferred stock to Immunex in repayment of advances	2,807,316	—	(2,807,316)	—	—	—
Sale of 3,675,986 shares of Series B preferred stock, net of issuance costs of \$772,415	16,597,399	—	—	—	—	16,597,399
Issuance of 120,000 shares of common stock as compensation	—	66,000	—	—	—	66,000
Net loss — 1992	—	—	—	—	(1,394,462)	(1,394,462)
Balance at December 31, 1992	19,404,715	93,600	—	—	(4,201,778)	15,296,537
Net loss — 1993	—	—	—	—	(5,065,512)	(5,065,512)
Balance at December 31, 1993	19,404,715	93,600	—	—	(9,267,290)	10,231,025
Sale of 2,154,345 shares of common stock in initial public offering, net of issuance costs of \$1,404,056	—	11,522,014	—	—	—	11,522,014
Conversion of Series A and B preferred stock to 5,595,986 shares of common stock	(19,404,715)	19,404,715	—	—	—	—
Exercise of stock options	—	4,555	—	—	—	4,555
Unrealized losses on securities available for sale	—	—	—	(116,104)	—	(116,104)
Net loss — 1994	—	—	—	—	(8,399,345)	(8,399,345)
Balance at December 31, 1994	—	31,024,884	—	(116,104)	(17,666,635)	13,242,145
Sale of 3,322,392 shares of common stock and 830,598 warrants, net of issuance costs of \$214,509	—	12,244,461	—	—	—	12,244,461
Exercise of stock options	—	26,091	—	—	—	26,091
Unrealized gains on securities available for sale	—	—	—	182,423	—	182,423
Net loss — 1995	—	—	—	—	(9,922,284)	(9,922,284)
Balance at December 31, 1995	\$ —	\$ 43,295,436	\$ —	\$ 66,319	\$ (27,588,919)	\$ 15,772,836

See accompanying notes to financial statements.

STATEMENTS OF CASH FLOWS

December 31,	1995	1994	1993	Period from 3-9-89 (date of inception) through 12-31-95
Operating activities:				
Net loss	\$ (9,922,284)	\$ (8,399,345)	\$ (5,065,512)	\$ (27,588,919)
Adjustments to reconcile net loss to net cash used in operating activities:				
Compensation expense on common stock issuance	—	—	—	66,000
Depreciation and amortization	1,484,549	1,264,848	411,652	3,162,881
Increase in deposits, prepaid expenses and other	(49,865)	(161,827)	(8,610)	(295,290)
(Increase) decrease in accrued interest on securities available for sale	(9,287)	(29,750)	124,180	(82,928)
Increase (decrease) in current liabilities	(17,955)	88,493	133,735	769,991
Net cash used in operating activities	(8,514,842)	(7,237,581)	(4,404,555)	(23,968,265)
Investing activities:				
Purchases of property, plant and equipment	(1,335,876)	(885,604)	(4,546,933)	(7,170,597)
Purchases of securities available for sale	(13,047,852)	(12,990,428)	(8,770,199)	(55,090,522)
Sales of securities available for sale	10,119,622	9,369,127	14,049,110	42,952,020
Increase in other assets	(76,500)	(177,500)	(199,749)	(574,179)
Net cash provided by (used in) investing activities	(4,340,606)	(4,684,405)	532,229	(19,883,278)
Financing activities:				
Advances from Immunex	—	—	—	2,807,316
Net proceeds from sale of capital stock	12,270,552	11,526,569	—	40,422,120
Proceeds from equipment financing	1,089,789	1,950,391	806,114	3,846,294
Payments under capital leases and installment loans	(657,058)	(412,315)	—	(1,069,373)
Net cash provided by financing activities	12,703,283	13,064,645	806,114	46,006,357
Net increase (decrease) in cash and cash equivalents	(152,165)	1,142,659	(3,066,212)	2,154,814
Cash and cash equivalents, beginning of period	2,306,979	1,164,320	4,230,532	—
Cash and cash equivalents, end of period	\$ 2,154,814	\$ 2,306,979	\$ 1,164,320	\$ 2,154,814
Supplemental disclosures of non-cash investing and financing activities:				
Deferred sales tax on leasehold improvements and equipment	\$ 16,407	\$ 114,589	\$ 363,933	\$ 509,588
Preferred stock issued to Immunex in payment of advances	\$ —	\$ —	\$ —	\$ 2,807,316

See accompanying notes to financial statements.

