GENOME THERAPEUTICS CORP
Form S-3
March 05, 2004
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As filed with the Securities and Exchange Commission on March 5, 2004

Registration No. 333-

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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 Number)**

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)

with copies to:

Patrick O Brien

Ropes & Gray LLP

One International Place

Boston, Massachusetts 02110-2624

(617) 951-7000

Approximate date of commencement of proposed sale to the public: As soon as practicable after this registration statement becomes 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, as amended (the Securities Act) 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	Amount of Registration Fee(2)
Common Stock, $0.10 par value per share	9,102,511	$ 5.88	$ 53,522,764	$ 6781.35

(1) 3,358,964 shares issuable upon the potential conversion of $22,309,647 aggregate principal amount of convertible notes, 930,000 shares issuable upon the potential conversion of interest accrued on the convertible notes and 4,813,547 shares previously issued as payment of interest and related amounts on the convertible notes. In addition to the shares set forth in the table, the amount to be registered includes an indeterminate number of shares issuable upon conversion of the convertible notes, 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 Registrant s Common Stock as reported on the Nasdaq National Market on March 3, 2004.

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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 MARCH 5, 2004

PROSPECTUS

9,102,511 Shares

Genome Therapeutics Corp.

Common Stock

These shares are being offered for sale by the selling stockholders listed on page 17. 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 19.

The common stock is traded on the Nasdaq National Market under the symbol GENE . On March 3, 2004, the reported closing price of the common stock was $5.88 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 March , 2004.

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THE COMPANY

We are a biopharmaceutical company committed to the clinical development and commercialization of new therapeutics to serve unmet medical needs. On February 6, 2004, we announced the completion of our merger with GeneSoft Pharmaceuticals, Inc., referred to as Genesoft, a privately-held pharmaceutical company based in South San Francisco.

Our product portfolio is now led by the FDA-approved fluoroquinolone antibiotic FACTIVE® (gemifloxacin mesylate) tablets, indicated for the treatment of community-acquired pneumonia of mild-to-moderate severity and acute bacterial exacerbations of chronic bronchitis.

In addition, we are developing a novel antibiotic candidate, Ramoplanin, which is currently in clinical trials for the prevention and treatment of serious hospital-acquired infections. Ramoplanin is in a Phase III trial for the prevention of bloodstream infections caused by vancomycin-resistant enterococci and in a Phase II trial for the treatment of *Clostridium difficile*-associated diarrhea.

Our preclinical development programs include an oral peptide deformylase inhibitor series for the potential treatment of respiratory tract infections as well as development of a FACTIVE intravenous formulation. We also have six pharmaceutical alliances focused on the development of novel therapeutics and diagnostics for chronic human diseases and certain infectious diseases. These alliances were formed in previous years based on our genomics drug discovery expertise. Our business strategy has shifted away from gene discovery and partnerships of this type to focus on development and commercialization of our own products.

The address for our executive offices is 100 Beaver Street, Waltham, Massachusetts 02453 and our telephone number is (781) 398-2300.

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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.

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 $29,789,000 for the fiscal year ended December 31, 2003 and as of December 31, 2003, we had an accumulated deficit of approximately $155,564,000. 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.

Prior to the merger, Genesoft had a net loss of approximately $26,089,000 for the fiscal year ended December 31, 2003 and as of December 31, 2003, Genesoft had an accumulated deficit of approximately $91,381,000. Genesoft had a net loss of approximately $25,569,000 for the fiscal year ended December 31, 2002, and, as of December 31, 2002, Genesoft had an accumulated deficit of approximately $55,568,000. For the fiscal year ended December 31, 2001, Genesoft had a net loss of approximately $18,321,000, and for the fiscal year ended December 31, 2000, Genesoft had a net loss of approximately $7,921,000. The losses have resulted primarily from costs incurred in research and development, including Genesoft s clinical trials, and from general and administrative costs associated with our operations. These costs have exceeded Genesoft s revenues which to date have been generated principally from funding from the U.S. government.

We anticipate that we will incur additional losses in the current year and in future years and cannot predict when, if ever, we will achieve profitability. These losses are expected to increase in the current year as we will significantly increase our expenditures in the sales and marketing area to prepare for the commercial launch of FACTIVE tablets. We also plan to continue to 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.

Our business will be very dependent on the commercial success of FACTIVE tablets.

FACTIVE tablets are currently our only commercial product and we expect they will account for substantially all of our revenues for at least the next several years. FACTIVE tablets have FDA marketing approval for the treatment of community-acquired pneumonia of mild to moderate

severity, or CAP, and acute bacterial exacerbations of chronic bronchitis, or ABECB. The commercial success of FACTIVE tablets will depend upon their acceptance by regulators, physicians, patients and other key decision-makers as a safe, therapeutic and cost-effective alternative to other anti-infectives and other products used, or currently being developed, to treat CAP and ABECB. If FACTIVE tablets are not commercially successful, we will have to find additional sources of funding or curtail or cease operations.

