

TARGETED GENETICS CORP /WA/
Form 424B5
February 03, 2004

PROSPECTUS SUPPLEMENT
(To Prospectus dated August 21, 2003)

10,854,257 SHARES

Common Stock

We are offering up to 10,854,257 shares of our common stock. In connection with this offering, we will pay fees to the placement agents. See "Plan of Distribution" beginning on page S-15 of this prospectus supplement for more information regarding these arrangements.

Our common stock is quoted on the Nasdaq SmallCap Market under the symbol TGEN. On January 30, 2004, the last reported sales price of our common stock on the Nasdaq SmallCap Market was \$2.55 per share.

Our business and an investment in our common stock involves significant risks. These risks are described under the Risk Factors beginning on page S-7 of this prospectus supplement and on page 5 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement and/or the accompanying prospectus. Any representation to the contrary is a criminal offense.

| | <u>Per share</u> | <u>Maximum Offering</u> |
|----------------------------------|------------------|-----------------------------|
| Public offering price | \$ <u>2.350</u> | \$ <u>25,507,504</u> |
| Placement agents' fee | \$ <u>0.141</u> | \$ <u>1,530,450</u> |
| Proceeds, before expenses, to us | \$ <u>2.209</u> | \$ <u>23,977,054</u> |

We estimate the total expenses of this offering, excluding the placement agents' fee, will be approximately \$200,000. The placement agents are not required to sell any specific number or dollar amount of the shares of common stock offered by this offering, but will use their best efforts to sell the shares of common stock offered. The offering will end on or prior to February 5, 2004. Pursuant to an escrow agreement between us, the placement agents and an escrow agent, certain funds received in payment for the shares sold in this offering will be wired to an interest bearing escrow account and held until we and the placement agents notify the escrow agent that the offering has closed, indicating the date on which the shares are to be delivered to the purchasers and the proceeds are to be delivered to us. Because there is no minimum offering amount required as a condition to closing in this offering, the actual public offering amount, placement agents' fee and net proceeds to us, if any, in this offering are not presently determinable and may be substantially less than the maximum offering amounts set forth above.

SG Cowen

Roth Capital Partners

January 30, 2004

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The purpose of this prospectus supplement is to provide supplemental information regarding Targeted Genetics Corporation in connection with the offering. You should read this prospectus supplement, along with the accompanying prospectus, carefully before you invest. Both documents contain important information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus.

You should rely only on information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference in this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with information that is different. We are offering the common stock only in jurisdictions where such offers are permitted. The information contained in this prospectus supplement and the accompanying prospectus is accurate only as of their respective dates, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a shelf registration statement that we have filed with the Securities and Exchange Commission, or SEC. Each time we sell our common stock under the accompanying prospectus we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the price, the amount of common stock being offered and the plan of distribution. The shelf registration was declared effective by the SEC on August 21, 2003. This prospectus supplement describes the specific details regarding this offering, including the price, the amount of common stock being offered, the risks of investing in our common stock and the placement arrangements. The accompanying prospectus provides general information about us, some of which, such as the section entitled Plan of Distribution, may not apply to this offering.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or the information incorporated by reference, you should rely on this prospectus supplement. You should read both this prospectus supplement and the accompanying prospectus together with

the additional information about Targeted Genetics to which we refer you in the section of this prospectus entitled "Where You Can Find More Information."

TARGETED GENETICS CORPORATION

This summary does not contain all the information about Targeted Genetics Corporation that may be important to you. You should read the more detailed information and financial statements and related notes that are incorporated by reference and are considered to be a part of this prospectus supplement.

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

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

We have an AAV-based product candidate under development for treating cystic fibrosis that has been evaluated in a Phase II clinical trial. In June 2003, we announced the final results of this Phase II trial. Final data from this repeat dosing trial indicate that our cystic fibrosis product candidate met safety and tolerability targets. In addition, final data from the Phase II trial indicate statistically significant improvement in lung function, decreases in levels of inflammatory cytokines and transfer of the gene targeted for delivery into cells of the lung. In July 2003, we initiated a larger confirmatory Phase II clinical trial for this cystic fibrosis product candidate. We designed this trial to enroll up to 100 patients and are conducting it in collaboration with the Cystic Fibrosis Foundation, or CF Foundation. We also are developing an AAV-based vaccine candidate for high-risk populations to protect against the progression of HIV infection to AIDS in partnership with the International AIDS Vaccine Initiative, or IAVI, a public health organization. In June 2003, we announced preclinical results that supported commencement of clinical trials of our AIDS vaccine candidate and our rheumatoid arthritis product candidate. In December 2003, we initiated a Phase I initial dose escalation safety study in humans for our AIDS vaccine

product candidate in Belgium. We designed this clinical trial to enroll up to 50 volunteers who are uninfected with HIV and in good health. Each subject in this study will receive a single injection of the vaccine candidate and they will be monitored for safety and immune response. In January 2004, we received regulatory approval from the U.S. Food and Drug Administration, or FDA, and Health Canada to begin our rheumatoid arthritis candidate Phase I clinical trial. We plan to dose the first patient during the first quarter of 2004. The rheumatoid arthritis product candidate trial will be conducted in up to 32 patients at up to eight sites in the US and Canada. We expect patient accrual in this study to be completed by the first quarter of 2005.

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We suspended further development of our cancer and hemophilia programs until we can find development partners to help fund development costs or find other sources of funding for the programs.

We believe that our successes in assembling a broad platform of proprietary intellectual property for developing and manufacturing potential products supports our potential to develop and manufacture gene therapy product candidates to treat a range of diseases. We have developed processes to manufacture our potential products, and the products of third parties, at a scale amenable to clinical development and expandable to large-scale production for advancing our potential products to clinical evaluation and commercialization. In March 2003, we entered into a manufacturing services agreement with GenVec Inc., or GenVec, to conduct initial feasibility studies to evaluate our ability to manufacture GenVec's cancer product candidate, TNFerade. In October 2003, we successfully completed the feasibility study and began manufacturing TNFerade for clinical use, which we completed in January 2004.

A wide range of diseases potentially may be treated, or prevented, with gene-based products, including cancer, genetic diseases and infectious diseases. We believe that there is also a significant opportunity to treat diseases currently treated using recombinant DNA proteins and monoclonal antibodies or small molecules that may be more effectively treated by gene-based therapies due to their ability to provide a long-term or a localized method of treatment. Our business strategy is to develop multiple gene delivery systems, which we believe will maximize our product opportunities. Using these gene delivery systems, we are developing product candidates across multiple diseases with the belief that gene-based therapies may provide a means to treat disease not achievable with current biologic and pharmaceutical drugs. We believe that, if successful, we can establish significant market potential for our product candidates. Because there are no commercially available gene therapy products in the U.S., we intend to pursue product development programs to enable us to demonstrate proof of concept and eventually commercialize gene-based therapeutics to address currently unmet medical needs in treating disease.