NOTES TO FINANCIAL STATEMENTS

1. Organization

Targeted Genetics Corporation (the "Company") is developing gene therapy products for the treatment of certain acquired and inherited diseases. As a development stage company, the Company has devoted substantially all of its efforts to date to conducting research and development activities, recruiting personnel and raising capital.

The Company was incorporated in the state of Washington in March 1989 as a wholly owned subsidiary of Immunex Corporation ("Immunex"). In February 1992, the Company issued 1,920,000 shares of Series A convertible preferred stock to Immunex in exchange for the grant of a license to certain technology, settlement of advances from Immunex and cancellation of 40,000 shares of common stock issued by the Company to Immunex on March 28, 1989. At December 31, 1995, Immunex held 21% of the outstanding stock of the Company.

The Company estimates that, at its current rate of expenditures, its existing cash, cash equivalents and securities available for sale will be sufficient to meet operating requirements through the end of 1996. Accordingly, the Company is pursuing one or more collaborative arrangements with corporate partners, with the intent of generating both research and development funding and equity capital. The Company may also elect to seek additional equity capital via the public or private markets, depending on market conditions.

2. Summary of Significant Accounting Policies

Cash Equivalents

The Company considers all short-term investments with a purchased maturity of three months or less to be cash equivalents. Cash equivalents, valued at cost which approximates market, consist principally of money market accounts and short-term government obligations.

Securities Available for Sale

Securities available for sale consist primarily of corporate debt securities and U.S. Government notes, all of which mature within two years. Management currently classifies the Company's entire investment portfolio, other than cash equivalents, as securities available for sale. Such securities are stated at market value, with the unrealized gains and losses included in 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.

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, ranging from five 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.

Net Loss Per Share

Net loss per share is computed based upon the weighted average number of common shares outstanding during the period. Common equivalent shares are not included in the computation because the effect of their inclusion would be antidilutive, except that, in accordance with Securities and Exchange Commission

Common equivalent shares issued during the twelve months prior to the Company's initial public offering have been included in the calculation as if they were outstanding for all periods through

the date of the Company's initial public offering, all 5,595,986 shares of preferred stock converted to common stock. Unaudited pro forma net loss per share reflects the assumption that all such shares had been common stock as of the beginning of the periods reported.

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.

Securities Available for Sale

Securities available for sale consist of the following:

	Amortized cost	Gross unrealized gains	Gross unrealized losses	Market value
1995:				
Equity securities	\$ 2,473,549	\$ 8,803	\$ —	\$ 2,482,352
Debt obligations	9,747,880	57,516	—	9,805,396
	<u>\$ 12,221,429</u>	<u>\$ 66,319</u>	<u>\$ —</u>	<u>\$ 12,287,748</u>
1994:				
Equity securities	\$ 3,349,999	\$ 2,961	\$ 34,653	\$ 3,318,307
Debt obligations	5,933,913	—	84,412	5,849,501
	<u>\$ 9,283,912</u>	<u>\$ 2,961</u>	<u>\$ 119,065</u>	<u>\$ 9,167,808</u>

Net gains on sales of securities available for sale totaled \$25,047 and \$15,901, and the gross unrealized gains totaled \$48,013 and \$55,576 in 1995 and 1994, respectively.