In December 2000, the FDA issued a non-approvable letter to the prior owner of rights to FACTIVE due, in part, to safety concerns arising out of an increased rate of rash relative to comparator drugs, especially in young women. While the FDA did approve FACTIVE tablets for marketing in April 2003, it required, as a postmarketing study commitment, that we conduct a prospective, randomized study comparing the FACTIVE tablet (5,000 patients) to an active comparator (2,500 patients) in patients with CAP or ABECB. This study will include patients of different ethnicities, to gain safety information in populations not substantially represented in the existing clinical trial program, specifically as it relates to rash. Patients will be evaluated for clinical and laboratory safety. This Phase IV trial is in the design stage and the FDA required, as a condition to its approval, that the trial be initiated by March 2004. We have requested permission from the FDA to commence the Phase IV trial at a later date that is consistent with the planned launch of FACTIVE tablets. The FDA has indicated its willingness to grant this request. If our request is not granted, however, we will commence the Phase IV trial as soon as possible thereafter, which may not be before the end of March 2004. In connection with the approval of FACTIVE tablets, the FDA has also required us to obtain data on the prescribing patterns and use of FACTIVE tablets for the first three years after their initial marketing in the U.S. As part of this

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requirement, we will furnish periodic reports to the FDA on the number of prescriptions issued, including refills, and the diagnoses for which the prescriptions are dispensed. The results of the Phase IV trial and the periodic reports we are required to provide to the FDA, as well as other safety information arising out of the marketing of the product, could restrict our ability to commercialize FACTIVE tablets.

We will need to raise additional funds in the future.

In connection with the merger with Genesoft, we raised approximately $81,020,000, after deducting placement agents fees and estimated offering expenses payable by us. We believe that these funds along with our pre-existing cash and marketable securities and borrowings under equipment financing arrangements and anticipated cash flows from operations would be sufficient to support our current plans for at least 18 months. We expect to raise additional capital in the future to fund our operations. In particular, we expect we will raise additional funds to support our sales and marketing activities, and fund clinical trials and other research and development activities. 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, among other factors, the investment market for biotechnology companies and the progress of the FACTIVE and Ramoplanin commercial and clinical development programs over that period. Additional financing may not be available to us 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 the outstanding shares of our common stock in order to fund our operating plans, potentially requiring a stockholder vote. In addition, we may have to sell securities at a discount to the prevailing market price, resulting in further dilution to our stockholders.

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

FACTIVE tablets are our first FDA approved product. To date, we have very limited marketing and sales experience. We will need to develop a marketing and sales staff to successfully commercialize FACTIVE tablets and our other product candidates, including Ramoplanin. In order to launch FACTIVE tablets in the second half of 2004, we will need to rapidly assemble a sales and marketing force. The development of these 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 and regulatory compliant manner or to find suitable sales and marketing partners may prevent us from successfully launching FACTIVE tablets in 2004, which would materially adversely affect our business and results of operations.

We will depend on third parties to manufacture our product candidates, including FACTIVE tablets and Ramoplanin.

We will not have the internal capability to manufacture commercial quantities of pharmaceutical products under the FDA s current Good Manufacturing Practices. We are party to an agreement with LG Life Sciences to manufacture bulk quantities of FACTIVE. We have also

entered into an agreement with Biosearch (which merged with Versicor Inc. in March 2003 and subsequently changed its name to Vicuron Pharmaceuticals Inc.) to manufacture bulk quantities of Ramoplanin, and we expect to enter into similar agreements with third parties for the manufacture of future product candidates. Although the LG Life Sciences facilities have previously been inspected by the FDA, they had not been actively manufacturing product for 32 months until their re-start of activity in October 2003. Future inspections may find deficiencies in the facilities or processes that may delay or prevent the manufacture or sale of FACTIVE tablets.

LG Life Sciences is obligated to provide us with finished product until the termination or expiration of its existing agreement with SB Pharmco Puerto Rico, Inc., or SB Pharmco, which provides for the supply of finished FACTIVE product by SB Pharmco. The term of this agreement ends on June 30, 2004 but, subject to the satisfaction of certain requirements, may be extended by LG Life Sciences to September 30, 2004. We are currently in discussions with other potential providers of finished products to assume these responsibilities for subsequent periods. We estimate that it will take 12 to 18 months to qualify a new provider of finished products. We expect to obtain quantities of FACTIVE tablets from SB Pharmco that will provide us with sufficient inventory until the new provider can be qualified. If we are unable to qualify a new provider by the time that our supply of finished product to be received from SB Pharmco is exhausted, our supply of FACTIVE product would be interrupted and our business may be materially adversely affected. In addition, we cannot assure you that SB Pharmco or any new secondary manufacturer will be able to avoid batch failures or other production delays.

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We cannot be certain that LG Life Sciences, 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. Currently, the only source of supply for FACTIVE bulk drug product is LG Life Sciences facility in South Korea, and if such facility were damaged or otherwise unavailable, we would incur substantial costs and delay in the commercialization of FACTIVE tablets. If we are forced to find an alternative source for Ramoplanin or other product candidates, we could also incur substantial costs and delays in the further commercialization of such products. 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.

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, it 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.

We cannot expand the indications for which we will market FACTIVE unless we receive FDA approval for each additional indication. Failure to expand these indications will limit the size of the commercial market for FACTIVE.

In April 2003, FACTIVE tablets were approved by the FDA for the treatment of community-acquired pneumonia of mild to moderate severity and acute bacterial exacerbations of chronic bronchitis. One of the objectives of ours is to expand the indications for which FACTIVE is approved for marketing by the FDA, including for the indication of acute bacterial sinusitis. While clinical trials for acute bacterial sinusitis have previously been completed, we may need to conduct additional clinical trials in order to market FACTIVE for this indication. In order to market FACTIVE for other indications, we will need to conduct additional clinical trials, obtain positive results from those trials and obtain FDA approval for such proposed indications. If we are unsuccessful in expanding the approved indications for the use of FACTIVE, the size of the commercial market for FACTIVE will be limited.

Failure to obtain regulatory approval in foreign jurisdictions will prevent us from marketing FACTIVE abroad.

In order to market FACTIVE in the European Union and other foreign jurisdictions for which we have rights to market the product, we or our distribution partners must obtain separate regulatory approvals. Obtaining foreign approvals may require additional trials and expense. We may not be able to obtain approval or may be delayed in obtaining approval from any or all of the jurisdictions in which we seek approval to market FACTIVE.

Sales of FACTIVE in European countries in which we do not have rights to market the product could adversely affect sales in the European countries in which we have exclusive rights to market the product.

Our exclusive rights to market FACTIVE in Europe are limited to France, Germany, the United Kingdom, Luxembourg, Ireland, Italy, Spain, Portugal, Belgium, the Netherlands, Austria, Greece, Sweden, Denmark, Finland, Norway, Iceland, Switzerland, Andorra, Monaco, San Marino and Vatican City. These countries include the current members of the European Union. However, in the future, a number of additional European countries in which we do not have rights to market FACTIVE may be admitted as members of the European Union. If LG Life Sciences were to sell FACTIVE or license a third party to sell FACTIVE in such countries after they are admitted to the European Union, our ability to maintain our projected profit margins based on sales in the territories covered by the LG Life Sciences license agreement may be adversely affected

because customers in our territory may purchase FACTIVE from neighboring countries in the European Union and our ability to prohibit such purchases may be limited under European Union antitrust restrictions.

Failure to secure distribution partners in foreign jurisdictions will prevent us from marketing FACTIVE abroad.

We intend to market FACTIVE through distribution partners in most, if not all, of the international markets for which we have a license to market the product. This will include the European Union, Canada and Mexico. We may not be able to secure distribution partners at all, or those that we do secure may not be successful in marketing and distributing FACTIVE. If we are not able to secure distribution partners or those partners are unsuccessful in their efforts, it would significantly limit the revenues that we expect to obtain from the sales of FACTIVE.

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The development and commercialization of our products may be terminated or delayed, and the costs of development and commercialization may increase, if third parties who we rely on to manufacture and support the development and commercialization of our products do not fulfill their obligations.

Our development and commercialization strategy entails entering into arrangements with corporate and academic collaborators, contract research organizations, distributors, third-party manufacturers, licensors, licensees and others to conduct development work, manage our clinical trials, manufacture our products and market and sell our products outside of the United States. We will not have the expertise or the resources to conduct such activities on our own and, as a result, we will be particularly dependent on third parties in these areas.

We may not be able to maintain our existing arrangements with respect to the commercialization of FACTIVE or establish and maintain arrangements to develop and commercialize Ramoplanin or any additional product candidates or products we may acquire on terms that are acceptable to us. Any current or future arrangements for development and commercialization may not be successful. If we are not able to establish or maintain agreements relating to FACTIVE, Ramoplanin or any additional products we may acquire on terms which we deem favorable, our results of operations would be materially adversely affected.

Third parties may not perform their obligations as expected. The amount and timing of resources that third parties devote to developing, manufacturing and commercializing our products are not within our control. Furthermore, our interests may differ from those of third parties that manufacture or commercialize our products. Disagreements that may arise with these third parties could delay or lead to the termination of the development or commercialization of our product candidates, or result in litigation or arbitration, which would be time consuming and expensive.

If any third party that manufactures or supports the development or commercialization of our products breaches or terminates its agreement with us, or fails to conduct its activities in a timely and regulatory compliant manner, such breach, termination or failure could:

- delay or otherwise adversely impact the development or commercialization of FACTIVE tablets, Ramoplanin, our other product candidates or any additional product candidates that we may acquire or develop;
- require us to undertake unforeseen additional responsibilities or devote unforeseen additional resources to the development or commercialization of our products; or
- result in the termination of the development or commercialization of our products.

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

Our lead product, FACTIVE tablets, will need to complete a Phase IV post-approval clinical trial in compliance with FDA requirements pursuant to the product s approval. Additionally, clinical trials may be necessary to gain approval to market the product for the treatment of acute bacterial sinusitis. Additional clinical trials will be required to gain approval to market FACTIVE for other indications. 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, a Phase II clinical trial to assess the safety and efficacy of Ramoplanin to treat *Clostridium difficile*-associated diarrhea, or CDAD, and a pilot study into the use of Ramoplanin to reduce the transmission of VRE in the hospital setting. Prior clinical and preclinical trials

for Ramoplanin were conducted by Biosearch Italia S.p.A. and its licensees, from whom we acquired our license to develop Ramoplanin. We currently expect to complete the Phase II trial of Ramoplanin for CDAD in the first half of 2004 and commence a Phase III CDAD trial before the end of 2004. The pilot study is expected to conclude in the first half of 2004. The Phase III trial of Rampolanin to prevent VRE bloodstream infections continues, but at a slow pace. Many patients are ineligible to participate in this trial because they are participating in other experimental protocols to treat their underlying cancers. We received approval from the FDA to introduce the capsule formulation into the study; however, based on the pace of enrollment, we do not expect to file a New Drug Application, or NDA, based on the results of this trial prior to the end of 2005. We continue to review with the FDA alternative approaches to facilitate filing an NDA for the VRE bloodstream infection prevention indication. We may not be able to complete these trials or make the filings within the timeframes we currently expect. If we are delayed in completing the trials or making the filings, our business may be adversely affected, including as a result of increased costs.

We may not be able to demonstrate the safety and efficacy of FACTIVE in indications other than those for which it has already been approved or of our other products including Ramoplanin, in each case, to the satisfaction of the FDA, or other regulatory authorities. We may also be required to demonstrate that our proposed products represent an improved form of treatment over existing therapies and we may be unable to do so without conducting further clinical studies. Negative,

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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 are able to 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 and applicable regulations;
- prior regulatory agency review and approval of our applications and procedures;
- analysis of data obtained from preclinical 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 preclinical 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 preclinical 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 gains regulatory approval, the product and the manufacturer of the product will be subject to continuing regulatory review, including the requirement to conduct post-approval clinical studies. 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 will face significant competition in the marketplace.

FACTIVE tablets are approved for the treatment of community-acquired pneumonia of mild to moderate severity and acute bacterial exacerbations of chronic bronchitis. There are several classes of antibiotics that are primary competitors for the treatment of these indications, including:

- other fluoroquinolones such as Levaquin® (levofloxacin), a product of Ortho-McNeil Pharmaceutical, Inc., Tequin® (gatifloxacin), a product of Bristol-Myers Squibb Company, and Cipro® (ciprofloxacin) and Avelox® (moxifloxacin), both products of Bayer Corporation;

- macrolides such as Biaxin® (clarithromycin), a product of Abbott Laboratories and Zithromax® (azithromycin), a product of Pfizer Inc.; and

- penicillins such as Augmentin® (amoxicillin/clavulanate potassium), a product of GlaxoSmithKline.

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In addition, a new drug application for Ketek®, a ketolide antibiotic from Aventis Pharmaceuticals, has been submitted to the FDA and Ketek is currently marketed in Europe. Many generic antibiotics are also currently prescribed to treat these infections. Moreover, a number of the antibiotic products that are competitors of FACTIVE tablets will be going off patent at dates ranging from 2003 to 2010. As these competitors lose patent protection, makers of generic drugs will likely begin to produce some of these competing products and this could result in pressure on the price at which we are able to sell FACTIVE tablets and reduce our profit margins.

Ramoplanin is currently in development for the prevention of bloodstream infections caused by vancomycin-resistant enterococci (VRE). We have no knowledge of any product currently approved by the 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® (vancomycin), 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 Phase I/II; and Acambis in Phase I/II. It is also possible that other companies are developing competitive products for this indication. We are aware that Vicuron and Novartis Pharma are jointly developing PDF inhibitor agents that may compete with any PDF products developed by us.

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 preclinical 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 will have substantially greater capital resources, facilities and human resources than us. Furthermore, many of those competitors are more experienced than us in drug discovery, development and commercialization, and in obtaining regulatory approvals. As a result, those 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.

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

Our ability to commercialize FACTIVE tablets, 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 FACTIVE tablets, Ramoplanin or other products in the future to market, we cannot assure you that third-party payers will pay for such 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. In addition, in December 2003 President Bush signed into law new Medicare prescription drug coverage legislation. While we cannot yet predict the impact the new legislation could have on our ability to commercialize FACTIVE tablets, Ramoplanin and any future products, the new legislation could adversely affect our anticipated revenues and results of operations, possibly materially.

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 FACTIVE tablets, Ramoplanin or any of our future products will be added to payers 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 our receiving lower or discounted prices for FACTIVE tablets, Ramoplanin or future products.

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We will rely upon existing and prospective alliance partners, licensees and government grants and contracts 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 AstraZeneca, bioMérieux, Schering-Plough and Wyeth. Over the past several years, we have received a substantial portion of our revenue from these alliances. However, our research obligations under our strategic alliances have been fulfilled or are anticipated to be completed in the near future. As a result, any substantial additional revenues under these alliances will consist of milestone payments based on the achievement by the alliance partner of development milestones or royalties based on the sale of products arising from the alliance. The achievement of any of the development milestones and successful development of any products under these alliances are dependent on the alliance partners activities and are beyond our control. We cannot assure you that any milestones will be attained, that any products will be successfully developed by the alliance partners or that we will receive any substantial additional revenues under these alliances.

In order to maintain the collaboration agreement with Wyeth, we must fulfill certain obligations, including providing reasonable technical assistance in using the know-how or other information that we have licensed to them. We believe that we are currently in compliance with our obligations under our collaboration agreement, but there can be no assurance that we will be able to successfully complete our obligations in the future.

If our partners develop products using our discoveries, 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 its alliance agreements. Our agreements with our partners typically allow the partners significant discretion in electing whether to pursue any of these activities. We will not be able to control the amount and timing of resources our partners may devote to our programs or potential products. As a result, there can be no assurance that our partners will perform their obligations as expected.

Our strategy will include entering into multiple, concurrent alliances and business partnerships, including, but not limited to in-licensing and co-promotion agreements. There can be no assurance that we will be able to manage multiple alliances and partnerships successfully. The risks we will face in managing multiple alliances and partnerships include maintaining confidentiality among partners, avoiding conflicts between partners and avoiding conflicts between us and our partners. If we fail to manage our alliances and partnerships 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, or an adverse effect on, sales and marketing efforts for our products,
- delay in development activities,
- legal claims involving significant time,
- significant expense,

loss of reputation, and

termination of one or more alliances, or loss of capital and loss of revenues.

We have applied for and received grants from the U.S. government in the past. Our strategy going forward will include the continued pursuit of government grants and contracts. We can not assure you that we will obtain any additional grants or that our existing grants will continue to be funded. If we are unable to obtain additional grants or maintain our existing grants, our revenues would be adversely affected.

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. Successful development and commercialization will be subject to numerous risks at each stage. For example, there can be no assurance that the high-throughput screening or lead optimization processes for a given strategic alliance will identify any

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compounds suitable for clinical development. Even if product candidates based on our discoveries undergo clinical trials, there can be no assurance that those clinical trials will indicate that the product candidates are safe or effective. The pace at which the clinical trials proceed is also uncertain. 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.

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.

New product candidates acquired or in-licensed by us may require additional research and development efforts prior to commercial sale, including extensive preclinical 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, it is uncertain whether any approved products that we develop or acquire will be:

- manufactured or produced economically;
- successfully commercialized; or
- widely accepted in the marketplace.

Future acquisitions may absorb significant resources and may be unsuccessful.

As part of our strategy, we may pursue acquisitions of businesses or assets or investments in or other relationships and alliances with third parties. 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 or at all;

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 business. Any acquisitions or investments by us may ultimately have a negative impact on our business, financial condition and results of operations.

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

We will be highly dependent on the principal members of our senior management and key scientific and technical personnel. The loss of any of its personnel could have a material adverse effect on its ability to achieve its goals. We currently

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maintain employment agreements with the following senior officers: Steven M. Rauscher, President and Chief Executive Officer; Stephen Cohen, Senior Vice President and Chief Financial Officer; Martin D. Williams, Senior Vice President, Corporate Development & Marketing; and Gary Patou, M.D., Executive Vice President, Chief Medical Officer. The term of each employment agreement continues until it is terminated by the officer or us, except for Dr. Patou s agreement which runs through January 1, 2005, after which he becomes a consultant for one year. We do not currently maintain key person life insurance on any of our employees.

Our future success is dependent upon our ability to attract and retain additional qualified sales and marketing, clinical development, scientific and managerial personnel. The plan to launch the commercial sale of FACTIVE tablets during the second half of 2004 will require us to significantly increase our hiring of new employees, primarily with expertise in the areas of sales and marketing. Like others in our industry, we may face, and in the past we 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 own or license approximately 50 issued U.S. patents, approximately 127 pending U.S. patent applications, 50 issued foreign patents and approximately 143 pending foreign patent applications. These patents and patent applications primarily relate to (1) the field of human and pathogen genetics, (2) the chemical composition, use, and method of manufacturing FACTIVE, (3) metalloenzyme inhibitors, their uses, and their targets, and (4) DNA-Nanobinder compounds and their use as anti-infective therapeutics. Our material patents are as follows:

U.S. Patent No. 5,633,262 granted May 27, 1997, relating to quinoline carboxylic acid derivatives having 7-(4-amino-methyl-3-oxime) pyrrolidine substituent; licensed from LG Life Sciences; expiring June 15, 2015

U.S. Patent No. 5,776,944 granted July 7, 1998, relating to 7-(4-aminomethyl-3-methyloxyiminopyrroplidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid ; licensed from LG Life Sciences; expiring June 15, 2015

U.S. Patent No. 5,869,670 granted February 9, 1999, relating to 7-(4-aminomethyl-3-methyloxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid; licensed from LG Life Sciences; expiring June 15, 2015

U.S. Patent No. 5,962,468 granted October 5, 1999, relating to 7-(4-aminomethyl-3-methyloxyiminopyrrolidin-1-yl)-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid; licensed from LG Life Sciences; expiring June 15, 2015

U.S. Patent No. 6,340,689 granted January 22, 2002, relating to methods of using quinolone compounds against atypical upper respiratory pathogenic bacteria; licensed from LG Life Sciences; expiring September 14, 2019

U.S. Patent No. 6,262,071 granted July 17, 2001, relating to methods of using antimicrobial compounds against pathogenic Mycoplasma bacteria; licensed from LG Life Sciences; expiring September 21, 2019

U.S. Patent No. 6,331,550 granted December 18, 2001, relating to methods of using of quinolone compounds against anaerobic pathogenic bacteria; licensed from LG Life Sciences; expiring September 21, 2019

U.S. Patent No. 6,455,540 granted September 24, 2002, relating to methods of Use of quinolone compounds against anaerobic pathogenic bacteria; licensed from LG Life Sciences; expiring September 21, 2019

U.S. Patent No. 6,423,690 granted July 23, 2002, relating to antibacterial agents; licensed from Vernalis; expiring February 5, 2019

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U.S. Patent No. 6,441,042 granted August 27, 2002, relating to hydroxamic acid derivatives as antibacterials; licensed from Vernalis; expiring May 14, 2019

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

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* and *leprae*; expiring June 24, 2020

U.S. Patent No. 6,605,709 granted August 12, 2003, relating to *Proteus mirabilis*; expiring April 5, 2020

U.S. Patent No. 6,6105,836 granted August 26, 2003, relating to *Klebsiella pneumoniae*; expiring January 27, 2020

U.S. Patent No. 6,617,156 granted September 9, 2003, relating to *Enterococcus faecalis*; expiring August 13, 2018

While it is difficult to assess the value of our intellectual property portfolio, the patents named above may 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. However, there is no assurance that any of these patents, if challenged, will be found to be enforceable or that any of these patents will provide us with a competitive advantage.

We are not currently involved in any litigation, settlement negotiations, or other legal action regarding patent issues and we 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 the applicable technology fields are still evolving. Therefore, the degree of future protection for our proprietary rights is uncertain.

Under our license agreement with LG Life Sciences, we obtained an exclusive license to develop and market gemifloxacin in certain territories. This license covers 11 issued U.S. patents and a broad portfolio of corresponding foreign patents and pending patent applications. These patents include claims that relate to the chemical composition of FACTIVE, methods of manufacturing and their use for the prophylaxis and treatment of bacterial infections. The U.S. patents are currently set to expire at various dates, ranging from 2015, in the case of the principal patents relating to FACTIVE, to 2019. We have filed patent term extension applications, covering the regulatory review process, for the principal patents. If granted, these extensions would extend the exclusivity period through 2017. We also have the exclusive right to use FACTIVE trademarks, trade names, domain names and logos in conjunction with the use or sale of the product in the territories covered by the license.

LG Life Sciences, as owner of U.S. Patent Nos. 5,776,944 and 5,962,468, submitted requests for reexamination to the U.S. Patent & Trademark Office, or PTO, in order to place additional references into the record of each patent. Both requests were granted by the PTO. Patent 468 has been reexamined with relatively minor modifications to the claims and confirmed patentable over the submitted references. The reexamination

of Patent 944 is currently pending. If the PTO does not confirm the claims in this patent as patentable, our patent protection with respect to FACTIVE in the U.S. may be weakened.

The patents that we license to Ramoplanin under our 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, and intend to rely on the five year data exclusivity provisions under the Hatch-Waxman Act.

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

- the pending patent applications that we have filed or to which they have exclusive rights may not result in issued patents or may take longer than expected to result in issued patents;
- the claims of any patents which are issued may be limited from those in the 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 partners may not provide a competitive advantage;
- other companies may challenge patents licensed or issued to us or our partners;
- 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.

In addition, we are aware that some companies have published patent applications relating to nucleic acids and proteins from various pathogenic organisms. If these companies receive issued patents, their patents may limit our ability and the ability of our collaborators to practice under any patents that may be issued to us or our collaborators. Because of this, we or our collaborators may not be able to obtain patents with respect to the genes of infectious agents 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.

We will bear substantial responsibilities under our license agreements for FACTIVE and Ramoplanin, and there can be no assurance that we will successfully fulfill our responsibilities.

In connection with the merger, we have assumed Genesoft s exclusive license from LG Life Sciences to develop and market FACTIVE in North America and France, Germany, the United Kingdom, Luxembourg, Ireland, Italy, Spain, Portugal, Belgium, the Netherlands, Austria, Greece, Sweden, Denmark, Finland, Norway, Iceland, Switzerland, Andorra, Monaco, San Marino and Vatican City. Under this agreement, we are responsible, at our expense and through consultation with LG Life Sciences, for the clinical and commercial development of FACTIVE in the countries covered by the license, including the conduct of clinical trials, the filing of drug approval applications with the FDA and other applicable regulatory authorities and the marketing, distribution and sale of FACTIVE in our territory; provided, that LG Life Sciences has the right to co-promote the product on terms to be negotiated in our territory for 2008 and periods commencing thereafter, in which case our royalty obligations to LG Life Sciences would cease. The agreement also requires a minimum sales commitment over a period of time, which if not met, would result in the technology being returned to LG Life Sciences. We believe that we are currently in compliance with our obligations under the agreement with LG Life Sciences, 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 preclinical and clinical trials for our product candidates and the challenges inherent in the commercialization of new products as described above in Our product candidates will face significant competition in the marketplace .

LG Life Sciences has the obligation under the agreement to diligently maintain its patents and the patents of third parties to which it has rights that, in each case, relate to gemifloxacin, the active ingredient in FACTIVE tablets. We have the right, at our expense, to control any litigation relating to suits brought by a third party alleging that the manufacture, use or sale of gemifloxacin in its licensed field in the territories covered by the license infringes upon our rights. We also have the primary right to pursue actions for infringement of any patent licensed from LG Life Sciences under the license agreement within the territories covered by the license. If we elect not to pursue any infringement action, LG Life Sciences has the right to pursue it. The costs of any infringement actions are first paid out of any damages recovered. If we are the plaintiff, the remainder of the damages are retained by us, subject to our royalty obligations to LG Life Sciences. If LG Life Sciences is the plaintiff, the remainder of the damages are divided evenly between us and LG Life Sciences, subject to our royalty obligations to LG Life Sciences. The costs of pursuing any such action could substantially diminish our resources.

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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 FDA 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 preclinical 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 s 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 our 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 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 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 action 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 upon trademarks, unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We generally protect this information with confidentiality agreements that provide that all confidential information developed or made known to others during the course of the employment, consulting or business relationship shall be kept confidential except in specified circumstances. Agreements with employees provide that all inventions conceived by the individual while employed by us are our exclusive property. We cannot guarantee, however, that these agreements will be honored, that we will have adequate remedies for breach if they are not honored or that our trade secrets will not otherwise become known or be independently discovered by competitors.

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 us, are generally uncertain and involve complex legal, scientific and factual questions. Our success in developing and commercializing biopharmaceutical products 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 biopharmaceutical 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 competitors in the biopharmaceutical industry. 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 expect to maintain separate insurance to cover intellectual property infringement. Our general liability insurance policy may not cover our infringement of the intellectual property rights of others, depending upon the circumstances. The aggregate coverage provided under our existing general liability insurance policy is $10 million. We do not currently intend to increase the amount of this insurance, though we will continue to evaluate the sufficiency of its coverage levels periodically. 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.

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

Under our government grants and contracts, the government will have 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 our part 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 will have 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 will have ownership rights in the data and discoveries derived from any materials furnished to us by the government.

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.

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

Our research and development activities will involve the controlled use of hazardous and radioactive materials and biological waste. We will be 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 existing safety procedures for handling and disposing of these materials comply with legally prescribed standards, we will not be able to 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 expect our company to maintain separate insurance to cover contamination or injuries relating to hazardous materials. Such liabilities may not be covered by our existing general liability insurance coverage, depending upon the circumstances. The aggregate coverage provided under our general liability insurance policy is $10 million. We do not currently intend to increase the amount of this insurance, though we will continue to evaluate the sufficiency of its coverage levels periodically.

If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could be forced to pay substantial damage awards.

The use of any of our product candidates in clinical trials, and the sale of any approved products, might expose us to product liability claims. We currently maintain, and we expect that we will continue to maintain, product liability insurance coverage in the amount of $10 million per occurrence and $10 million in the aggregate. Such insurance coverage might not protect us against all of the claims to which we might become subject. We might not be able to maintain adequate insurance coverage at a reasonable cost or in sufficient amounts or scope to protect us against potential losses. In the event a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damage awards resulting from a claim brought successfully against us. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct financial and managerial resources to such defense and adverse publicity could result, all of which could harm our business.

We may not realize all of the anticipated benefits of the merger with Genesoft.

The success of our merger with Genesoft will depend, in part, on our ability to realize the anticipated synergies, cost savings and growth opportunities from integrating our business with the former business of Genesoft. Our success in realizing these benefits and the timing of this realization depends upon the successful integration of the former operations of Genesoft. The full integration of two independent companies, especially when one company is located on the West Coast and the other on the East Coast, is a complex, costly and time-consuming process. The difficulties of combining the operations of the companies and realizing the expected benefits of the merger include, among others:

coordinating commercial and clinical development initiatives and staffs for FACTIVE and Ramoplanin;

raising sufficient capital to fund the significant expenditures that are needed to launch and successfully commercialize FACTIVE and the further clinical development of Ramoplanin;

retaining key employees;

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consolidating research and development operations;

consolidating corporate and administrative infrastructures and physical plant;

integrating and managing the technology of two companies; and

minimizing the diversion of management s attention from ongoing business concerns.

We cannot assure you that we will realize the full benefits anticipated by us to result from the merger. In addition, we may not have sufficient capital to fully implement our strategies following the merger which may cause a delay in the launch of FACTIVE tablets and could further prevent us from realizing the anticipated benefits of the merger.

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:

our ability to successfully launch and commercialize FACTIVE tablets;

the revenues that we may derive from the sale of FACTIVE tablets, as compared to analyst estimates;

the results of our clinical trials for Ramoplanin and additional indications for FACTIVE and the pace of our progress in those clinical trials;

our ability to license or develop other compounds for clinical development;

the timing of the 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 February 27, 2004 the closing price of our common stock as reported on the Nasdaq National Market ranged from a high of $7.01 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 3,245,806 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 that are exercisable to purchase 535,806 shares of common stock at an exercise price of $3.37 per share (subject to anti-dilution and other adjustments), which are exercisable and expire on June 4, 2008. In connection with the issuance of these convertible notes, we are also obligated to issue additional warrants that are exercisable to purchase up to 100,000 shares of common stock at an exercise price of $15.00 per share, which warrants expire on March 5, 2005. On September 29, 2003 and October 15, 2003, we had closings of a private placement transaction in which we issued warrants to purchase 1,910,000 and 700,000 shares of common stock, respectively, at an exercise price of $3.48. The September 2003 warrants become exercisable on March 29, 2004 and remain exercisable until September 29, 2008. The October 2003 warrants become exercisable on April 15, 2004 and remain exercisable until October 15, 2008. The shares underlying all of these warrants have been registered for re-sale and are therefore freely tradeable without restriction. The exercise of all or a

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substantial portion of these warrants would cause a significant reduction in the relative percentage interests of our stockholders in our earnings, voting power, liquidation value and book and market value. In addition, if all or a substantial portion of these warrants were exercised and sold, the market price of our common stock could decline significantly.

The $22,309,647 in aggregate original principal amount of convertible notes that we issued at the closing of the merger with Genesoft will, if converted into our common stock, substantially reduce the percentage interests of our stockholders.

At the closing of the merger, we assumed approximately $24 million of debt of Genesoft, of which approximately $1.7 million was paid at closing. The remainder of the debt consists of promissory notes of Genesoft that we exchanged with holders of such notes for our convertible promissory notes, which will bear interest at 5% per annum and have a maturity date of five years from the closing date. If these notes are not converted into shares of our common stock during the five-year period, the subsequent payment of these notes at maturity may require us to expend a significant portion of our capital resources. Depending upon the combined company s capital resources at the maturity date, the payment of these notes could impair the combined company s working capital and prevent it from pursuing important clinical development and commercialization programs.

The $22,309,647 in aggregate original principal amount of our convertible notes issued at the closing of the merger, including accrued interest, are convertible into shares of our common stock at the holder s election at any time after the closing of the merger at a price per share equal to $6.6418, subject to subsequent adjustments. In addition, following the one year anniversary of the closing of the merger, we have the right to force conversion if the price of our common stock closes above 150% of the then effective conversion price for 15 consecutive days. The conversion of all or a substantial portion of these convertible notes would cause a significant reduction in the relative percentage interests of our stockholders in our earnings, voting power, liquidation value and book and market value.

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 pace of our commercial launch of FACTIVE tablets;
- the level of acceptance by physicians and third party payors of FACTIVE;
- the progress of our clinical trials for FACTIVE, Ramoplanin and our other product candidates;
- our success in concluding deals to acquire additional approved products and product candidates;
- the introduction of new products and services by our competitors;
- regulatory actions; and

expenses related to, and the results of, litigation and other proceedings relating to intellectual property rights.

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 materially adversely affect its ability to satisfy any claims we might have arising from its provision of auditing and other services to us.

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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

At the time of signing the merger agreement between Genome and Genesoft Pharmaceuticals, Inc. on Novermber 17, 2003, we entered into a note amendment and exchange agreement with Genesoft and the holders of promissory notes issued by Genesoft, referred to as the Genesoft notes, during its financing rounds in December 2002-January 2003 and April-May 2003. Pursuant to the note amendment and exchange agreement, at the closing of the merger on February 6, 2004, we issued convertible notes of Genome, or the Genome notes, in an aggregate principal amount of $22,309,647, in exchange for the Genesoft notes. The Genome notes, including any accrued interest, are convertible, at the option of the holder, into shares of Genome common stock at a price of $6.6418 per share (subject to anti-dilution and other adjustments) pursuant to the provisions of the note amendment and exchange agreement. In addition, following the one year anniversary of the closing of the merger, we have the right to force conversion if the price of our common stock closes above 150% of the then effective conversion price for 15 consecutive trading days. At the closing of the merger, the holders of the Genesoft notes also received an aggregate 4,813,547 shares of Genome common stock representing the payment of accrued interest and related amounts on their respective Genesoft notes. The shares of our common stock registered for resale in the registration statement of which this prospectus is a part and the shares offered in this prospectus represent (i) the shares underlying the Genome notes (subject to antidilution and other adjustments), (ii) shares issuable upon conversion of interest to be accrued on the Genome notes and (iii) the aggregate 4,813,547 shares issued to the holders of the Genesoft notes as payment of accrued interest and related amounts on their respective Genesoft notes at the closing of the merger. 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 a holder of a Genome note elects to convert the Genome note into shares of our common stock; (2) the amount of interest that has accrued on a given Genome note at the time of conversion; (3) whether we elect to require the conversion of the Genome notes upon the market price of our common stock meeting a specified price threshold; and (4) the conversion price at the time of conversion of the Genome 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 a selling stockholder includes the number of shares of common stock that would be issuable upon conversion of the principal amount of Genome notes as of February 27, 2004 and the shares issued to a selling stockholder as payment of accrued interest and related amounts on their respective Genesoft notes at the closing of the merger. However, the actual number of shares of common stock issuable upon conversion of the convertible notes is presently indeterminable, and could be materially more or less than the amounts listed on the table due to possible conversion price adjustments due to stock splits, stock dividends or similar transactions. The selling stockholders may sell all, part, or none of the shares listed. 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 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.

Name of Selling Shareholder	Shares Owned Prior To Offering	Shares of Common Stock Offered Hereby(4)	Shares Owned After Offering(5)	Percentage of Class Owned After Offering
Banca del Gottardo Lugano	53,863	53,863	0	*
BB BioVentures LP (6)	7,416,793	2,413,847	5,002,946	6.49%
BSI SA	584,895	222,179	362,716	*
BSI-New Biomedical Frontier (SICAV)	391,495	70,089	321,406	*

Carmichael, James	3,541	2,693	848	*
Gretchen and John Bergguen Trust	2,693	2,693	0	*
Klein, Joseph III	64,605	24,240	40,365	*
Klingenstein, Paul	44,542	8,648	35,894	*
Lombard Odier Darier Hentsch & Cie	624,935	161,588	463,347	*
Lysander, LLC	75,121	17,522	57,599	*
Maverick Fund II, Ltd.	181,518	181,518	0	*
Maverick Fund LDC	988,117	988,117	0	*

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Name of Selling Shareholder	Shares Owned Prior To Offering	Shares of Common Stock Offered Hereby(4)	Shares Owned After Offering(5)	Percentage of Class Owned After Offering
Maverick Fund USA	446,255	446,255	0	*
MPM Asset Management Investors 1998 LLC (6)	97,322	31,506	65,816	*
MPM BioVentures Parallel Fund, L.P. (6)	948,963	294,371	654,592	*
Novartis Venture Fund	2,590,190	971,970	1,618,220	2.10%
Private Equity Direct Finance	1,034,123	350,446	683,677	*
Prosper Partners	44,542	8,648	35,894	*
Rajagopal, Asha (7)	182,628(1)	24,255	158,373(1)	*
Rutter, Cynthia S.	67,328	67,328	0	*
Rutter, William H. (9)	67,328	67,328	0	*
Singer, David (8)	1,467,100(2)	70,074	1,397,026(2)	1.81%
SunAmerica Investments, Inc.	1,346,575	1,346,575	0	*
Warburg, Richard	6,626	1,877	4,749	*
William J. Rutter Revocable Trust (9)	1,147,352(3)	344,881	802,471(3)	1.04%

* Less than 1%.

(1) Includes 81,289 shares issuable upon the exercise of exercisable options or options that are to become exercisable within 60 days of February 27, 2004.

(2) Includes 1,054,150 shares issuable upon the exercise of exercisable options or options that are to become exercisable within 60 days of February 27, 2004.

(3) Includes 21,639 shares issuable upon the exercise of exercisable options or options that are to become exercisable within 60 days of February 27, 2004.

(4) In addition to the amounts listed in the table, upon conversion of a Genome note, each holder will also convert any accrued interest on his note into shares of Genome common stock at the price of $6.6418 per share (subject to anti-dilution and other adjustments). The amount of interest shares attributable to a given note holder is currently indeterminable, since it is uncertain when, if ever, such holder will convert its Genome note. The Company has reserved a total of 930,000 shares of its common stock for issuance upon potential conversion of accrued interest on the Genome notes.

(5) The number of shares owned by a selling stockholder after the offering assumes that all of the shares offered hereby by the selling stockholder are sold. However, as described above, a selling stockholder may sell all, part, or none of his or its shares.

(6) Luke Evnin has shared voting and dispositive power over shares held by BB BioVentures L.P., MPM Asset Management Investors 1998 LLC and MPM BioVentures Parallel Fund, L.P. Dr. Evnin joined the Company s board following the completion of its merger with Genesoft in February 2004. Dr. Evnin was a member of the Board of Directors of Genesoft from October 1998 to February 2004.

(7) Ms. Rajagopal became an employee of the Company as a result of its merger with Genesoft in February 2004. Ms. Rajogopal served as the Director of Finance of Genesoft from June 2001 to February 2004.

(8) Mr. Singer joined the Company s board as Chairman following the completion of its merger with Genesoft in February 2004. