GENOME THERAPEUTICS CORP
Form S-3/A
September 12, 2003
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As filed with the Securities and Exchange Commission on September 12, 2003

Registration No. 333-106602

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

AMENDMENT NO. 2 TO

FORM S-3

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

GENOME THERAPEUTICS CORP.

(Exact name of registrant as specified in its charter)

Massachusetts	**04-2297484**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

100 Beaver Street

Waltham, Massachusetts 02453

(781) 398-2300

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Stephen Cohen

Senior Vice President and Chief Financial Officer

Genome Therapeutics Corp.

100 Beaver Street

Waltham, Massachusetts 02453

(781) 398-2300

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Patrick O Brien

Ropes & Gray

One International Place

Boston, MA 02110-2624

(617) 951-7000

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement is declared effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box . x

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title of shares to be registered	Amount to be registered [1]	Proposed maximum offering price per share [2]	Proposed maximum aggregate offering price [2]	Amount of registration fee [2]
Common Stock $0.10 Par Value	486,646 Shares	$2.63	$1,279,878.98	$103.54

(1) Represents shares issuable upon the exercise of the warrants. In addition to the shares set forth in the table, the amount to be registered may include an indeterminate number of shares issuable upon exercise of the warrants, as this amount may be adjusted as a result of stock splits, stock dividends and similar transactions in accordance with Rule 416.

(2) In accordance with Rule 457(c), the price is estimated solely for purposes of calculating the registration fee and is based upon the average of the reported high and low sales prices of the Common Stock as reported on the Nasdaq National Market on June 25, 2003. This registration fee was previously paid on June 27, 2003.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until this registration statement shall become effective on such date as the Commission, acting pursuant to Section 8(a), may determine.

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The information in this Prospectus is not complete and may be changed. The selling stockholders may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 12, 2003.

PROSPECTUS

486,646 Shares

Genome Therapeutics Corp.

Common Stock

These shares are being offered for sale by the selling stockholders listed on page 12. 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 13.

The common stock is traded on the Nasdaq National Market under the symbol GENE . On September 5, 2003, the reported closing price of the common stock was $2.89 per share.

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

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.

The date of this prospectus is September __, 2003.

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THE COMPANY

We are a biopharmaceutical company focused on the discovery, development and commercialization of pharmaceutical and diagnostic products. Our strategic goal is to directly participate in the commercialization of products that are used primarily in hospitals. For diseases treated by larger physician audiences, we seek to discover, develop and commercialize products through alliances with major pharmaceutical companies.

We have nine established product development programs. We are managing the development and commercialization of our lead product candidate, Ramoplanin, in the United States and Canada. This product is in a Phase III clinical trial for the prevention of bloodstream infections caused by vancomycin-resistant enterococci (VRE) and a Phase II trial for the treatment of patients with Clostridium difficile-associated diarrhea (CDAD). We have seven product discovery and development alliances with pharmaceutical companies including Amgen, AstraZeneca, bioMerieux, Schering-Plough and Wyeth. Our biopharmaceutical product candidates are all currently in discovery or development phases and are neither approved by the U.S. Food and Drug Administration nor available for commercial sale.

Over the past two years, our primary business focus has evolved from providing basic research and genomic services for pharmaceutical companies to more downstream efforts emphasizing clinical development and commercialization of our own product candidates. We continue to reduce our expenditures in the early-stage product discovery and development research areas, including genomics research, and to focus our resources on later stage drug discovery and development. This evolution in our strategic focus reflects our goals of getting products to market more rapidly and generating more substantial revenues and, ultimately, profits for our shareholders.

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.

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Risks Related to Our Business

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 $22,643,000 for the six months ended June 30, 2003 and as of June 30, 2003, we had an accumulated deficit of approximately $148,419,000. We had a net loss of approximately $34,017,000 for the fiscal year ended December 31, 2002, and, as of December 31, 2002, we had an accumulated deficit of approximately $125,775,000. For the fiscal year ended December 31, 2001, we had a net loss of approximately $10,090,000, and for the fiscal year ended December 31, 2000, we had a net loss of approximately $5,847,000. The losses have resulted primarily from costs incurred in research and development, including our clinical trials, 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 genomic discoveries 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.