Property and Equipment

Property and equipment consist of the following:

	1995	1994
Equipment	\$ 3,862,632	\$ 2,835,223
Intangible assets	3,948,678	3,608,599
	<u>7,811,310</u>	<u>6,443,822</u>
Accumulated depreciation and amortization	<u>2,851,808</u>	<u>1,405,010</u>
	<u>\$ 4,959,502</u>	<u>\$ 5,038,812</u>

The Company has leased furniture and equipment, primarily laboratory equipment, under three capital leases. The total cost of furniture and equipment leased at December 31, 1995 and 1994 was \$2,655,998 and \$2,009,604, respectively, with related accumulated depreciation of \$1,076,712 and \$489,541 at December 31, 1995 and 1994, respectively.

At December 31, 1995 and 1994, the Company had pledged furniture and equipment, having a total cost of \$853,900 and \$616,441, respectively, as collateral under an installment loan agreement. Accumulated depreciation related to these assets was \$221,410 and \$63,911 at December 31, 1995 and 1994, respectively.

5. Long-Term Obligations

Long-term obligations consist of the following:

December 31,	1995	1994
Deferred state sales tax	\$ 509,588	\$ 493,181
Installment note payable, effective rate of 16.73%, due in monthly installments through 1999	822,214	741,004
Capitalized lease obligations (see note 7)	1,954,706	1,603,185
	3,286,508	2,837,370
Less current portion	881,210	584,371
	<u>\$ 2,405,298</u>	<u>\$ 2,252,999</u>

The state of Washington granted the Company a deferral of state sales tax on new construction and equipment used in research and development activities. The related obligation is payable over six years beginning in 1996.

Principal payments related to long-term obligations for each of the five years ending December 31, 2000 are \$881,210, \$1,024,238, \$658,800, \$430,932 and \$162,539, respectively.

6. Shareholders' Equity

Common Stock

The Company sold 1,200,000 shares of common stock to its scientific advisors and founders in February and November 1992. The Company has the right to repurchase certain of these shares in the event the holder's relationship with the Company terminates. The repurchase rights expire in annual increments ending in 1996. The shares were sold at prices ranging from \$0.03 to \$0.55 per share. At December 31, 1995, 216,000 shares were subject to repurchase at the original sales price.

Stock Options

The Company has adopted two stock option plans under which 1,520,000 shares of common stock were reserved for issuance. Generally, options vest in annual increments over a three- or five-year period. All options expire ten years from date of grant. Options have been granted at market value or, prior to the Company's initial public offering, at fair value at the date of grant as established by the Company's Board of Directors. As of December 31, 1995, options on 268,620 shares were exercisable and 443,123 shares were available for future grant.

activity related to the Company's stock option plans follows:

	Shares Under Option	Option Price
January 1, 1995	838,000	\$0.50–6.25
	(22,860)	0.55–6.25
	253,237	4.00–5.13
	(35,960)	0.50–5.00
December 31, 1995	<u>1,032,417</u>	<u>\$0.50–6.25</u>

The Company issued warrants to purchase 830,598 shares in conjunction with an offering of its common stock. The warrants are immediately exercisable at a price of \$4.68 per share, expiring July 1997. The Company issued a total of 62,016 warrants related to equipment financing agreements. The warrants have an exercise price of \$6.00 per share and expire from May 1999 to December 2003. At December 31, 1995, 1,032,417 shares of common stock were reserved for these warrants.

Leases

The Company leases its research and office facility under a noncancellable operating lease which expires December 31, 1997. The lease may be extended under three five-year renewal options at the then prevailing fair market rate.

Rental payments under noncancellable leases at December 31, 1995 are as follows:

	Operating	Capital
December 31:		
	\$ 433,880	\$ 873,814
	457,446	873,814
	474,233	303,740
	119,607	358,866
	<u>—</u>	<u>—</u>
Lease payments	<u>\$1,485,166</u>	2,410,234
Presenting interest		<u>455,528</u>
Minimum capitalized lease payments		<u>\$1,954,706</u>

The amount of expense for operating leases for the years ended December 31, 1995, 1994 and 1993 was \$396,220, \$56,354, respectively.