The development of pharmaceutical products involves extensive preclinical development, followed by human clinical trials that take several years or more to complete. The length of time required to completely develop any product candidate varies substantially according to the type, complexity and novelty of the product candidate, the degree of involvement by a development partner and the intended use of the product candidate. Our commencement and rate of completion of clinical trials may vary or be delayed for many reasons, including those discussed in the section of this prospectus supplement entitled Risk Factors.

We were incorporated in the state of Washington in 1989. Our executive offices are located at 1100 Olive Way, Suite 100, Seattle, Washington 98101, and our telephone number is (206) 623-7612. In this prospectus supplement, references to Targeted Genetics include our subsidiaries.

For more information about Targeted Genetics, you should read the accompanying prospectus and the information described in the section of this prospectus supplement entitled Where You Can Find More Information, including our consolidated financial statements and related notes.

In this prospectus supplement, Targeted Genetics, we, us and our refer to Targeted Genetics Corporation and its subsidiaries.

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THE OFFERING

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|--|--|
| Common stock offered by Targeted Genetics | 10,854,257 shares |
| Common stock to be outstanding after this offering | 77,054,887 shares |
| Use of proceeds | For working capital and other general corporate purposes |
| Nasdaq SmallCap Market symbol | TGEN |

The number of shares of common stock to be outstanding after this offering is based on 66,200,630 shares outstanding on September 30, 2003. It excludes:

4,143,924 shares of common stock issuable upon exercise of options outstanding as of September 30, 2003, of which 2,479,524 shares are exercisable, under our 1992 Restated Stock Option Plan, our Stock Option Plan for Non-employee Directors, our 1999 Stock Option Plan and our 2000 Genovo, Inc. Roll-over Stock Option Plan at a weighted average exercise price of \$3.68 per share; and

365,826 shares available for grant as of September 30, 2003 under our stock option plans.

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RISK FACTORS

This offering involves a high degree of risk. Before you invest in our common stock, you should carefully read and consider the risk factors described below in this section and the risks described in the documents incorporated by reference in this prospectus supplement and in the accompanying prospectus. If any of these risks actually occur, our business, operating results or financial condition could be harmed. This could cause the trading price of our stock to decline, and you could lose all or part of your investment.

Risks Related to Our Business

We expect to continue to operate at a loss and may never become profitable, which could result in a decline in the value of our common stock and a loss of your investment.

Substantially all of our revenue has been derived under collaborative research and development agreements relating to the development of our potential product candidates. We have incurred, and will continue to incur for the foreseeable future, significant expense to develop our research and development programs, conduct preclinical studies and clinical trials, seek regulatory approval for our product candidates and provide general and administrative support for these activities. As a result, we have incurred significant net losses since inception, and we expect to continue to incur substantial additional losses in the future. As of September 30, 2003, we had an accumulated deficit of approximately \$210 million. We may never generate profits and, if we do become profitable, we may be unable to sustain or increase profitability.

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

In June 2003, we announced the final results of the initial Phase II clinical trial for our cystic fibrosis candidate. In July 2003, we initiated a confirmatory Phase II clinical trial for this product candidate. In December 2003, we initiated the equivalent of a Phase I trial for our AIDS vaccine in Belgium. We also plan to dose the first patient in our rheumatoid arthritis product candidate Phase I clinical trial during the first quarter of 2004. Our product candidates for cancer have been evaluated in Phase I and Phase II clinical trials. In connection with the operational changes that we implemented in 2002 and the termination of our collaboration with Wyeth in February 2003, we suspended further development of our cancer and hemophilia product development programs. We will not generate any product revenue for at least several years and only then if we can successfully develop and commercialize our product candidates. Commercializing our potential products depends on successful completion of additional research and development and testing, in both preclinical development and clinical trials. Clinical trials may take several years or more to complete. The commencement, cost and rate of completion of our clinical trials may vary or be delayed for many reasons, including the risks discussed elsewhere in this section. If we are unable to successfully complete preclinical and clinical development of some or all of our product candidates in a timely manner, we may be unable to generate sufficient product revenue to maintain our business.

Even if our potential products succeed in clinical trials and are approved for marketing, these products may never achieve market acceptance. If we are unsuccessful in commercializing our product candidates for any reason, including greater effectiveness or economic

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

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

To our knowledge, no gene therapy products have received regulatory approval for marketing from the FDA. Because our product candidates involve new and unproven technologies, we believe that the regulatory approval process may proceed more slowly compared to clinical trials involving traditional drugs. The FDA and applicable state and foreign regulators must conclude at each stage of clinical testing that our clinical data suggest acceptable levels of safety in order for us to proceed to the next stage of clinical trials. In addition, gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the National Institutes of Health, or NIH, are subject to review by the NIH's Office of Biotechnology Activities Recombinant DNA Advisory Committee, or RAC. Although NIH guidelines do not have regulatory

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status, the RAC review process can impede the initiation of the trial, even if the FDA has reviewed the trial and approved its initiation. Moreover, before a clinical trial can begin at an NIH-funded institution, that institution's Institutional Biosafety Committee must review the proposed clinical trial to assess the safety of the trial.

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

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

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

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

the timing, costs and scope of, and our success in, conducting clinical trials, obtaining regulatory approvals and pursuing patent prosecutions;

competing technological and market developments;

the timing and costs of, and our success in, any commercialization activities and facility expansions, if and as required; and

the existence and/or outcome of any litigation or administrative proceedings involving our intellectual property.

As of September 30, 2003, we had approximately \$26.1 million in cash and cash equivalents. We believe that our cash and cash equivalents will be sufficient to fund our operations into 2005. We are pursuing opportunities to obtain additional capital to fund our operations beyond that time. Additional sources of financing could involve one or more of the following:

- extending or expanding our current collaborations;
- entering into additional product development collaborations;
- selling or licensing our technology or product candidates;
- issuing equity; or
- issuing debt.

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

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

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If we lose either IAVI or the CF Foundation as partners or if our collaborative relationships are unsuccessful, we may be unable to develop our potential products.

A significant portion of our operating and clinical trial expenses are funded through our collaborative agreements with IAVI and the CF Foundation. We have a collaborative development agreement with IAVI, which expires in December 2006, that provides us with funding to reimburse research and development and manufacturing expenses we incurred in connection with the collaboration. In addition, our collaboration with IAVI provides us with the funding for our Phase I clinical trial for our AIDS vaccine candidate. We also have a collaboration with the CF Foundation related to our current confirmatory Phase II clinical trial for our product candidate for treating cystic fibrosis. Under this collaboration, the CF Foundation is providing funding to the sites conducting this study to cover their direct costs of the trial.

If we were to lose the collaborative funding relationship with IAVI or the CF Foundation and were unable to obtain alternative sources of funding for the AIDS vaccine product candidate covered by the IAVI collaboration or the cystic fibrosis product candidate, which is funded under the agreement with the CF Foundation, we may be unable to continue our research and development or clinical program for those product candidates. In addition, the loss of significant amounts of collaborative or clinical trial funding could cause the delay, reduction or termination of the related research and development programs, and a reduction in capital expenditures and other operating activities necessary to support general operations. Such a reduction could further impede our ability to develop our product candidates. IAVI has the right to terminate the collaboration or its obligation to provide funding at any time for any reason with 90 days' notice. The CF Foundation has the right to terminate our funding agreement at any time for any reason. Termination of our IAVI collaboration would significantly affect our operating activities and termination of our CF Foundation collaboration would significantly affect the development of our cystic fibrosis product candidate.

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

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

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

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

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development of product candidates could be delayed and we could experience difficulty in generating sufficient revenue to maintain our business.

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

We have entered into exclusive and nonexclusive license agreements that give us and our partners rights to use technologies owned or licensed by commercial and academic organizations in the research, development and commercialization of our potential products. For example, we have licensed several issued and pending patents for the vector and gene delivered in our product candidate for cystic fibrosis and the processes that we use to manufacture our AAV-based product candidates. We believe that we will need to obtain additional licenses to use patents and unpatented technology owned or licensed by others for compositions, methods, processes to manufacture compositions, processes to manufacture and purify gene delivery product candidates and other technologies and processes for our present and potential product candidates. If we are unable to maintain our current licenses for third-party technology or obtain additional licenses on acceptable terms, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates. In addition, the license agreements for technology for which we hold exclusive licenses typically contain provisions that require us to meet minimum development milestones in order to maintain the license on an exclusive basis for some or all fields of the license. We also have license agreements for some of our technologies, which may require us to sublicense certain of

our rights. If we do not meet these requirements, our licensor may convert all or a portion of the license to a nonexclusive license or in some cases, terminate the license.

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

the scope of rights granted under the license agreement and other interpretation-related issues;

the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

the sublicensing of patent and other rights under our collaborative development relationships;

the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and

the priority of invention of patented technology.

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

The success of our clinical trials and preclinical studies may not be indicative of results in a large number of patients or predictive of long-term efficacy.

The successful results of our technology in preclinical studies using animal models may not be predictive of the results that we will see in our clinical trials. In addition, results in early-stage clinical trials are based on limited numbers of patients and generally test for drug safety rather than efficacy. Our reported progress and results from our early phases of clinical testing of our product candidates may not be indicative of progress or results that will be achieved from larger populations, which could be less favorable. Moreover, we do not know if the favorable results we have achieved in clinical trials will have a lasting effect. If a larger group of patients does not experience positive results, or if any favorable results do not demonstrate a beneficial effect, our product candidate for cystic fibrosis, or any other potential products that we advance to clinical trials, may not receive approval from the FDA for further clinical trials or commercialization. Any report of clinical trial results that are below the expectations of financial analysts or investors could result in a decline in our stock price.

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

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

of potential products will be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether.

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

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

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

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

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

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

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

While we believe that we have developed AAV manufacturing processes that can enable large scale manufacturing, we currently do not have the physical capacity to manufacture large-scale quantities of our potential products. This could limit our ability to conduct large clinical trials of a product candidate and to commercially launch a successful product candidate. In order to manufacture product at such scale, we will need to expand or improve our current facilities and staff or supplement them through the use of contract providers. If we are unable to obtain and maintain the necessary manufacturing capabilities, either alone or through third parties, we will be unable to manufacture our potential products in quantities sufficient to sustain our business. Moreover, we are unlikely to become profitable if we, or our contract providers, are unable to manufacture our potential products in a cost-effective manner.

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

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

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

Risks Related to Our Industry

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Common Stock

Concentration of ownership of our common stock may give certain shareholders significant influence over our business and the ability to disproportionately affect our stock price.

A significant number of shares of our common stock are held by a small number of investors, including holdings by Biogen of approximately 12.1 million shares, or 18.3 percent of our current common shares outstanding, and holdings by Elan and its affiliates of approximately 7.7 million shares, or 11.7 percent of our current common shares outstanding. Elan also holds convertible preferred stock that, if converted, would result in Elan obtaining approximately 4.8 million additional shares. At any time that Elan's ownership exceeds 10 percent of our common stock, it has the right to nominate one director, who shall be a member of the senior management of Elan or otherwise acceptable to Targeted Genetics, for election to Targeted Genetics' board of directors. This concentration of stock ownership may allow these shareholders to exercise significant control over our strategic decisions and block, delay or substantially influence all matters requiring shareholder approval, such as:

election of directors;

amendment of our charter documents; or

approval of significant corporate transactions, such as a change of control of Targeted Genetics.

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

Further, Elan has registration rights with respect to its holdings pursuant to a registration rights agreement dated July 21, 1999. Registration of Elan's shares for resale would permit Elan to sell large quantities of stock which could adversely impact the price of the Company's stock. In

connection with the filing of the shelf registration statement underlying this prospectus supplement, Elan was entitled to written notice of such filing, which we failed to provide.

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

The stock market in general and the market for biotechnology-related companies in particular have experienced extreme price and volume fluctuations, often unrelated to the operating performance of the affected companies. The market price of the securities of biotechnology companies, particularly companies such as ours without earnings and product revenue, has been highly volatile and is likely to remain so in the future. We believe that in the past, similar levels of volatility have contributed to the decline in the market price of our common stock, and may do so again in the future. Recently, trading volumes of our common stock increased dramatically, resulting in a volatile market price for our common stock. In addition, the trading price of our common stock could decline significantly as a result of sales of a substantial number of shares of our common stock, or the perception that significant sales could occur. In the past, securities class action litigation has been brought against companies that experience volatility in the market price of their securities. Market fluctuations in the price of our common stock could also adversely affect our collaborative opportunities and our future ability to sell equity securities at a price we deem appropriate. As a result, you could lose all or part of your investment.

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

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

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$23.8 million, after deducting certain fees due to the placement agents and our estimated offering expenses, as described in "Plan of Distribution." We intend to use any net proceeds from the sale of common stock offered by this prospectus supplement and the accompanying prospectus for working capital and other general corporate purposes. Although from time to time we evaluate potential acquisitions of complementary businesses or technologies, we currently have no

present understandings, commitments or agreements with respect to any such transactions. Pending any of these uses, we intend to invest the net proceeds of this offering in short-term marketable securities. Within the parameters set by our investment policy, we will retain broad discretion in allocating the net proceeds of this offering.

DILUTION

If you invest in our common stock, your interest will be diluted by an amount equal to the difference between the public offering price and the net tangible book value per share of common stock after this offering. We calculate net tangible book value per share by dividing our net tangible book value (total assets less intangible assets and total liabilities) by the number of outstanding shares of common stock.

Our net tangible book value at September 30, 2003 was \$8.9 million, or \$0.13 per share of common stock. After giving effect to the sale of 10,854,257 shares of common stock in this offering at the fixed price of \$2.35 per share, and our receipt of the net proceeds from the sale of those shares, our adjusted net tangible book value at September 30, 2003 would be \$32.6 million, or \$0.42 per share. This represents an immediate increase in pro forma net tangible book value of \$0.29 per share to existing shareholders and an immediate and substantial dilution of \$1.93 per share to new investors. The following table illustrates this per share dilution:

| | | |
|---|--------|--------|
| Public offering price per share | | \$2.35 |
| | | <hr/> |
| Net tangible book value per share at September 30, 2003 | \$0.13 | <hr/> |
| Increase in net tangible book value per share attributable to offering | 0.29 | <hr/> |
| Pro forma net tangible book value per share as of September 30, 2003, after giving effect to the offering | | 0.42 |
| | | <hr/> |
| Dilution per share to new investors in the offering | | \$1.93 |
| | | <hr/> |

These calculations exclude

4,143,924 shares of common stock issuable upon exercise of options outstanding as of September 30, 2003, of which 2,479,524 shares are exercisable, under our 1992 Restated Stock Option Plan, our Stock Option Plan for Non-employee Directors, our 1999 Stock Option Plan and our 2000 Genovo, Inc. Roll-over Stock Option Plan at a weighted average exercise price of \$3.68 per share; and

365,826 shares available for grant as of September 30, 2003 under our stock option plans.

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PLAN OF DISTRIBUTION

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We are offering the shares of our common stock through placement agents. Subject to the terms and conditions contained in the placement agent agreement dated January 30, 2004, SG Cowen Securities Corporation and Roth Capital Partners, LLC have agreed to act as the placement agents for the sale of up to 10,854,257 shares of our common stock. The placement agents are not purchasing or selling any shares by this prospectus supplement or accompanying prospectus, nor are they required to arrange the purchase or sale of any specific number or dollar amount of shares, but have agreed to use best efforts to arrange for the sale of all 10,854,257 shares.

The placement agent agreement provides that the obligations of the placement agents and the investors are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of certain opinions, letters and certificates from our counsel, our independent auditors and us.

Confirmations and definitive prospectuses will be distributed to all investors who agree to purchase shares of the common stock, informing investors of the closing date as to such shares. We currently anticipate that closing of the sale of 10,854,257 shares of common stock will take place on or about February 5, 2004. Investors will also be informed of the date and manner in which they must transmit the purchase price for their shares.

On the scheduled closing date, the following will occur:

we will receive funds in the amount of the aggregate purchase price; and

SG Cowen Securities Corporation, as representative of the placement agents, will receive the placement agents' fees on behalf of the placement agents for further distribution between the placement agents in accordance with the terms of the placement agent agreement.

We will pay the placement agents an aggregate commission equal to 6% of the gross proceeds of the sale of shares of common stock in the offering. In no event will the total amount of compensation paid to the placement agents and other securities brokers and dealers upon completion of this offering exceed 8% of the maximum gross proceeds of the offering. The estimated offering expenses payable by us, in addition to the placement agents' fees, are approximately \$200,000, which includes legal, accounting and printing costs and various other fees associated with registering and listing the shares of common stock. After deducting certain fees due to the placement agents and our estimated offering expenses, we expect the net proceeds from this offering to be up to approximately \$23.8 million.

We have agreed to indemnify the placement agents against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the placement agent agreement. We have also agreed to contribute to payments the placement agents may be required to make in respect of such liabilities.

We, along with our executive officers and directors, have agreed to certain lock-up provisions with regard to future sales of our common stock for a period of 60 days after the offering as set forth in the placement agent agreement.

The lock-up does not prevent (i) the issuance of shares or options to purchase shares pursuant to qualified stock option plans, currently outstanding options, warrants or rights and (ii) the issuance of shares of common stock valued at \$375,000 to Itochu Corporation at a negotiated per share price in exchange for the preferred stock of CellExSys held by Itochu in connection with dissolution of an abandoned joint venture and mutual settlement of claims.

The placement agent agreement with SG Cowen Securities Corporation and Roth Capital Partners, LLC is included as an exhibit to our Current Report on Form 8-K that will be filed with the Securities and Exchange Commission in connection with the consummation of this offering.

The transfer agent for our common stock is Mellon Investor Services, LLC.

Our common stock is traded on the Nasdaq SmallCap Market under the symbol TGEN.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, that are subject to the "safe harbor" created by those securities. Such forward-looking statements provide information regarding our current expectations, plans, objectives and forecasts of future events. Forward-looking statements include, without limitation:

statements about our product development and commercialization goals and expectations;

potential market opportunities;

our plans for and anticipated results of our clinical development activities;

the potential advantage of our product candidates;

statements about our future capital requirements, the sufficiency of our capital resources to meet those requirements and the expected composition of our capital resources; and

other statements that are not historical facts.

Words such as may, will, believe, estimate, anticipate, plan, expect and intend, or statements concerning potential or opportunity, or similar expressions or the negative thereof, may identify forward-looking statements, but the absence of these words does not mean that the statement is not forward-looking. Forward-looking statements are based on the judgment of management at the time the statements are made. Inaccurate assumptions and known and unknown risks and uncertainties can affect the accuracy of forward-looking statements. Our actual results could differ materially from those stated in or implied by forward-looking statements for a number of reasons, including the risks described in the sections of this prospectus supplement and the accompanying prospectus entitled Risk Factors. Other factors besides those described in this prospectus supplement and the accompanying prospectus could also affect actual results.

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

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement under the Securities Act relating to the common stock being offered by this prospectus. As permitted by the SEC rules, this prospectus omits some information included in the registration statement. For a more complete understanding of the common stock and this offering, you should refer to the registration statement, including its exhibits.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. SEC rules allow us to incorporate by reference into this prospectus supplement the information we file with the SEC, which means we can disclose important information to you by referring you to those documents. The information included in the following documents is incorporated by reference and is considered to be a part of this prospectus:

1. Our quarterly report on Form 10-Q for the quarter ended September 30, 2003, filed with the SEC on October 31, 2003.
2. Our annual report on Form 10-K for the year ended December 31, 2002, filed with the SEC on March 27, 2003;
3. Our current reports on Form 8-K filed with the SEC on January 27, 2004, January 22, 2004, January 13, 2004, December 9, 2003, October 30, 2003, October 1, 2003, August 21, 2003, August 18, 2003, July 31, 2003, July 22, 2003, July 17, 2003, June 23, 2003, June 18, 2003, June 13, 2003, June 10, 2003, May 6, 2003, April 7, 2003 and January 8, 2003;

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4. Our definitive proxy statement dated April 7, 2003, relating to our May 8, 2003 annual meeting of shareholders; and
 5. The description of our common stock contained in our registration statements on Form 8-A filed on April 26, 1994 and October 22, 1996 under Section 12(g) of the Exchange Act, including any amendments or reports filed for the purpose of updating that description.

We also incorporate by reference all documents we file under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, (a) after the filing date of the initial registration statement of which this prospectus is a part and before the effectiveness of the registration statement and (b) after the effectiveness of the registration statement and before all of the shares registered under the registration statement are sold. The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be part of this prospectus supplement as of the date on which the document is filed, and any older information that has been modified or superseded will not be deemed to be a part of this prospectus supplement. Unless specifically stated to the contrary, none of the information that we disclose under Item 9 or 12 of any Current Report on Form 8-K that we may from time to time furnish to the SEC will be incorporated by reference into, or otherwise included in, this prospectus supplement.

Upon request, we will provide without charge to each person who receives a prospectus supplement, including any beneficial owner, a copy of the information that has been incorporated by reference into this prospectus supplement. Please direct your request, either in writing or by telephone, to the Secretary, Targeted Genetics Corporation, 1100 Olive Way, Suite 100, Seattle, Washington 98101, (206) 623-7612.

You may also inspect and copy the registration statement and other documents that we have filed with the SEC, at prescribed rates, at the public reference facility maintained by the SEC at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549. You may obtain information regarding the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the registration statement and other documents we have filed with the SEC are publicly available through the SEC's web site at <http://www.sec.gov> or through our website at www.targetedgenetics.com.

LEGAL MATTERS

Dorsey & Whitney LLP, Seattle, Washington has provided us with an opinion regarding the validity of the shares of common stock to be offered by this prospectus supplement. Brown Raysman Millstein Felder & Steiner LLP is acting as counsel for the placement agents in connection with various legal matters relating to the shares of common stock offered hereby.

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Prospectus

TARGETED GENETICS CORPORATION

11,600,000 SHARES OF COMMON STOCK

We may sell from time to time up to 11,600,000 shares of the common stock offered by this prospectus. We will describe the specific terms and amounts of the common stock offered in a prospectus supplement that will accompany this prospectus. You should read both the prospectus supplement and this prospectus carefully before you invest in our common stock. This prospectus may not be used to sell securities unless accompanied by a prospectus supplement.

Our common stock is quoted on the NASDAQ SmallCap Market under the symbol TGEN. The reported last sales price of our common stock on August 6, 2003 was \$1.71 per share.

Investing in our common stock involves risks. See Risk Factors on page 5.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is August 21, 2003

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ABOUT THIS PROSPECTUS

This prospectus is part of a shelf registration statement that we have filed with the Securities and Exchange Commission, or SEC. Each time we sell our common stock under this prospectus we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the price, the amount of common stock being offered and the plan of distribution. The prospectus supplement for a particular offering may also add, update or change information contained in this prospectus. In addition, we may update or supplement any prospectus supplement relating to a particular offering. You should read both this prospectus and any applicable prospectus supplement together with the additional information about Targeted Genetics to which we refer you in the section of this prospectus entitled "Where You Can Find More Information."

You should rely only on the information provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than its date, regardless of the time of delivery of the prospectus or prospectus supplement or any sale of common stock.

This prospectus and any prospectus supplement is an offer to sell and a solicitation of an offer to buy the securities offered by this prospectus and any prospectus supplement only in jurisdictions where the offer or sale is permitted.

TARGETED GENETICS CORPORATION

This summary does not contain all the information about Targeted Genetics Corporation that may be important to you. You should read the more detailed information and financial statements and related notes that are incorporated by reference and are considered to be a part of this prospectus.

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

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

We have an AAV-based product candidate under development for treating cystic fibrosis that has been evaluated in a Phase II clinical trial. In June 2003, we announced the final results of this Phase II trial. The final data indicate that our cystic fibrosis product candidate met safety and tolerability targets in this repeat dosing trial. In addition, the final data from the Phase II trial indicate statistically significant improvement in lung function, decreases in levels of inflammatory cytokines and transfer of the correct genes into cells of the lung. In July 2003, we initiated a

larger confirmatory Phase II clinical trial for this cystic fibrosis product candidate. This trial is being conducted in collaboration with the Cystic Fibrosis Foundation, or CF Foundation. We also are developing an AAV-based vaccine candidate for high-risk populations to protect against the progression of HIV infection to AIDS in partnership with the International Aids Vaccine Initiative, or IAVI, a public health

organization. In June 2003, we announced preclinical results that support commencement of initial clinical trials in humans of our AIDS vaccine. We expect to begin initial clinical trials of our AIDS vaccine product candidate by the end of 2003. In the first half of 2003, we announced preclinical results that support commencement of a Phase I clinical trial for our AAV-based arthritis product candidate. We expect to submit regulatory filings in the second half of 2003 to support a Phase I clinical trial of our rheumatoid arthritis product candidate.

We also have a pipeline of product candidates focused on treating cancer and hemophilia. During 2002, we restructured our operations to concentrate resources on key product development programs and business development activities. In connection with these operational changes, we suspended further clinical development of our cancer and hemophilia programs until we can find development partners to help fund development costs or find other sources of funding for the programs. We have focused our efforts on advancing the clinical development of our product candidate to treat cystic fibrosis and on initiating clinical trials of our product development candidates to treat arthritis and AIDS.

We believe that our successes in assembling a broad platform of proprietary intellectual property for developing and manufacturing potential products supports our potential to develop and manufacture gene therapy product candidates to treat a range of diseases. We have developed processes to manufacture our potential products, and the products of third parties, at a scale amenable to clinical development and expandable to large-scale production for advancing our potential products to clinical evaluation and commercialization. In March 2003, we entered into our first manufacturing services agreement, under which we are conducting initial feasibility studies regarding the potential manufacturing of clinical-grade biologic materials for a third-party biotechnology company.

A wide range of diseases may potentially be treated with gene-based products, including cancer, genetic diseases and infectious diseases. We believe that there is also a significant opportunity to treat diseases currently treated with proteins using recombinant DNA technology, monoclonal antibodies or small molecules that may be more effectively treated by gene-based therapies due to their ability to provide a long-term or a localized method of treatment. Our business strategy is to develop multiple gene delivery systems, which we believe will maximize our product opportunities. Using these gene delivery systems, we are developing product candidates across multiple diseases with the belief that gene-based therapies may provide a means to treat disease in ways not currently achievable with traditional pharmaceuticals. We believe that, if successful, we can establish significant market potential for our product candidates. Because there are currently no commercially available gene therapy products, we intend to pursue product development programs to enable us to demonstrate proof of concept and eventually commercialize gene-based therapeutics to address currently unmet medical needs in treating disease. If this is achieved, we believe that the value of our assets can be leveraged into multiple product opportunities.

The development of pharmaceutical products involves extensive preclinical development, followed by human clinical trials that take several years or more to complete. The length of time required to completely develop any product candidate varies substantially according to the type, complexity and novelty of the product candidate, the degree of involvement by a development partner and the intended use of the product candidate. Our commencement and rate of completion of clinical trials may vary or be delayed for many reasons, including those discussed in the section of this prospectus entitled Risk Factors.

We were incorporated in the state of Washington in 1989. Our executive offices are located at 1100 Olive Way, Suite 100, Seattle, Washington 98101, and our telephone number is (206) 623-7612. In this prospectus, references to Targeted Genetics include our subsidiaries.

For more information about Targeted Genetics, you should read the accompanying prospectus and the information described in the section of this prospectus entitled Where You Can Find More Information, including our consolidated financial statements and related notes.

In this prospectus, Targeted Genetics, we, us and our refer to Targeted Genetics Corporation and its subsidiaries.

RISK FACTORS

This offering involves a high degree of risk. Before you invest in our common stock, you should carefully read and consider the following risk factors. If any of these risks actually occur, our business, operating results or financial condition could be harmed. This could cause the trading price of our stock to decline, and you could lose all or part of your investment.

Risks Related to Our Business

We expect to continue to operate at a loss and may never become profitable, which could result in a decline in the value of our common stock and a loss of your investment.

Substantially all of our revenue has been earned under collaborative research and development agreements relating to the development of our potential product candidates. We have incurred, and will continue to incur for the foreseeable future, significant expense to develop our research and development programs, conduct preclinical studies and clinical trials, seek regulatory approval for our product candidates and provide general and administrative support for these activities. As a result, we have incurred significant net losses since inception, and we expect to continue to incur substantial additional losses in the future. As of June 30, 2003, we had an accumulated deficit of approximately \$209 million. We may never generate profits and, if we do become profitable, we may be unable to sustain or increase profitability.

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

In June 2003, we announced the final results of the initial Phase II clinical trial for our cystic fibrosis candidate. In July 2003, we initiated a confirmatory Phase II clinical trial for this product candidate. We expect to begin initial clinical trials of our AIDS vaccine product candidate by the end of 2003. We expect to submit regulatory filings in the second half of 2003 that support a Phase I clinical trial of our rheumatoid arthritis product candidate. Our product candidates for cancer have been evaluated in Phase I and Phase II clinical trials. We have preclinical development programs for treating hemophilia and cancer. In connection with the operational changes that we implemented in 2002 and the termination of our collaboration with Wyeth in February 2003, we suspended further development of our cancer and hemophilia product development programs. We will not generate any product revenue for at least several years and only then if we can successfully develop and commercialize our product candidates. Commercializing our potential products depends on successful completion of additional research and development and testing, in both preclinical development and clinical trials. Clinical trials may take several years or more to complete. The commencement, cost and rate of completion of our clinical trials may vary or be delayed for many reasons, including the risks discussed elsewhere in this section. If we are unable to successfully complete preclinical and clinical development of some or all of our product candidates in a timely manner, we will be unable to generate sufficient product revenue to maintain our business.

Even if our potential products succeed in clinical trials and are approved for marketing, these products may never achieve market acceptance. If we are unsuccessful in commercializing our product candidates for any reason, including greater effectiveness or economic feasibility of competing products or treatments, the failure of the medical community or the public to accept or use any products based on gene delivery, inadequate marketing and distribution capabilities or other reasons discussed elsewhere in this section, we will be unable to generate sufficient product revenue to maintain our business.

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

To our knowledge, no gene therapy products have received regulatory approval for marketing from the U.S. Food and Drug Administration, or FDA, or similar regulatory agencies in other countries. Because our product candidates involve new and unproven technologies, we believe

that the regulatory approval process may proceed more slowly compared to clinical trials involving traditional drugs. The FDA and applicable state and foreign regulators must conclude at each stage of clinical testing that our clinical data suggest acceptable levels of safety and efficacy in order for us to proceed to the next stage of clinical trials. In addition, gene therapy clinical trials conducted at institutions that receive funding from the National Institutes of Health, or NIH, are subject to review by the NIH's Office of Biotechnology Activities Recombinant DNA Advisory Committee, or RAC. Although NIH guidelines do not have regulatory status, the RAC review process can impede

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the initiation of the trial, even if the FDA has reviewed the trial and approved its initiation. Moreover, before a clinical trial can begin at an NIH-funded institution, that institution's Institutional Biosafety Committee must review the proposed clinical trial to assess the safety of the trial.

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

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

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

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

the timing, costs and scope of, and our success in, conducting clinical trials, obtaining regulatory approvals and pursuing patent prosecutions;

competing technological and market developments;

the timing and costs of, and our success in, any commercialization activities and facility terminations or expansions, if and as required; and

the existence and/or outcome of any litigation or administrative proceedings involving our intellectual property.

As of June 30, 2003, we had approximately \$24.8 million in cash and cash equivalents. In addition, we expect to receive additional collaborative funding of up to \$4.0 million under our collaborations with Biogen, Inc., which ends in September 2003, and IAVI, which ends in December 2003. We believe that our cash and cash equivalents and the funding anticipated under our collaborations will be sufficient to fund our operations through at least the end of 2004. We are pursuing opportunities to obtain additional capital to fund our operations beyond that time. Additional sources of financing could involve one or more of the following:

extending or expanding our current collaborations;

entering into additional product development collaborations;

selling or licensing our technology or product candidates;

issuing equity in the public or private markets; or

issuing debt.

Additional funding may be unavailable to us on reasonable terms, if at all.

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

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If we lose our strategic partners or if our collaborative relationships are unsuccessful, we may be unable to develop our potential products.

A significant portion of our operating expenses is funded through our collaborative agreements with third parties. We have collaborative development agreements with Biogen and IAVI under which we expect to receive approximately \$4.0 million in additional funding for research activities to be conducted in 2003. This funding is to reimburse research and development expenses we incur in connection with the applicable development collaboration. If we were to lose the collaborative funding expected from IAVI and were unable to obtain alternative sources of funding for the AIDS vaccine product candidate covered by the collaboration, we may be unable to continue our research and development program for that product candidate. In addition, the loss of significant amounts of collaborative funding could cause the delay, reduction or termination of the related research and development programs, and a reduction in capital expenditures and other operating activities necessary to support general operations. Such a reduction could further impede our ability to develop our product candidates. IAVI has the right to terminate its collaboration or its obligation to provide research funding at any time for scientific or business reasons with 90 days' notice. Termination of our IAVI collaboration would significantly affect our operating activities.

If our strategic partners terminate or decline to extend our collaborations, we may be unable to develop our potential products.

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

intense. We may be unable to successfully maintain our existing relationships or establish additional relationships necessary for the development of our product candidates on acceptable terms, if at all. If we are unable to do so, our research and development programs may be delayed or we may lose access to important intellectual property or know-how.

A significant portion of our research is funded through collaborations with third parties. We have the following active strategic partnerships:

- a collaboration with IAVI to develop an AIDS vaccine, the development period of which will conclude in December 2003;
- a collaboration with CF Foundation to fund our current Phase II clinical trial for our product candidate for treating cystic fibrosis; and
- a multiple-product collaboration with Biogen, the initial development period of which will conclude in September 2003.

One or all of these strategic partners may choose not to continue the collaboration, or may choose to terminate the collaboration at any time. As a result, the development of the affected product candidate could be delayed or terminated.

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

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

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

We have entered into license agreements, both exclusive and nonexclusive, that give us and our partners rights to use technologies owned or licensed by commercial and academic organizations in the research, development and commercialization of our potential products. For example, we have licensed several issued and pending patents for the gene used in our cancer product development programs, the vector and gene delivered in our product candidate for cystic fibrosis and the processes that we use to manufacture our AAV-based product candidates. If we are unable to maintain our current licenses for third-party technology or, if necessary, obtain additional licenses on acceptable terms, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates. In addition, the license agreements for technology for which we hold exclusive licenses, such as the license for part of the process that we use to manufacture our AAV-based product candidates, typically contain provisions requiring us to meet minimum development milestones in order to maintain the license on an exclusive basis. If we do not meet these requirements, our licensor may convert the license to a nonexclusive license or terminate the license.

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

scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

the scope of rights granted under the license agreement and other interpretation-related issues;

the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

the sublicensing of patent and other rights under our collaborative development relationships;

the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our strategic partners; and

the priority of invention of patented technology.

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

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

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

clinical trials or commercialization. Any report of clinical trial results that are below the expectations of financial analysts or investors could result in a decline in our stock price.

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

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

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

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

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

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

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

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

company could significantly harm our reputation and make it more difficult to obtain the funding and collaborative partnerships necessary to maintain our business.

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

We currently do not have the capacity to manufacture large-scale commercial quantities of our potential products. To do so, we will need to expand or improve our current facilities and staff or supplement them through the use of contract providers. If we are unable to obtain and maintain the necessary manufacturing capabilities, either alone or through third parties, we will be unable to manufacture our potential products in quantities sufficient to sustain our business. Moreover, we are unlikely to become profitable if we, or our contract providers, are unable to manufacture our potential products in a cost-effective manner.

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

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

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

Risks Related to Our Industry

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

Public perception of our product candidates could be harmed by negative events in the field of gene therapy. For example, in late 2002, two patients in a French academic clinical study being treated for x-linked severe combined immunodeficiency in a gene therapy trial using a retroviral vector acquired leukemia. Patient deaths, related and unrelated to gene therapy, have occurred in other clinical trials. These adverse events and the resulting publicity, as well as any other adverse events in the field of gene therapy that may occur in the future, could result in a decrease in demand for any products that we may develop. The commercial success of our product candidates will depend in part on public acceptance of the use of gene therapy for preventing or treating human diseases. If public perception is influenced by claims that gene therapy is unsafe, our product candidates may not be accepted by the general public or the medical community. For example, there is concern regarding the potential safety and efficacy of gene therapy products. The public and the medical community may conclude that our technology is unsafe. Moreover, to the extent that unfavorable publicity or negative public perception arising from other biotechnology-related fields such as human cloning and stem-cell research are linked in the public mind to gene therapy, our industry will be harmed.

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

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

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

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

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

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

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

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

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

Sales of medical products and treatments substantially depend, both domestically and abroad, on the availability of reimbursement to the consumer from third-party payors. Our potential products may not be considered cost-effective by

third-party payors, who may not provide coverage at the price set for our products, if at all. If purchasers or users of our products are unable to obtain adequate reimbursement, they may forego or reduce their use of our products. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

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

Risks Related to Our Common Stock

Concentration of ownership of our common stock may give certain shareholders significant influence over our business and the ability to disproportionately affect our stock price.

A significant number of shares of our common stock are held by a small number of investors, including holdings by Biogen of approximately 9.6 million shares and holdings by Elan International Services, Ltd., or Elan, and its affiliates of approximately 2.5 million shares of common stock. Elan also holds convertible debt and equity securities that, if converted, would result in Elan holding approximately 8.3 million additional shares. This concentration of stock ownership may allow these shareholders to exercise significant control over our strategic decisions and block, delay or substantially influence all matters requiring shareholder approval, such as:

election of directors;

amendment of our charter documents; or

approval of significant corporate transactions, such as a change of control of Targeted Genetics.

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

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

The stock market in general and the market for biotechnology-related companies in particular have experienced extreme price and volume fluctuations, often unrelated to the operating performance of the affected companies. The market price of the securities of biotechnology companies, particularly companies such as ours without earnings and product revenue, has been highly volatile and is likely to remain so in the future. We believe that in the past, similar levels of volatility have contributed to the decline in the market price of our common stock, and may do so again in the future. Recently, trading volumes of our common stock increased dramatically, resulting in a volatile market price for our common stock. In addition, the trading price of our common stock could decline significantly as a result of sales of a substantial number of shares of our common stock, or the perception that significant sales could occur. In the past, securities class action litigation has been brought against companies that experience volatility in the market price of their securities. Market fluctuations in the price of our common stock could also adversely affect our collaborative opportunities and our future ability to sell equity securities at a price we deem appropriate. As a result, you could lose all or part of your investment.

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

To meet all or a portion our long-term funding requirements, we may sell securities in the public or private equity markets if and when conditions are favorable, even if we do not have an immediate need for additional capital at that time. Raising funds through the issuance of equity securities will dilute the ownership of our existing shareholders. Furthermore,

we may enter into financing transactions at prices that represent a substantial discount to market price. A negative reaction by investors and securities analysts to any discounted sale of our equity securities could result in a decline in the trading price of our common stock.

USE OF PROCEEDS

Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of common stock offered by this prospectus for additional working capital and other general corporate purposes, as well as the possible acquisition of or investment in complementary businesses and technologies. Until we have used the net proceeds, we may invest them in short-term marketable securities.

PLAN OF DISTRIBUTION

Distributions by the Company

We may sell the common stock offered by this prospectus in one or more transactions

- to or through underwriters;
- through dealers, agents or institutional investors;
- directly to purchasers; or
- through a combination of these methods.

We may sell the common stock at a fixed price or prices that may change, at prevailing market prices, at prices relating to prevailing market prices or at negotiated prices. Each time we sell common stock in a particular offering, we will provide a prospectus supplement or, if required, amend this prospectus, to disclose the following information with respect to that offering:

- the material terms of the distribution, including the number of shares and the consideration to be paid;
- the identity of any underwriters, dealers, agents or purchasers that will purchase the common stock;
- the amount of any compensation, discounts or commissions to be received by underwriters, dealers or agents;
- the nature of any transactions by underwriters, dealers or agents during the offering that are intended to stabilize or maintain the market price of the common stock; and
- the terms of any indemnification provisions.

Underwriters, dealers, agents or other purchasers may sell the common stock at a fixed price or prices that may change, at prices set at or relating to prevailing market prices or at negotiated prices.

Underwriters

We may sell all or a portion of the shares offered by this prospectus in one or more transactions to or through underwriters. In connection with the sale of our common stock, underwriters, dealers or agents may receive compensation from us, or from the purchasers of the common stock for whom they may act as agents, in the form of discounts, concessions or commissions. Underwriters, dealers, agents or purchasers that participate in the distribution of the common stock, and any broker-dealers or other persons acting on behalf of parties that participate in the distribution of the common stock, are underwriters under the Securities Act of 1933, or the Securities Act. Any discounts or commissions they receive and any profit on the resale of the common stock they receive constitute underwriting discounts and commissions under the Securities Act. Any person deemed to be an underwriter under the Securities Act may be subject to statutory liabilities, including those under Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Securities Exchange Act of 1934, or the Exchange Act.

Only underwriters named in the amended prospectus, if any, will be underwriters of the common stock offered through that amended prospectus. Any underwriters used in an offering will acquire the common stock for their own account and may resell the common stock from time to time in one or more transactions, at a fixed public offering price or at varying prices

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determined at the time of sale. We may offer the common stock to the public through underwriting syndicates represented by managing underwriters or through underwriters without a syndicate. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

Agents; Direct Sales

We may designate agents to distribute the common stock offered by this prospectus. Unless the applicable prospectus supplement states otherwise, any such agent will act on a best-efforts basis for the period of appointment. We may authorize dealers or other persons acting as our agents to solicit offers by institutional investors to purchase the common stock from us under contracts that provide for payment and delivery on a future date. We may enter into agreements directly with purchasers that provide for the sale of the common stock over a period of time by means of draw-downs at our election, which the purchaser would be obligated to accept under specified conditions. Under a draw-down agreement, we may sell common stock at a per-share purchase price discounted from the market price of our common stock. We may also enter into agreements for sales of common stock based on combinations of or variations from these methods. We will describe in the applicable prospectus supplement the terms and conditions of any such agreements and any related commissions we will pay. Agents and underwriters may also engage in transactions with us or perform services for us in the ordinary course of business.

Stabilization Activities

In connection with a firm commitment underwritten offering of our common stock, underwriters and purchasers that are deemed to be underwriters under the Securities Act may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. For example, they may

over-allot in connection with the offering, creating a syndicate short position for their own account;

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bid for and purchase our common stock in the open market to cover short positions or to stabilize the price of our common stock;
or

reclaim selling concessions allowed for distributing our common stock in the offering if the underwriters repurchase previously distributed common stock in transactions to cover short positions, stabilization transactions or otherwise.

Any of these activities may stabilize or maintain the market price above independent market levels. These activities may be conducted only in conjunction with a firm commitment underwritten offering. Underwriters are not required to engage in these activities and may terminate any such activity at any time. In engaging in any such activities, underwriters will be subject to the applicable provisions of the Securities Act and the Exchange Act and the rules and regulations under those acts. Regulation M under the Securities Act, for example, may restrict the ability of any person engaged in the distribution of the common stock to engage in market-making activities with respect to the common stock, and the anti-manipulation rules under the Exchange Act may also apply to market sales of the common stock. These provisions may affect the marketability of the common stock and the ability of any person to engage in market-making activities with respect to the common stock.

Indemnification

We may agree to indemnify underwriters, dealers, agents or other purchasers against civil liabilities they may incur in connection with the offer and sale of the common stock offered by this prospectus, including liabilities under the Securities Act. We may also agree to contribute to payments that these persons may be required to make with respect to these liabilities.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Our disclosure and analysis in this prospectus, the applicable prospectus supplement and the documents incorporated by reference into this prospectus and the applicable prospectus supplement contain forward-looking statements, which provide information regarding our current expectations, plans, objectives and forecasts of future events. Forward-looking statements include, without limitation:

statements about our product development and commercialization goals and expectations;

potential market opportunities;

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our plans for and anticipated results of our clinical development activities;

the potential advantage of our product candidates;

statements about our future capital requirements, the sufficiency of our capital resources to meet those requirements and the expected composition of our capital resources; and

other statements that are not historical facts.

Words such as may, will, believe, estimate, anticipate, plan, expect and intend, or statements concerning potential or opportunity, or similar expressions or the negative thereof, may identify forward-looking statements, but the absence of these words does not mean that the statement is not forward-looking. Forward-looking statements are based on the judgment of management at the time the statements are made.

Inaccurate assumptions and known and unknown risks and uncertainties can affect the accuracy of forward-looking statements. Our actual results could differ materially from those stated in or implied by forward-looking statements for a number of reasons, including the risks described in the sections of this prospectus and the applicable prospectus supplement entitled Risk Factors. Other factors besides those described in this prospectus and the applicable prospectus supplement could also affect actual results.

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

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement under the Securities Act relating to the common stock being offered by this prospectus. As permitted by the SEC rules, this prospectus omits some information included in the registration statement. For a more complete understanding of the common stock and this offering, you should refer to the registration statement, including its exhibits.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. SEC rules allow us to incorporate by reference into this prospectus the information we file with the SEC, which means we can disclose important information to you by referring you to those documents. The information included in the following documents is incorporated by reference and is considered to be a part of this prospectus:

1. Our quarterly report on Form 10-Q for the quarter ended June 30, 2003, filed with the SEC on August 1, 2003.
2. Our annual report on Form 10-K for the year ended December 31, 2002, filed with the SEC on March 27, 2003;
3. Our current reports on Form 8-K filed with the SEC on July 31, 2003, July 22, 2003, July 17, 2003, June 23, 2003, June 18, 2003, June 13, 2003, June 10, 2003, May 6, 2003, April 7, 2003, and January 8, 2003;
4. Our definitive proxy statement dated April 7, 2003, relating to our May 8, 2003 annual meeting of shareholders; and
5. The description of our common stock contained in our registration statements on Form 8-A filed on April 26, 1994 and October 22, 1996 under Section 12(g) of the Exchange Act, including any amendments or reports filed for the purpose of updating that description.

We also incorporate by reference all documents we file under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, (a) after the filing date of the initial registration statement of which this prospectus is a part and before the effectiveness of the registration statement and (b) after the effectiveness of the registration statement and before all of the shares registered under the registration statement are sold. The most recent information that we file with the SEC automatically updates and supersedes older information. The information contained in any such filing will be deemed to be part of this prospectus as of the date on which the document is filed, and any older information that has been modified or superseded will not be deemed to be a part of this prospectus. Unless specifically stated to the contrary, none of the information that we disclose under Item 9 or 12 of any Current Report on Form 8-K that we may from time to time furnish to the SEC will be incorporated by reference into, or otherwise included in, this prospectus

Upon request, we will provide without charge to each person who receives a prospectus, including any beneficial owner, a copy of the information that has been incorporated by reference into this prospectus or the applicable prospectus supplement. Please direct your request, either in writing or by telephone, to the Secretary, Targeted Genetics Corporation, 1100 Olive Way, Suite 100, Seattle, Washington 98101, (206)

623-7612.

You may also inspect and copy the registration statement and other documents that we have filed with the SEC, at prescribed rates, at the public reference facility maintained by the SEC at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549. You may obtain information regarding the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the registration statement and other documents we have filed with the SEC are publicly available through the SEC's web site at <http://www.sec.gov> or through our website at www.targetedgenetics.com.

LEGAL MATTERS

Dorsey & Whitney LLP, Seattle, Washington has provided us with an opinion regarding the validity of the shares of common stock to be offered by this prospectus.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements included in our annual report on Form 10-K for the year ended December 31, 2002, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

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10,854,257 Shares

TARGETED GENETICS CORPORATION

Common Stock

PROSPECTUS SUPPLEMENT

SG Cowen

Roth Capital Partners

January 30, 2004