We will need 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 fourteen months. We expect to raise additional capital over the course of the next twelve months. In particular, we will 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. Our ability to raise additional capital, however, will be heavily influenced by the investment market for biotechnology companies and the progress of our clinical development programs over that period. 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.

Future fund raising could dilute the ownership interests of our stockholders.

In order to raise additional funds, we may issue equity or convertible debt securities in the future. Depending upon the market price of our shares at the time of any transaction, we may be required to sell a significant percentage of our outstanding shares of common stock in order to fund our operating plans, potentially requiring a shareholder vote. In addition, we may have to sell our securities at a discount to the prevailing market price, resulting in further dilution to our stockholders.

Clinical trials 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 lead product candidate, Ramoplanin, is in a Phase III clinical trial for the prevention of bloodstream infections caused by vancomycin-resistant enterococci, also known as VRE, and a Phase II clinical trial to assess the safety and efficacy of Ramoplanin to treat

Clostridium difficile-associated diarrhea (CDAD). Prior clinical and pre-clinical trials for Ramoplanin were conducted by Biosearch Italia S.p.A. and its licensees, from whom we acquired our license to develop Ramoplanin. We may not be able to demonstrate the safety and efficacy of Ramoplanin or our other 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.

The speed with which we complete 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;

- fluctuations in the infection rates for patients enrolled in our trials;

- compliance of patients and investigators with the protocol;

- 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;

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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.

Our product candidates may face significant competition in the marketplace.

Our lead product candidate, Ramoplanin, is currently in development for the prevention of blood stream infections caused by vancomycin-resistant enterococci (VRE). We have no knowledge of any product currently approved by the Food and Drug Administration (FDA) for this indication, nor are we aware of any product candidate currently in clinical trials for this indication. It is possible that competition exists without our knowledge and that current discovery and preclinical efforts are ongoing for this indication. Ramoplanin is also in clinical development for the treatment of Clostridium difficile-associated diarrhea (CDAD). We are aware of two products currently utilized in the marketplace Vancocin, a product of Eli Lilly, and Metronidazole, a generic product for treatment of this indication. We are also aware of at least three companies with products in development for the treatment of CDAD Geltex/Genzyme in Phase II; ImmuCell in PhaseI/II; and Acambis in Phase I/II. It is also possible that other companies are developing competitive products for this indication. All of our other internal product programs are in earlier stages and have not yet reached clinical development and are not yet indication specific. Our alliance-related product development programs are also all in pre-clinical stages, and it is therefore not possible to identify any product profiles or competitors for these product development programs at this time. Our industry is very competitive and it therefore is likely that if and when product candidates from our early stage internal programs or our alliance programs reach the clinical development stage or are commercialized for sale, these products will also face competition.

Many of our competitors have substantially greater capital resources, facilities and human resources than us. Furthermore, many of our competitors are more experienced than we are in drug discovery, development and commercialization, and in obtaining regulatory approvals. As a result, our competitors may discover, develop and commercialize pharmaceutical products or services before us. In addition, our competitors may discover, develop and commercialize products or services that are more effective than, or otherwise render non-competitive or obsolete, the products or services that we or our collaborators are seeking to develop and commercialize. Moreover, these competitors may obtain patent protection or other intellectual property rights that would limit our rights or the ability of our collaborators to develop or commercialize pharmaceutical products or services.

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. 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 discoveries. If our partners are unable to use the genomic information that we provide to them to develop such products, they may cease to pursue our alliance, and our business may suffer as a result.

We rely heavily upon existing and prospective alliance partners and licensees as a source of revenue for our operations and as a means of developing and commercializing our products.

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

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AstraZeneca, Amgen, bioMerieux, Schering-Plough and Wyeth-Ayerst. We have received a 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 order to maintain our collaboration agreements with each of Amgen, bioMerieux and Wyeth, we must fulfill certain obligations, including carrying out research programs agreed to by the parties, keeping records of our research activities, providing periodic reports on the status of each research program, devoting qualified personnel to each research program, and providing our collaborators with reasonable technical assistance in using the know-how or other information that we have licensed to them. Under our other collaboration agreements, we have fulfilled all of our research and development obligations and have no material obligations going forward. We believe that we are currently in compliance with our obligations under our collaboration agreements, but there can be no assurance that we will be able to successfully complete our obligations in the future due to, among other things, an inability to achieve scientific goals or a lack of qualified personnel.

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.

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.

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 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.

Development of therapeutic, diagnostic and vaccine products by our strategic alliance partners based on our discoveries will be subject to the high risks of failure inherent in the development or commercialization of biopharmaceutical products.

There can be no assurance of the successful development or commercialization of any products by our strategic alliance partners based on our discoveries. Successful development and commercialization will be subject to numerous risks at each stage. For example, we cannot be certain that the high-throughput screening or lead optimization processes for a given strategic alliance will identify any compounds suitable for clinical development. Even if product candidates based on our discoveries undergo clinical trials, we cannot be certain that those clinical trials will indicate that the product candidates are safe or effective.

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We also cannot know the pace at which the clinical trials will proceed. Furthermore, after the completion of clinical trials, a product could fail to receive necessary regulatory approvals due to negative, inconclusive or insufficient clinical data or other reasons beyond our control. Even if the necessary regulatory approvals for a product are obtained, it may be difficult or impossible to manufacture the product 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.

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 results of operations. 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.

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 (which merged with Versicor Inc. in March 2003 and subsequently changed its name to Vicuron Pharmaceuticals Inc.) 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 Vicuron 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.

Our failure to acquire and develop additional product candidates or approved products will impair our ability to grow.

As part of our growth strategy, we intend to acquire and develop additional product candidates or approved products. The success of this strategy depends upon our ability to identify, select and acquire biopharmaceutical products that meet our criteria. We may not be able to acquire the rights to additional product candidates and approved products on terms that we find acceptable, or at all.

Any product candidate we acquire will require additional research and development efforts prior to commercial sale, including extensive pre-clinical and/or clinical testing and approval by the FDA and corresponding foreign regulatory authorities. All product candidates are prone to the risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate will not be safe, non-toxic and effective or approved by regulatory authorities. In addition, we cannot assure you that any approved products that we develop or acquire will be:

manufactured or produced economically;

successfully commercialized; or

widely accepted in the marketplace.

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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.

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 our personnel could have a material adverse effect on our ability to achieve our goals. We maintain employment agreements with each of our officers, who are: Steven M. Rauscher, President and Chief Executive Officer; Stephen Cohen, Senior Vice President and Chief Financial Officer; Richard Labaudiniere, Senior Vice President of Research and Development; and Martin D. Williams, Senior Vice President, Corporate Development & Marketing. The term of each employment agreement continues until it is terminated by the officer or us. In the event that an officer s employment is terminated by us for reasons other than for cause, or is terminated with good reason by the officer, the officer s employment agreement provides for the continuation of all compensation and benefits for a period of up to 12 months in the case of Mr. Rauscher, or up to 9 months in the cases of Messrs. Cohen, Labaudiniere and Williams, or until such time as he is re-employed, whichever occurs first. We do not maintain key person life insurance on any of our employees.

Our future success is 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. Like others in our industry, we may face and in the past have faced from time to time difficulties in attracting and retaining certain employees with the requisite expertise and qualifications. We believe that our historical recruiting periods and employee turnover rates are similar to those of others in our industry, however, we cannot be certain that we will not encounter greater difficulties in the future.

Our intellectual property protection and other protections may be inadequate to protect our products.

Our success will depend, in part, on our ability to obtain commercially valuable patent claims and protect our intellectual property. We currently have 12 issued U.S. patents, 99 pending U.S. patent applications, 10 issued foreign patents and 46 pending foreign patent applications. These patents and patent applications primarily relate to the field of human and pathogen genetics. Our material patents are as follows:

U.S. Patent No. 6,380,370 granted April 30, 2002, relating to *Staphylococcus epidermidis;* expiring August 13, 2018

U.S. Patent No. 6,551,795 granted April 22, 2003, relating to *Pseudomonas aeruginosa;* expiring February 18, 2019

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U.S. Patent No. 6,562,958 granted May 13, 2003, relating to *Acinetobacter baumannii;* expiring June 4, 2019

U.S. Patent No. 6,583,275 granted June 24, 2003, relating to *Enterococcus faecium;* expiring June 30, 2018

U.S. Patent No. 6,583,266 granted June 24, 2003, relating to *Mycobacterium tuberculosis;* expiring June 24, 2020

While it is difficult to assess the value of our intellectual property portfolio, we anticipate that the patents named above will provide a competitive advantage in certain instances in the pathogen and anti-infective field by requiring others to obtain a license from us if they wish to produce competing products.

We are not currently involved in any litigation, settlement negotiations, or other legal action regarding patent issues and are not aware of any patent litigation threatened against us. 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 patents that we license to Ramoplanin under the License and Supply Agreement with Vicuron include claims relating to methods of manufacturing Ramoplanin as well as methods increasing the yield of the active compound. We also have applications pending relating to various novel uses of Ramoplanin. The patent covering the chemical composition of Ramoplanin has expired. To provide additional protection for Ramoplanin, we rely on proprietary know-how relating to maximizing yields in the manufacture of Ramoplanin, as well as the five year data exclusivity provisions under the Hatch-Waxman Act.

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.

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.

Under our agreement with Vicuron, we have obtained an exclusive license to develop and market oral Ramoplanin in the United States and Canada. Under this agreement, we are responsible, at our expense, for the clinical and non-clinical development of Ramoplanin in our field, the prevention and treatment of human disease, in the United States and Canada, including the conduct of clinical trials and the filing of drug approval applications with the Food and Drug Administration and other applicable regulatory authorities. Vicuron is responsible for providing us with all information in its possession relating to Ramoplanin in our licensed field, for cooperating with us in obtaining regulatory approvals of Ramoplanin and for using diligent efforts to provide us with bulk Ramoplanin sufficient to carry out our clinical development activities. We believe that we are currently in compliance with our obligations under the License and Supply Agreement, but there can be no assurance that we will be able to remain in compliance due to the limitations on our resources and the many risks of conducting clinical trials, as described above in Clinical trials are costly, time consuming and unpredictable, and we have limited experience conducting and managing necessary pre-clinical and clinical trials for our product candidates .

Under our agreement with Vicuron, Vicuron has the obligation to prosecute patents relating to Ramoplanin that are made by Vicuron personnel or conceived jointly by our personnel and Vicuron personnel. We have the obligation to prosecute patents relating to Ramoplanin that are made solely by our personnel. We have the right to control any suits brought by a third party alleging that the manufacture, use or sale of Ramoplanin in our licensed field in the United States or Canada infringes upon their rights. We will bear the costs of any such actions, which could be substantial; provided that if we are obligated to pay any royalties or other payments to a third party to sell Ramoplanin as a result of this litigation, including any settlement reached with Vicuron s consent, Vicuron is obligated to pay that expense.

We also have the primary right to pursue actions for infringement of any patent licensed from Vicuron under the License and Supply Agreement within the United States and Canada within our licensed field. Vicuron has the primary right to pursue actions for infringement of any patents that it licenses to us under the License and Supply Agreement outside of our licensed field within the United States and Canada and for all purposes outside of the United States and Canada. If the party with the primary right to pursue the infringement actions elects not to pursue it, the other party generally has the right to pursue it. The costs of any infringement actions are first paid out of any damages recovered and are then allocated to the parties depending upon their interest in the suit. The costs of pursuing any such action could substantially diminish our resources.

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. We do not maintain separate insurance to cover intellectual property infringement. Our general liability insurance policy may not cover infringement by us of the intellectual property rights of others, depending upon the circumstances.

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The aggregate coverage provided under our general liability insurance policy is $10,000,000. 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 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.

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 do not maintain separate insurance to cover contamination or injuries relating to hazardous materials. Such liabilities may not be covered by our general liability insurance coverage, depending upon the circumstances. The aggregate coverage provided under our general liability insurance policy is $10,000,000.

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.

Risks Related to Our Industry

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.

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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.

Risks Related to The Securities Market and This Offering

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:

- the results of our clinical trials for Ramoplanin and the pace of our progress in those clinical trials;
- our ability to license or develop other compounds for clinical development;
- the timing of achievement of our development milestones and other payments under our strategic alliance agreements;
- termination of, or an adverse development in, our strategic alliances;
- conditions and publicity regarding the biopharmaceutical industry 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.

Over the two-year period ending September 5, 2003, the closing price of our common stock as reported on the Nasdaq National Market ranged from a high of $8.27 to a low of $1.03. 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.

We have issued warrants to purchase 486,646 shares of common stock and the re-sale of the shares underlying these warrants could cause a dilution of our existing shareholders.

On June 4, 2003, as part of the Amendment, Redemption and Exchange Agreement pertaining to our convertible notes held by two institutional investors, we issued warrants to purchase 486,646 shares of common stock at an exercise price of $3.71 per share (subject to anti-dilution and other adjustments), which become exercisable immediately and expire on June 4, 2008. The shares underlying the warrants will be registered for re-sale (pursuant to this prospectus) and if the warrants are exercised, these shares could be sold into the market creating dilution of the ownership of our shareholders at that time.

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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:

- the progress of our pre-clinical and clinical trials;
- 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 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;
- 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.

Certain of our financial statements have been audited by Arthur Andersen LLP, and the ability to recover damages from Arthur Andersen may be limited.

Prior to June 24, 2002, Arthur Andersen LLP served as our independent public accountants. Our inability to obtain the consent of Arthur Andersen to include its report on certain financial statements audited by Arthur Andersen and incorporated by reference in this prospectus may limit your recovery against Arthur Andersen. SEC rules require us to include or incorporate by reference in this prospectus certain historical financial statements for the years ended December 31, 2001 and 2000 that were audited by Arthur Andersen. As a result of the well-publicized events concerning Arthur Andersen, we have not been able to obtain the consent of Arthur Andersen to the inclusion of its audit report in this prospectus and will not be able to obtain Arthur Andersen s consent in the future. The absence of this consent may limit any recovery to which you might be entitled against Arthur Andersen. It is also likely that these events concerning Arthur Andersen would adversely affect its ability to satisfy any claims we might have arising from its provision of auditing and other services to us.

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 June 4, 2003, we entered into an Amendment, Redemption and Exchange Agreement with the selling stockholders named below pursuant to which we redeemed in cash a portion of the convertible notes held by the selling stockholders and converted the remaining portion of the notes into our common stock. In addition, the selling stockholders received new warrants to purchase up to 486,646 shares of our common stock in exchange for the warrants they previously held. The shares of our common stock registered for resale in the registration statement of which this prospectus is a part are the shares underlying these new warrants (subject to antidilution adjustments).

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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 exercise of the warrants (subject to antidilution adjustments). 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 warrants exercise their warrants; and (2) the exercise price of the warrants at the time of their exercise.

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 exercise of the warrants as of September 12, 2003. The number of shares set forth on the table as being offered hereby represents the 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 exercise of the warrants (subject to antidilution adjustments). This amount includes 100% of the number of shares of common stock issuable as of September 12, 2003, upon exercise of the warrants. However, the actual number of shares of common stock issuable upon exercise of the warrants is indeterminable, and could be materially more or less than the amounts listed on the table due to possible exercise price adjustments. 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 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	389,317(1)	389,317(1)	0
The Tail Wind Fund, Ltd.	496,566(2)	97,329(1)	399,237(3)

(1) Represents shares of common stock issuable upon exercise of the warrants held by the selling stockholder.
(2) Represents 399,237 shares of common stock owned by the selling stockholder and 97,329 shares of common stock issuable upon exercise of the warrants.
(3) Represents 399,237 shares of common stock owned by the selling stockholder or 1.5% of the issued and outstanding shares of common stock as of September 5, 2003.

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 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).

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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.

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;
- 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 June 4, 2008. 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.

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EXPERTS

The consolidated financial statements of Genome Therapeutics Corporation appearing in Genome Therapeutics Corporation s Annual Report on Form 10-K for the year ended and as of December 31, 2002 (2002 Annual Report), are incorporated herein by reference. Our consolidated financial statements for the year ended December 31, 2002 included in our 2002 Annual Report have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements for the years ended December 31, 2001 and 2000 and as of December 31, 2001, and included in our 2002 Annual Report had been audited by Arthur Andersen LLP, independent accountants, as indicated in their report thereon included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given the authority of such firm as experts in auditing and accounting. Arthur Andersen has not consented to the inclusion of their report in this prospectus, and in reliance on Rule 437a under the Securities Act, we have not obtained their consent to do so. We refer you to Risk Factors Risks Related to This Offering and Our Common Stock Certain of our financial statements have been audited by Arthur Andersen LLP, and the ability to recover damages from Arthur Andersen may be limited.

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.

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. 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, 2002.

(b) Our Quarterly Report on Form 10-Q for the fiscal quarter ended March 29, 2003.

(c) Our Quarterly Report on Form 10-Q for the fiscal quarter ended June 28, 2003.

(d) Our Current Report on Form 8-K as filed on June 5, 2003.

(e) Our Current Report on Form 8-K as filed on June 13, 2003.

(f) 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

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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.

486,646 Shares of

Common Stock

PROSPECTUS

September __, 2003

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the estimated costs and expenses of the sale and distribution of the securities being registered, all of which are being borne by us.

Securities and Exchange Commission registration fee	$ 103.54
Printing and engraving expenses	1,000
Accountant s fees and expenses	5,000
Legal fees and expenses	5,000
Miscellaneous expenses	3,000
Total	$ 14,103.54

All of the amounts shown are estimates except for the fee payable to the Commission.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

The Company is organized under the laws of The Commonwealth of Massachusetts. The Massachusetts Business Corporation Law provides that indemnification of directors, officers, employees, and other agents of another organization, or who serve at its request in any capacity with respect to any employee benefit plan, may be provided by the corporation to whatever extent specified in its charter documents or votes adopted by its shareholders, except that no indemnification may be provided for any person with respect to any matter as to which the person shall have been adjudicated in any proceeding not to have acted in good faith in the reasonable belief that his action was in the best interest of the corporation. Under Massachusetts law, a corporation can purchase and maintain insurance on behalf of any person against any liability incurred as a director, officer, employee, agent, or person serving at the request of the corporation as a director, officer, employee, or other agent of another organization or with respect to any employee benefit plan, in his capacity as such, whether or not the corporation would have power to itself indemnify him against such liability.

The Company s Restated Articles of Organization, as amended to date, provide that its directors shall not be liable to the Company or its stockholders for monetary damages for breach of fiduciary duty as a director, except to the extent that the exculpation from liabilities is not permitted under the Massachusetts Business Corporation Law as in effect at the time such liability is determined. The By-Laws provide that the Company shall indemnify its directors and officers to the full extent permitted by the laws of The Commonwealth of Massachusetts. In addition, the Company holds a Directors and Officer Liability and Corporate Indemnification Policy.

ITEM 16. EXHIBITS

The following is a list of exhibits filed as part of this registration statement.

Exhibit Number	Description
4.1	Specimen Common Stock Certificate. (1)
4.2	Amendment, Redemption and Exchange Agreement by and between Genome Therapeutics Corp. and Smithfield Fiduciary LLC dated as of June 4, 2003. (2)
4.3	Amendment, Redemption and Exchange Agreement by and between Genome Therapeutics Corp. and The Tail Wind Fund Ltd. dated as of June 4, 2003. (2)

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4.4	Form of Warrant issued to Smithfield Fiduciary LLC. (2)
4.5	Form of Warrant issued to The Tail Wind Fund Ltd. (2)
5.1	Opinion of Ropes & Gray. (3)
23.1	Consent of Ropes & Gray. (included in Opinion filed as Exhibit 5.1)
23.2	Consent of Ernst & Young. (4)
24.1	Power of Attorney. (included on the signature page of this registration statement) (3)

(1) Incorporated by reference to our Registration Statement on Form S-3 (File No. 333-00127).
(2) Incorporated by reference to our Current Report on Form 8-K filed June 5, 2003.
(3) Previously filed.
(4) Filed herewith.

ITEM 17. UNDERTAKINGS

A. Rule 415 Offering

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement.

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (1)(i) and (1)(ii) above do not apply if the registration statement is on Form S-3 or Form S-8, and the information required to be, included in a post-effective amendment by those paragraphs is contained in periodic reports filed by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

B. Filings Incorporating Subsequent Exchange Act Documents by Reference

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant s annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan s annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration

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relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

C. Request for Acceleration of Effective Date

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised 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. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

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SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 2 to the registration statement (File No. 333-106602) to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, The Commonwealth of Massachusetts, on September 12, 2003.

GENOME THERAPEUTICS CORP.

By: /s/ STEVEN M. RAUSCHER

Steven M. Rauscher

President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 2 to the registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ STEVEN M. RAUSCHER Steven M. Rauscher	Director, Chairman of the Board, President and Chief Executive Officer (Principal Executive Officer)	September 12, 2003
/s/ STEPHEN COHEN Stephen Cohen	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	September 12, 2003
* Robert J. Hennessey	Director	September 12, 2003
* Marc B. Garnick, M.D.	Director	September 12, 2003
* Philip Leder, M.D.	Director	September 12, 2003
* Lawrence Levy	Director	September 12, 2003
*	Director	September 12, 2003

Norbert G. Riedel, Ph.D.		
*	Director	September 12, 2003
David K. Stone		
*	Director	September 12, 2003
William S. Reardon		

*By: /s/ Stephen Cohen

Stephen Cohen

Attorney-in-Fact

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EXHIBIT INDEX

Number Exhibit	Description
4.1	Specimen Common Stock Certificate. (1)
4.2	Amendment, Redemption and Exchange Agreement by and between Genome Therapeutics Corp. and Smithfield Fiduciary LLC dated as of June 4, 2003. (2)
4.3	Amendment, Redemption and Exchange Agreement by and between Genome Therapeutics Corp. and The Tail Wind Fund Ltd. dated as of June 4, 2003. (2)
4.4	Form of Warrant issued to Smithfield Fiduciary LLC. (2)
4.5	Form of Warrant issued to The Tail Wind Fund Ltd. (2)
5.1	Opinion of Ropes & Gray. (3)
23.1	Consent of Ropes & Gray. (included in Opinion filed as Exhibit 5.1)
23.2	Consent of Ernst & Young. (4)
24.1	Power of Attorney. (included on the signature page of this registration statement) (3)

(1) Incorporated by reference to our Registration Statement on Form S-3 (File No. 333-00127).
(2) Incorporated by reference to our Current Report on Form 8-K filed June 5, 2003.
(3) Previously filed.

(4) Filed herewith.