8. Income Taxes

At December 31, 1995, the Company had net operating loss carryforwards of approximately \$24.2 million and research and experimental credit carryforwards of approximately \$817,000. The carryforwards are available to offset future federal income taxes and begin to expire in 2007. At December 31, 1995 and 1994, the Company recognized a valuation allowance to offset deferred tax assets due to the uncertainty of realizing the related benefits.

Significant components of the Company's deferred tax assets are as follows:

December 31,	1995	1994
Deferred tax assets:		
Net operating loss carryforwards	\$ 8,223,000	\$ 5,162,000
Research and experimental credit carryforwards	817,000	654,000
Depreciation	156,000	29,000
Other	54,000	55,000
Total deferred tax assets	\$ 9,250,000	\$ 5,900,000
Valuation allowance for deferred tax assets	\$ 9,250,000	\$ 5,900,000

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 (a development stage company) as of December 31, 1995 and 1994, and the related statements of operations, shareholders' equity and cash flows for each of the three years in the period ended December 31, 1995 and the period from March 9, 1989 (date of inception) through December 31, 1995. 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 generally accepted auditing standards. 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 (a development stage company) at December 31, 1995 and 1994, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1995 and the period from March 9, 1989 (date of inception) through December 31, 1995 in conformity with generally accepted accounting principles.

Seattle, Washington
February 9, 1996

Ernst & Young LLP

Scientific Advisory Board

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Vice President, Director
Department of Molecular Biology
Immunex R & D Corporation

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Research Center

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Research Laboratories
University of Washington School of Medicine

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Head of Division of Medical Genetics
Director of Markey Molecular
Medicine Center
University of Washington

Independent Auditors

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999 Third Avenue, Suite 3500
Seattle, Washington 98104

General Counsel

Perkins Coie
1201 Third Avenue
Seattle, Washington 98104

SEC Form 10-K

A copy of the Company's annual report to the Securities and Exchange Commission on Form 10-K is available without charge upon written request to the Investor Relations Department at the corporate headquarters.

Corporate Headquarters

1100 Olive Way, Suite 100
Seattle, Washington 98101
206/623-7612

Transfer Agent and Registrar

Communications concerning transfer requirements, lost certificates and changes of address should be directed to the Transfer Agent:

First Interstate Bank of Washington, N.A.
800/522-6645

Shareholder Inquiries

Inquiries regarding the Company and its activities may be directed to the Investor Relations Department at the corporate headquarters.

Targeted Genetics' news releases are available via automated Fax Back through Company News On-Call at 800/758-5804, ext. 832075. The Company's news releases are also available on the Web at:
<http://www.prnewswire.com>.

Price Range of Common Stock

The Company's initial public offering was completed in May 1994. From that date, the Company's common stock has traded on the Nasdaq National Market tier of the Nasdaq Stock Market under the symbol TGEN. At March 1, 1996, there were approximately 1,000 holders of the Company's common stock. The Company has never paid cash dividends and does not anticipate paying them in the foreseeable future. The following table sets forth for each calendar quarter indicated, the high and low sale prices for the Company's common stock.

1994	High	Low
Second Quarter (from May 20, 1994)	7 ¹ / ₈	5 ⁵ / ₈
Third Quarter	6 ¹ / ₈	3 ¹³ / ₁₆
Fourth Quarter	5 ³ / ₄	3 ³ / ₄
1995	High	Low
First Quarter	6 ³ / ₈	3 ⁷ / ₈
Second Quarter	5 ⁵ / ₈	3 ¹ / ₂
Third Quarter	6 ¹ / ₂	3 ⁵ / ₈
Fourth Quarter	5 ⁵ / ₈	3 ³ / ₄

Design: The Leonhardt Group
Copy: Words, Seattle, Washington
Photography: Davis Freeman

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