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GENOME THERAPEUTICS CORP  
Form 424B3  
April 19, 2002

This filing is made pursuant to rule  
424(b)(3) under the Securities Act of  
1933, as amended, in connection with  
Registration No. 333-85500

PROSPECTUS

2,962,500 Shares

Genome Therapeutics Corp.

Common Stock

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These shares, which are issuable upon the conversion or exercise of certain convertible notes and warrants issued by the Company in a private placement transaction on March 5, 2002, are being offered for sale by the selling stockholders listed on page 13. The selling stockholders may sell the common stock at prices and on terms determined by the market, in negotiated transactions or through underwriters. The selling stockholders may also sell the common stock under Rule 144 of the Securities Act of 1933. See "Plan of Distribution" beginning on page 14.

The common stock is traded on the Nasdaq National Market under the symbol "GENE". On April 17, 2002, the reported closing price of the common stock was \$4.75 per share.

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An investment in the shares offered hereby involves a high degree of risk. See "Risk Factors" beginning on page 2 of this prospectus.

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

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The date of this prospectus is April 19, 2002.

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### THE COMPANY

We are a biopharmaceutical company focused on the discovery and development of pharmaceutical and diagnostic products. We have eight established product development programs. Our lead product candidate, Ramoplanin, is in Phase III clinical trials for the prevention of bloodstream infections caused by vancomycin-resistant enterococci (VRE). We have six alliances with pharmaceutical companies including Schering-Plough, AstraZeneca, Wyeth-Ayerst and bioMerieux, and a joint venture with ArQule. In addition to these eight projects, we have a portfolio of earlier stage internal drug discovery programs. We also maintain an active service business, GenomeVision™ Services, providing drug discovery services to pharmaceutical and biotechnology companies and to the National Human Genome Research Institute.

### RISK FACTORS

This offering involves a high degree of risk. You should consider carefully the risks described below before you decide to buy our common stock. The risks and uncertainties described below are not the only ones facing us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business operations. If any of the following risks were to occur, our business, financial condition or results of operations would likely suffer. In that event, the trading price of our common stock could decline, and you could lose all or part of your investment.

We have a history of significant operating losses and expect these losses to continue in the future.

We have experienced significant operating losses each year since our inception and expect these losses to continue for the foreseeable future. We had a net loss of approximately \$10,090,000 for the fiscal year ended December 31, 2001, and, as of December 31, 2001, we had an accumulated net loss of approximately \$82,054,000. The losses have resulted primarily from costs incurred in research and development and from general and administrative costs associated with our operations. These costs have exceeded our revenues which to date have been generated principally from collaborations, government grants and sequencing services. We anticipate incurring additional losses this year and in future years and cannot predict when, if ever, we will achieve profitability. These losses may increase in the near future as we expand our research and development and clinical trial activities. In addition, our partners' product development efforts which utilize our products are at an early stage and, accordingly, we do not expect our losses to be substantially mitigated by revenues from milestone payments or royalties under those agreements for a number of years, if ever.

Use of genomic information to develop or commercialize products is unproven.

The development of new drugs and the diagnosis of disease based on genomic information is unproven. Our business strategy is based on the assumption that identifying and characterizing genes and sequencing select human genes and the genomes of select pathogens may help scientists better understand complex

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disease processes and develop drugs to treat these diseases. There is limited understanding of the roles of genes in diseases. Few therapeutic vaccine or diagnostic products based on genomic information have been developed and commercialized. To date, no one has developed or commercialized any pharmaceutical, diagnostic or vaccine products based on our technologies. If we fail to identify genes useful for the discovery and development of such products, or if partners are unable to use the genomic information that we provide to them to develop such products, our current and potential customers may lose confidence in our products or their value for drug discovery, and our business may suffer as a result.

We rely heavily upon existing and prospective alliance partners and licensees, and a significant portion of our revenue has been derived from one alliance partner.

Our strategy for developing and commercializing therapeutic, vaccine and diagnostic products depends, in part, on strategic alliances and licensing arrangements with pharmaceutical and biotechnology partners. We currently have alliances with AstraZeneca, bioMerieux, Schering-Plough and Wyeth-Ayerst. We have received a

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substantial portion of our revenue from these alliances, and we expect to continue to do so. Under these arrangements, we are entitled to receive payments and royalties based on the achievement by us and our partners of certain development milestones and the successful development of products arising from the collaborations. Although we have achieved many of the scientific milestones under our agreements, we cannot assure you that we will continue these achievements in the future or that milestones dependent on our partners' development and commercialization activities will be attained.

In addition, we cannot assure that we will maintain our current collaborations or establish additional collaborations. Competition among genomics companies for collaborations with pharmaceutical companies is intense. This competition is enhanced by the trend towards consolidation among large pharmaceutical companies. Consequently, we cannot be sure that we will be able to enter into new collaborations or maintain our existing ones, and any new or renewed collaborations may be on terms less favorable to us than past collaborations. Our failure to maintain existing collaborations or to enter into additional collaborations would have a material adverse effect on our business. In particular, if funding from partners were to become unavailable or were to be reduced, we would need to devote additional internal resources to our research programs or possibly scale back or terminate some programs.

Since 1996, we have received a significant amount of revenues based on payments under our alliances with Schering-Plough. We have two infectious disease alliances with Schering-Plough and a third collaboration with Schering-Plough that relates to asthma genetics. The funded research phase under these agreements have been extended and is scheduled to end on March 31, 2002 (with respect to the infectious disease alliances) and December 31, 2002 (with respect to the asthma alliance). For the fiscal years ended December 31, 1999, 2000 and 2001, revenues from Schering-Plough accounted for approximately 71%, 35% and 31%, respectively, of our total revenue. If Schering-Plough fails to continue to extend one or more of these agreements, we would lose research funding, which could have a material adverse effect on us.

Our strategy includes entering into multiple, concurrent alliances. We cannot assure that we will be able to manage multiple alliances successfully. The risks we face in managing multiple alliances include maintaining

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confidentiality among partners, avoiding conflicts between partners and avoiding conflicts between us and our partners. If we fail to manage our alliances effectively, or if any of the problems described above arise, one or more of the following could occur which could have a material adverse effect on our business:

- . use of significant resources to resolve conflicts,
- . delay in research effects,
- . legal claims involving significant time,
- . expense,
- . loss of reputation,
- . termination of one or more alliances, or
- . loss of capital and loss of revenues.

If our partners develop products using our genomic information, we will rely on these partners for product development, regulatory approval, manufacturing and marketing of those products before we can receive some of the milestone payments, royalties and other payments to which we may be entitled under the terms of some of our alliance agreements. Our agreements with our partners typically allow the partners significant discretion in electing whether to pursue any of these activities. We cannot control the amount and timing of resources our partners may devote to our programs or potential products. As a result, we cannot assure that our partners will perform their obligations as expected. In addition, if a partner is involved in a business combination, such as a merger or acquisition, or changes its business focus, its performance under our agreement may suffer and, as a result, we may not generate any revenues from the royalty, milestone and similar payment provisions of our collaboration agreement with that partner.

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Development of therapeutic, diagnostic and vaccine products based on our discoveries will be subject to the high risks of failure inherent in the development or commercialization of health care products. These risks include the possibility that any such products will be found to be toxic, be found to be ineffective, fail to receive necessary regulatory approvals, be difficult or impossible to manufacture on a large scale, be uneconomical to market, fail to be developed prior to the successful marketing of similar products by competitors or infringe on proprietary rights of third parties.

Our alliance partners may not be successful in developing or commercializing therapeutic, diagnostic or vaccine products under our agreements with them.

We derive a substantial portion of our revenues from fees paid by pharmaceutical companies for our information, products and services. We expect that pharmaceutical and biotechnology companies will be one of our primary source of revenues for the foreseeable future. As a result, we are subject to risks and uncertainties that affect the pharmaceutical and biotechnology industries and to reductions and delays in research and development expenditures by companies in these industries. These effects on the pharmaceutical and biotechnology industries may affect our ability to conclude deals with collaborative partners.

In addition, our future revenues may be adversely affected by mergers and

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consolidations in the pharmaceutical and biotechnology industries, which will reduce the number of our potential customers. Large pharmaceutical and biotechnology customers could also decide to conduct their own genomic programs, rely on publicly available information or joint consortia or seek other providers instead of using our products or services.

We may not succeed in obtaining regulatory approval for commercialization of our product candidates or maintain regulatory compliance with respect to products approved for commercial use.

On October 9, 2001, we acquired a license to develop the antibiotic Ramoplanin, our first product candidate, and we intend to expand our pipeline of clinical candidates, both through internal development efforts and acquisitions. The development, manufacture and marketing of pharmaceutical products are subject to government regulation in the United States and other countries. In the United States and most foreign countries, we must complete rigorous pre-clinical testing and extensive human clinical trials that demonstrate the safety and effectiveness of a product in order to apply for regulatory approval to market the product. These processes are expensive and can take many years to complete. We may not be able to demonstrate the safety and efficacy of our products to the satisfaction of the U.S. Food and Drug Administration, commonly referred to as the FDA, or other regulatory authorities. We may also be required to demonstrate that our proposed product represents an improved form of treatment over existing therapies and we may be unable to do so without conducting further clinical studies. Negative, inconclusive or inconsistent clinical trial results could prevent regulatory approval, increase the cost and timing of regulatory approval or require additional studies or a filing for a narrower indication.

In addition, regulatory approval may take longer than we expect as a result of a number of factors, including failure to qualify for priority review of our applications. Delays in obtaining regulatory approval can be extremely costly in terms of lost sales opportunities and increased clinical trial costs. Furthermore, all statutes and regulations governing the approval of our product candidates are subject to change in the future. These changes may increase the time or cost of regulatory approval, limit approval, or prevent it completely.

Even if we receive regulatory approval for our product candidates, the later discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions, including withdrawal of the product from the market. Approval of a product candidate may be conditioned upon certain limitations and restrictions as to the drug's use, or upon the conduct of further studies, and may be subject to continuous review. After approval of a product, we will have significant ongoing regulatory compliance obligations, and if we fail to comply with these requirements, we could be subject to penalties, including warning letters, fines, product recalls, withdrawal of regulatory approval, operating restrictions, injunctions, and criminal prosecution.

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Clinical studies are costly, time consuming and unpredictable, and we have limited experience conducting and managing necessary pre-clinical and clinical trials for our product candidates.

Our initial product candidate, Ramoplanin, is in Phase III clinical trials for the prevention of bloodstream infections caused by vancomycin-resistant enterococci, also known as VRE. Prior clinical and pre-clinical trials for Ramoplanin were conducted by Biosearch Italia and its licensees, from whom we acquired our license to develop Ramoplanin. The speed with which we complete

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our clinical trials and our applications for marketing approval will depend on several factors, including the following:

- . the rate of patient enrollment, which is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study and the nature of the protocol;
- . institutional review board approval of the protocol and the informed consent form;
- . prior regulatory agency review and approval of our applications and procedures;
- . analysis of data obtained from pre-clinical and clinical activities which are susceptible to varying interpretations, which interpretations could delay, limit or prevent regulatory approval;
- . changes in the policies of regulatory authorities for drug approval during the period of product development; and
- . the availability of skilled and experienced staff to conduct and monitor clinical studies, to accurately collect data and to prepare the appropriate regulatory applications.

In addition, the cost of human clinical trials varies dramatically based on a number of factors, including the order and timing of clinical indications pursued, the extent of development and financial support from alliance partners, the number of patients required for enrollment, the difficulty of obtaining clinical supplies of the product candidate, and the difficulty in obtaining sufficient patient populations and clinicians.

We have limited experience in conducting and managing the pre-clinical and clinical trials necessary to obtain regulatory marketing approvals. We may not be able to obtain the approvals necessary to conduct clinical studies. Also, the results of our clinical trials may not be consistent with the results obtained in pre-clinical studies or the results obtained in later phases of clinical trials may not be consistent with those obtained in earlier phases. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after experiencing promising results in early animal and human testing. If regulatory approval of a drug is granted, such approval is likely to limit the indicated uses for which it may be marketed. Furthermore, even if a product of ours gains regulatory approval, the product and the manufacturer of the product will be subject to continuing regulatory review. We may be restricted or prohibited from marketing or manufacturing a product, even after obtaining product approval, if previously unknown problems with the product or its manufacture are subsequently discovered.

We will need to develop marketing and sales capabilities to successfully commercialize our product candidates.

Because we have only recently acquired a license to develop our first product candidate, we currently have no marketing or sales experience. We will need to develop a marketing and sales staff to successfully commercialize our product candidates, including Ramoplanin. The development of marketing and sales capabilities will require significant expenditures, management resources and time. We may be unable to build such a sales force, the cost of establishing such a sales force may exceed any product revenues, or our marketing and sales efforts may be unsuccessful. Failure to successfully establish sales and marketing capabilities in a timely manner or find suitable sales and marketing partners may materially adversely affect our business and

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results of operation. Even if we are able to develop a sales force or find a suitable marketing partner, our products may not be accepted by health care providers or consumers.

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Health care insurers and other payers may not pay for our products or may impose limits on reimbursement.

Our ability to commercialize Ramoplanin and our future products will depend, in part, on the extent to which reimbursement for such products will be available from third-party payers, such as Medicare, Medicaid, health maintenance organizations, health insurers and other public and private payers. If we succeed in bringing Ramoplanin or other products in the future to market, we cannot assure you that third-party payers will pay for Ramoplanin or other products or will establish and maintain price levels sufficient for realization of an appropriate return on our investment in product development. If adequate coverage and reimbursement levels are not provided by government and private payers for use of our products, our products may fail to achieve market acceptance and our results of operations may be materially adversely affected.

Many health maintenance organizations and other third-party payers use formularies, or lists of drugs for which coverage is provided under a health care benefit plan, to control the costs of prescription drugs. Each payer that maintains a drug formulary makes its own determination as to whether a new drug will be added to the formulary and whether particular drugs in a therapeutic class will have preferred status over other drugs in the same class. This determination often involves an assessment of the clinical appropriateness of the drug and sometimes the cost of the drug in comparison to alternative products. We cannot assure you that Ramoplanin or any of our future products will be added to payer's formularies, whether our products will have preferred status to alternative therapies, nor whether the formulary decisions will be conducted in a timely manner. We may also decide to enter into discount or formulary fee arrangements with payers, which could result in us receiving lower or discounted prices for Ramoplanin or future products.

We currently depend and will in the future depend on third parties to manufacture our product candidates, including Ramoplanin.

We do not have the internal capability to manufacture commercial quantities of pharmaceutical products under the FDA's current Good Manufacturing Practices. We have entered into an agreement with Biosearch for the manufacture of Ramoplanin and expect to enter into similar agreements with third parties for the manufacture of future product candidates. We cannot be certain that Biosearch or future manufacturers will be able to deliver commercial quantities of product candidates to us or that such deliveries will be made on a timely basis. If we are required to find additional or alternative sources of supply for Ramoplanin or other future product candidates, we may face additional cost and delay in product development and commercialization. We may not be able to enter into alternative supply arrangements at commercially acceptable rates, if at all. Also, if we change the source or location of supply or modify the manufacturing process, regulatory authorities will require us to demonstrate that the product produced by the new source or from the modified process is equivalent to the product used in any clinical trials that we had conducted.

In addition, any contract manufacturers that we may use must adhere to the FDA's regulations on current Good Manufacturing Practices, which are enforced by the FDA through its facilities inspection program. These facilities are subject to periodic inspection by the FDA. The manufacture of products at these facilities will be subject to strict quality control testing and recordkeeping

requirements.

Moreover, while we may choose to manufacture products in the future, we have no experience in the manufacture of pharmaceutical products for clinical trials or commercial purposes. If we decide to manufacture products, we would be subject to the regulatory requirements described above. In addition, we would require substantial additional capital and would be subject to delays or difficulties encountered in manufacturing pharmaceutical products. No matter who manufactures the products, we will be subject to continuing obligations regarding the submission of safety reports and other post-market information.

The genomics industry is intensely competitive and evolving.

There is intense competition among entities attempting to sequence segments of the human genome and identify genes associated with specific diseases and develop products and services based on these discoveries.

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We face competition in these areas from genomic, pharmaceutical, biotechnology and diagnostic companies, academic and research institutions and government or other publicly-funded agencies, both in the United States and abroad. Some of our competitors are developing databases containing gene sequence, gene expression, genetic variation or other genomic information and are marketing or plan to market their data to pharmaceutical companies. Additional competitors may attempt to establish databases containing this information in the future. In addition, some entities are attempting to identify and patent randomly sequenced genes and gene fragments, while others are pursuing a gene identification, characterization and product development strategy based on positional cloning or other technologies. Numerous pharmaceutical companies also are developing genomic research programs, either alone or in partnership with our competitors. Competition among these entities to sequence genes, identify and characterize genes of interest, obtain patent protection and market this genomic information is intense and is expected to increase. In order to compete against existing and future technologies, we will need to demonstrate to potential customers that our technologies and capabilities are superior to competing technologies.

Many of our competitors have substantially greater capital resources, sequencing capabilities, research and developmental staffs, facilities, manufacturing and marketing experience, distribution channels and human resources than us. These competitors may discover, characterize or develop important genes, drug targets or leads, drug discovery technologies or drugs in advance of us or our customers or which are more effective than those developed by us or our customers, or may obtain regulatory approvals of their drugs more rapidly than our customers do, any of which could have a material adverse effect on any of our similar programs. Moreover, these competitors may obtain patent protection or other intellectual property rights that would limit our rights or our customers' ability to use our products to commercialize therapeutic, diagnostic or vaccine products.

Future competition will come from existing competitors as well as other companies seeking to develop new technologies for drug discovery based on gene sequencing, target gene identification, bioinformatics and related technologies. In addition, certain pharmaceutical and biotechnology companies have significant needs for genomic information and may choose to develop or acquire competing technologies to meet such needs. We also face competition from providers of software. A number of companies have announced their intent to develop and market software to assist pharmaceutical companies and academic researchers in managing and analyzing their own genomic data and publicly



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available data.

Our intellectual property protection may be inadequate to protect our proprietary rights.

Our success will depend, in part, on our ability to obtain commercially valuable patent claims and protect our intellectual property. Our patent position involves complex legal and factual questions, and legal standards relating to the validity and scope of claims in our technology field are still evolving. Therefore, the degree of future protection for our proprietary rights is uncertain.

The risks and uncertainties that we face with respect to our patents and other proprietary rights include the following:

- . the pending patent applications we have filed or to which we have exclusive rights may not result in issued patents or may take longer than we expect to result in issued patents;
- . the claims of any patents which are issued may be limited from those in our patent applications and may not provide meaningful protection;
- . we may not be able to develop additional proprietary technologies that are patentable;
- . the patents licensed or issued to us or our customers may not provide a competitive advantage;
- . other companies may challenge patents licensed or issued to us or our customers;
- . patents issued to other companies may harm our ability to do business;
- . other companies may independently develop similar or alternative technologies or duplicate our technologies; and
- . other companies may design around technologies we have licensed or developed.

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We may apply for patent protection for compositions and methods relating to gene expression and disease-specific patterns of gene expression that we identify and individual disease genes and targets that we discover. These patent applications may include claims relating to novel genes, gene fragments, single nucleotide polymorphisms (SNPs) or encoded protein and to novel uses for known genes, gene fragments, SNPs or proteins identified from the use of our genomic information and our databases.

We may not be able to obtain meaningful patent protection for our discoveries. Even if patents are issued, their scope of coverage or protection is uncertain. For example, we or our collaborators have filed patent applications with respect to a number of full length genes and corresponding proteins and partial genes of *H. pylori*, of *M. leprae* and several other organisms. These applications seek to protect these full-length and partial gene sequences and corresponding proteins, as well as equivalent sequences and products and uses derived from these sequences and proteins. Some court decisions and US Patent and Trademark Office guidelines indicate that disclosure of a partial sequence may not be sufficient to support the patentability of a full-length sequence.

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In addition, we are aware that some companies have published patent applications relating to nucleic acids encoding several H. pylori proteins and, in other disease programs, relating to genes for which we have found mutations of interest. If these companies are issued patents, their patents may limit our ability and the ability of our collaborators to practice under any patents that may be issued to our collaborators or us. Because of this, we or our collaborators may not be able to obtain patents with respect to the genes of infectious agents such as H. pylori, or the value of certain other patents issued to us or our collaborators may be limited. Also, even if a patent were issued to us, the scope of coverage or protection afforded to such patent may be limited.

Our proprietary position may depend on our ability to protect trade secrets.

We rely on trade secret protection for our confidential and proprietary information and procedures, including procedures related to sequencing genes and to searching and identifying important regions of genetic information. We currently protect such information and procedures as trade secrets. We protect our trade secrets through recognized practices, including access control, confidentiality agreements with employees, consultants, collaborators, and customers, and other security measures. These confidentiality agreements may be breached, however, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently developed by competition.

We may infringe the intellectual property rights of third parties and may become involved in expensive intellectual property litigation.

The intellectual property rights of biotechnology companies, including our company, are generally uncertain and involve complex legal, scientific and factual questions. Our success in the functional genomic field may depend, in part, on our ability to operate without infringing on the intellectual property rights of others and to prevent others from infringing on our intellectual property rights.

There has been substantial litigation regarding patents and other intellectual property rights in the genomic industry. We may become party to patent litigation or proceedings at the U.S. Patent and Trademark Office or a foreign patent office to determine our patent rights with respect to third parties which may include subscribers to our database information services. Interference proceedings in the U.S. Patent and Trademark Office or opposition proceedings in a foreign patent office may be necessary to establish which party was the first to discover such intellectual property. We may become involved in patent litigation against third parties to enforce our patent rights, to invalidate patents held by such third parties, or to defend against such claims. The cost to us of any patent litigation or similar proceeding could be substantial, and it may absorb significant management time. If an infringement litigation against us is resolved unfavorably, we may be enjoined from manufacturing or selling certain of our products or services without a license from a third party. We may not be able to obtain such a license on commercially acceptable terms, or at all.

We may not be able to obtain meaningful patent protection for discoveries under our government contracts.

Under our government grants and contracts, the government has a statutory right to practice or have practiced any inventions developed under the

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government research contracts. In addition, under certain circumstances, such as inaction on the part of us or our licensees to achieve practical application of the invention or a need to alleviate public health or safety concerns not reasonably satisfied by us or our licensees, the government has the right to grant to other parties licenses to any inventions first reduced to practice under the government grants and contracts. If the government grants such a license to a third party, our patent position may be jeopardized. In addition, the government has ownership rights in the data, clones, genes and other material derived from the material furnished to us by the government, while we have ownership rights in other technology developed solely by us. We are also obligated under certain government grants to submit sequencing data and materials resulting from our research to public databases within 24 hours from the date such data and materials are developed. Our ability to obtain patent protection for our discoveries and inventions may be adversely affected by this publication.

International patent protection is uncertain.

Patent law outside the United States is uncertain and is currently undergoing review and revision in many countries. Further, the laws of some foreign countries may not protect our intellectual property rights to the same extent as U.S. laws. We may participate in opposition proceedings to determine the validity of our or our competitors' foreign patents, which could result in substantial costs and diversion of our efforts. Finally, some of our patent protection in the United States is not available to us in foreign countries due to the laws of those countries.

We expect to raise additional funds in the future.

We believe that our existing cash and marketable securities together with borrowings under equipment financing arrangements and anticipated cash flow from operations will be sufficient to support our current plans for approximately two years. However, we expect to raise additional capital, subject to market conditions and strategic considerations over the course of the next 18 months. In particular, we may need additional funds to increase our research and development activities and fund our clinical trials. We may seek funding through additional public or private equity offerings, debt financings or agreements with customers. If we raise additional capital by issuing equity or convertible debt securities, the issuances may dilute share ownership of existing investors and future investors may be granted rights superior to those of current shareholders. Additional financing may not be available when needed, or, if available, may not be available on favorable terms. If we cannot obtain adequate financing on acceptable terms when such financing is required, our business will be adversely affected.

We have issued \$15 million of convertible notes due December 31, 2004, which contain restrictive covenants, including covenants that can cause early repayment of the Notes.

On March 5, 2002, we issued convertible notes, bearing interest at 6% per annum, to two institutional investors in the aggregate principal amount of \$15 million. The Notes are due on December 31, 2004, but if at any time on or after December 31, 2003, we maintain a net cash balance (i.e., cash and cash equivalents less obligations for borrowed money bearing interest) of less than \$35 million, then the holders of the notes can require that all or any part of the outstanding principal balance of the notes plus all accrued but unpaid interest be repaid. If we have to repay the notes early, our cash position and ability to execute our business plan could be adversely affected. The notes also contain provisions limiting Genome Therapeutics' ability to incur debt that is senior to the notes, with an exception for certain equipment financing, and provisions that can cause the payment of a premium to the holders of the notes on a change of control transaction.

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The notes are convertible into our common stock at a price of \$8 per share (subject to anti-dilution and other adjustments). As part of the transaction, the purchasers also received warrants to purchase up to 487,500 shares

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of our common stock at an exercise price of \$8.00 per share (subject to anti-dilution and other adjustments), which become exercisable to the extent the notes are converted or if certain other redemptions or repayments of the notes occur. The shares underlying the notes and the warrants will be registered for re-sale and if the notes are converted and the warrants exercised, these shares could be sold into the market creating dilution of the ownership of our shareholders at that time.

We rely on funding from the United States government.

As of December 31, 2001, we had approximately \$8.6 million of government research contracts outstanding under which we had not yet completed all of the services. Funding under our government grants and research contracts is subject to appropriation each year by the United States Congress and can be discontinued or reduced at any time. In addition, there can be no assurance that we will receive additional grants or contracts in the future. The government's failure to fund our research in this area not only would end our participation in the program, but might adversely affect the industry-wide perception of genomics and the utility of genomic information.

Our research and product development depends on access to tissue samples and other biological materials from individuals.

To continue to build our database products, we will need access to normal and diseased human and other tissue samples, other biological materials and related clinical and other information, which may be in limited supply. We compete with many other companies for these materials and information. We may not be able to obtain or maintain access to these materials and information on acceptable terms. In addition, government regulation in the United States and foreign countries could result in restricted access to, or use of, human and other tissue samples. If we lose access to sufficient numbers or sources of tissue samples, or if tighter restrictions are imposed on our use of the information generated from tissue samples, our business may be harmed. Competition among genomics companies is also increasing for access to unique data from related individuals that we use to identify genes for specific human diseases.

Ethical, legal and social issues related to the use of genetic information and genetic testing may cause less demand for our products.

Genetic testing has raised issues regarding confidentiality and the appropriate uses of the resulting information. For example, consumers have expressed concerns towards insurance carriers and employers using such tests to discriminate on the basis of such information, resulting in barriers to the acceptance of such tests. This could lead to governmental authorities calling for limits on or regulation of the use of genetic testing or prohibit testing for genetic predisposition to certain diseases, particularly those that have no known cure. Any of these scenarios could reduce the potential markets for our products.

We may not succeed in realizing any additional revenue from the PathoGenome Database.

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In 1997, we introduced the PathoGenome Database that consists of genetic information from more than thirty microbial organisms. In the past, our strategy for our database depended on entering into subscription agreements with pharmaceutical, biotechnology and other companies for the use of our database. Each of the agreements that we may have with our customers is for a specific term, and we anticipate that they may not be renewed upon expiration or may be renewed at a substantially lower price. If any agreements expire and are not renewed, our revenue would suffer.

Our sales cycle is lengthy and we may spend considerable resources on unsuccessful negotiation efforts or may not be able to complete deals on the schedule anticipated.

Our ability to obtain new customers for genomic information products depends on our customers' belief that we can help accelerate their drug discovery efforts. Our negotiation cycle is typically lengthy because we need to

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educate potential customers and sell the benefits of our products and services to a variety of constituencies within companies. In addition, each agreement involves the negotiation of unique terms. We may expend substantial funds and management effort with no assurance that an agreement will result. Actual and proposed consolidations of pharmaceutical companies have affected and may in the future affect the timing and progress of our ability to conclude deals with collaborative partners.

We depend on key personnel in a highly competitive market for skilled personnel.

We are highly dependent on the principal members of our senior management and key scientific and technical personnel. The loss of any of these personnel could have a material adverse effect on our ability to achieve our goals. Our future success is also dependent upon our ability to attract and retain additional qualified scientific, technical and managerial personnel. Our plan to expand our biopharmaceutical program will require us to hire a number of new personnel with expertise in the areas of clinical trials and sales and marketing. We experience intense competition for qualified personnel and may not be able to continue to attract and retain skilled personnel necessary for the development of our business.

Our activities involve hazardous materials and may subject us to environmental liability.

Our research and development involve the controlled use of hazardous and radioactive materials and biological waste. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials and certain waste products. Although we believe that our safety procedures for handling and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, we could be held liable for damages or penalized with fines, and this liability could exceed our resources.

We believe that we are in compliance in all material respects with applicable environmental laws and regulations and currently do not expect to make material additional capital expenditures for environmental control facilities in the near term. However, we may have to incur significant costs to comply with current or future environmental laws and regulations.

We may have difficulty managing our growth.

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We expect to continue to experience growth in the number of our employees and customers and the scope of our operations. In particular, we plan significant growth in our service (GenomeVision) and bioPharmaceutical business. This growth may continue to place a significant strain on our management and operations. Our ability to manage this growth will depend upon our ability to broaden our management team and our ability to attract, hire and retain skilled employees. Our success will also depend on the ability of our officers and key employees to continue to implement and improve our operational and other systems, to manage multiple, concurrent customer relationships and to hire, train and manage our employees.

Our stock price is highly volatile.

The market price of our stock has been and is likely to continue to be highly volatile due to the risks and uncertainties described in this section of the prospectus, as well as other factors, including:

- . conditions and publicity regarding the genomic or life sciences industries generally;
- . price and volume fluctuations in the stock market at large which do not relate to our operating performance; and
- . comments by securities analysts, or our failure to meet market expectations.

The stock market has from time to time experienced extreme price and volume fluctuations that are unrelated to the operating performance of particular companies. In the past, companies that have experienced volatility have sometimes been the subject of securities class action litigation. If litigation were instituted on this basis, it could result in substantial costs and a diversion of management's attention and resources.

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Multiple factors beyond our control may cause fluctuations in our operating results and may cause our business to suffer.

Our revenues and results of operations may fluctuate significantly, depending on a variety of factors, including the following:

- . our success in concluding deals for, and changes in the demand for, our products;
- . variations in the timing of payments from partners and customers and the recognition of these payments as revenues;
- . the terms we are able to negotiate in our deals;
- . the progress of our pre-clinical and clinical trials;
- . the timing of our new product introductions, if any;
- . changes in the research and development budgets of our customers and potential customers;
- . the introduction of new products and services by our competitors;
- . regulatory actions;

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- . expenses related to, and the results of, litigation and other proceedings relating to intellectual property rights;
- . the cost and timing of our adoption of new technologies;
- . the cost, quality and availability of cell and tissue samples, reagents and related components and technologies, including those supplied to us pursuant to contractual arrangements; and
- . the lengthy nature of our sales cycle for concluding alliances and other deals.

We will not be able to control many of these factors. In addition, if our revenues in a particular period do not meet expectations, we may not be able to adjust our expenditures in that period, which could cause our business to suffer. We believe that period-to-period comparisons of our financial results will not necessarily be meaningful. You should not rely on these comparisons as an indication of our future performance. If our operating results in any future period fall below the expectations of securities analysts and investors, our stock price may fall, possibly by a significant amount.

Future acquisitions may absorb significant resources and may be unsuccessful.

As part of our strategy, we may pursue acquisitions of businesses or assets, investments and other relationships and alliances. Acquisitions may involve significant cash expenditures, debt incurrence, additional operating losses, dilutive issuances of equity securities, and expenses that could have a material adverse effect on our financial condition and results of operations. For example, to the extent that we elect to pay the purchase price for such acquisitions in shares of our stock, the issuance of additional shares of our stock will be dilutive to our stockholders. Acquisitions involve numerous other risks, including:

- . difficulties integrating acquired technologies and personnel into our business;
- . diversion of management from daily operations;
- . inability to obtain required financing on favorable terms;
- . entering new markets in which we have little or no previous experience;
- . potential loss of key employees or customers of acquired companies;
- . assumption of the liabilities and exposure to unforeseen liabilities of acquired companies; and
- . amortization of the intangible assets of acquired companies.

It may be difficult for us to complete these types of transactions quickly and to integrate the businesses efficiently into our current business. Any acquisitions or investments by us may ultimately have a negative impact on our business and financial condition.

### USE OF PROCEEDS

The net proceeds from the sale of the securities will be received by the selling stockholders. We will not receive any proceeds from the sale of the securities by the selling stockholders.

SELLING STOCKHOLDERS

On March 5, 2002, we entered into a Purchase Agreement with the selling stockholders named below pursuant to which we issued convertible notes to such selling stockholders in the aggregate principal amount of \$15 million in a private placement. As part of the transaction, we also issued them warrants to purchase up to 487,500 shares of our common stock, which become exercisable to the extent the notes are converted or if certain other redemptions or repayments of the notes occur. The shares of our common stock registered for resale in the registration statement of which this prospectus is a part are the shares underlying the notes and warrants (subject to antidilution adjustments) as well as a certain number of shares to satisfy interest payment obligations on the notes.

The number of shares registered in the registration statement of which this prospectus is a part and the number of shares offered in this prospectus represents our bona fide estimate of the number of shares issuable upon conversion of the convertible notes and exercise of the warrants (subject, in each case, to antidilution adjustments) and payment of all interest on the notes in shares of common stock. The number of shares that will ultimately be issued to the selling stockholders cannot be determined at this time because it depends on: (1) whether the holders of the convertible notes elect to convert the convertible notes into shares of common stock; (2) whether we elect to require the conversion of the convertible notes upon the market price of the common stock meeting a specified price threshold; (3) whether the holders of the warrants exercise their warrants; (4) the conversion price of the convertible notes and the exercise price of the warrants at the time of conversion of the convertible notes and exercise of the warrants; (5) the period for which the convertible notes remain outstanding; and (6) the market price of our common stock at the time we make any interest payments on the convertible notes.

The table below sets forth information regarding ownership of our common stock by the selling stockholders and the number of shares that may be sold by them under this prospectus. The number of shares set forth in the table as being held by the selling stockholders includes the number of shares of common stock that are issuable upon conversion of the convertible notes and the exercise of the warrants as of March 29, 2002. The number of shares set forth on the table as being offered hereby represents the total number of shares we have registered for resale by the selling stockholders based on our bona fide estimate of the number of shares of common stock that we will need to issue to the selling stockholders on conversion of the notes and exercise of the warrants (subject, in each case, to antidilution adjustments) and payment of all interest on the notes. This amount includes 100% of the number of shares of common stock issuable as of March 29, 2002 upon conversion of the convertible notes and exercise of the warrants and 100% of the number of shares we believe will need to be issued as interest payments over the term of the notes. However, the actual number of shares of common stock issuable upon conversion of the convertible notes, exercise of the warrants and payment of interest is indeterminable, and could be materially more or less than the amounts listed on the table due to possible conversion and exercise price adjustments, and, in the case of interest payments, changes to the market price of our common stock. Because the selling stockholders may offer all or some portion of the common stock listed in the table pursuant to this prospectus or otherwise, no estimate can be given as to the amount of common stock that will be held by the selling stockholders upon termination of the offering. The selling stockholders may sell all, part, or none of the shares listed. The number of shares owned by the selling stockholders is determined by rules promulgated by the Commission for beneficial ownership and is not necessarily indicative of ownership for any



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other purpose. None of the selling stockholders has had any position, office or other material relationship with us, other than as a security holder, during the past three years.

Name of Selling Shareholder -----	Shares Owned Prior To Offering -----	Shares of Common Stock Offered Hereby -----	Shares Owned After Offering -----
Smithfield Fiduciary LLC	2,370,000 (1)	2,370,000	0
The Tail Wind Fund, Ltd.	592,500 (2)	592,500	0

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- (1) Includes 1,500,000 shares issuable upon conversion of \$12,000,000 of convertible notes, plus 390,000 shares issuable upon the exercise of warrants and 480,000 shares that may be issued upon payment of interest on convertible notes or upon antidilution adjustments.
- (2) Includes 375,000 shares issuable upon conversion of \$3,000,000 of convertible notes, plus 97,500 shares issuable upon the exercise of warrants and 120,000 shares that may be issued upon payment of interest on convertible notes or upon antidilution adjustments.

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### PLAN OF DISTRIBUTION

We are registering the shares of common stock on behalf of the selling stockholders. The selling stockholders will act independently of us in making decisions with respect to the timing, manner and size of each sale. All costs, expenses and fees in connection with the registration of the shares offered by this prospectus will be borne by us, other than brokerage commissions and similar selling expenses, if any, attributable to the sale of shares which will be borne by the selling stockholders. Sales of shares may be effected by selling stockholders from time to time in one or more types of transactions (which may include block transactions) on the Nasdaq National Market, in the over-the-counter market, in negotiated transactions, through put or call options transactions relating to the shares, through short sales of shares, or a combination of such methods of sale, at market prices prevailing at the time of sale, or at negotiated prices. Such transactions may or may not involve brokers or dealers. The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares, nor is there an underwriter or coordinated broker acting in connection with the proposed sale of shares by the selling stockholders.

The selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the shares or of securities convertible into or exchangeable for the shares in the course of hedging positions they assume with selling stockholders. The selling stockholders may also enter into options or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealers or other financial institutions of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as amended or supplemented to reflect such transaction).

The selling stockholders may make these transactions by selling shares

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directly to purchasers or to or through broker-dealers, which may act as agents or principals. Such broker-dealers may receive compensation in the form of discounts, concessions or commissions from selling stockholders and/or the purchasers of shares for whom such broker-dealers may act as agents or to whom they sell as principal, or both (which compensation as to a particular broker-dealer might be in excess of customary commissions).

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares owned by them. If the selling stockholders default in the performance of their secured obligations, the pledgees or secured parties may offer and sell their shares from time to time under a supplement to this prospectus or a post-effective amendment to the registration statement of which this prospectus is a part, as applicable law may require, amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer the shares in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus subject to filing any supplement to this prospectus or post-effective amendment to the registration statement required by applicable law.

The selling stockholders and any broker-dealers that act in connection with the sale of shares may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act, and any commissions received by such broker-dealers or any profit on the resale of the shares sold by them while acting as principals might be deemed to be underwriting discounts or commissions under the Securities Act. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares against certain liabilities, including liabilities arising under the Securities Act.

Because selling stockholders may be deemed to be "underwriters" within the meaning of Section 2(11) of the Securities Act, the selling stockholders will be subject to the prospectus delivery requirements of the Securities Act. We have informed the selling stockholders that the anti-manipulative provisions of Regulation M promulgated under the Exchange Act may apply to their sales in the market.

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Selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, provided they meet the criteria and conform to the requirements of Rule 144.

Upon our being notified by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing:

- . the name of each such selling stockholder and of the participating broker-dealer(s);
- . the number of shares involved;
- . the initial price at which such shares were sold;
- . the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable;

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- . that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus; and
- . other facts material to the transactions.

We have agreed to indemnify the selling stockholders in certain circumstances against some liabilities, including liabilities that could arise under the Securities Act. The selling stockholders have agreed to indemnify us, our directors and our officers who sign the registration statement against some liabilities in certain circumstances, including liabilities that could arise under the Securities Act.

We have agreed to maintain the effectiveness of this registration statement until the earlier of the sale of all the shares offered by this prospectus or the date that each holder of such shares can sell all of the shares it holds in compliance with Rule 144(k) promulgated under the Securities Act, but in no event beyond March 5, 2007. No sales may be made pursuant to this prospectus after the expiration date unless we amend or supplement this prospectus to indicate that we have agreed to extend the period of effectiveness. The selling stockholders may sell all, some or none of the shares offered by this prospectus.

### LEGAL MATTERS

Ropes & Gray, Boston, Massachusetts, will pass upon the validity of the shares of common stock we are offering.

### EXPERTS

The consolidated financial statements, incorporated by reference in this prospectus and elsewhere in the registration statement, have been audited by Arthur Andersen LLP, independent public accountants, as indicated in their reports with respect thereto, and are included herein in reliance upon the authority of said firm as experts in giving said report.

### AVAILABLE INFORMATION

This prospectus, which constitutes a part of a registration statement on Form S-3 (the "registration statement") filed by us with the Securities and Exchange Commission (the "Commission") under the Securities Act, omits certain of the information set forth in the registration statement. Reference is hereby made to the registration statement and to the exhibits thereto for further information with respect to us and the securities offered hereby. Copies of the registration statement and the exhibits thereto are on file at the offices of the Commission and may be obtained upon payment of the prescribed fee or may be examined without charge at the public reference facilities of the Commission described below or via the Commission's web site described below.

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Statements contained herein concerning the provisions of documents are necessarily summaries of such documents, and each statement is qualified in its entirety by reference to the copy of the applicable document filed with the Commission.

### INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The following documents or portions of documents filed by us (File No.

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0-10824) with the Commission are incorporated herein by reference:

- (a) Our Annual Report on Form 10-K for the fiscal year ended December 31, 2001.
- (b) Our Current Report on Form 8-K as filed on March 6, 2002.
- (c) The description of our common stock contained in our registration statement on Form 10/A filed with the Commission on January 9, 1996 under the Exchange Act, including any amendment or reports filed for the purpose of updating such description.

All reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the filing of a post-effective amendment that indicates that all securities offered hereby have been sold or which deregisters all securities remaining unsold, shall be deemed to be incorporated by reference into this prospectus and to be a part hereof from the date of the filing of such reports or documents. Any statement contained in a document, all or a portion of which is incorporated by reference herein, shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained or incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

Upon written or oral request, we will provide without charge to each person, including any beneficial owner, to whom this prospectus is delivered a copy of any or all of such documents which are incorporated herein by reference (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into the documents that this prospectus incorporates). Written or oral requests for copies should be directed to Manny Bougoulas, Comptroller, 100 Beaver Street, Waltham, Massachusetts 02453, telephone number (781) 398-2300.

We are subject to the informational requirements of the Exchange Act, and, accordingly, file reports, proxy statements and other information with the Commission. You can read our Commission filings, including the registration statement, over the Internet at the Commission's website at <http://www.sec.gov>. You may also read and copy any document we file with the Commission at its public reference facilities at 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549; and Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661. You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Commission at 450 Fifth Street, N.W., Washington D.C. 20549. Please call the Commission at 1-800-SEC-0330 for further information on the operation of public reference facilities.

### COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is therefore unenforceable.

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We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any shares in any jurisdiction where it is unlawful. The information in this prospectus is current as of the date shown on the cover page.

Genome Therapeutics Corp.

2,962,500 Shares of  
Common Stock

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PROSPECTUS  
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April 19, 2002

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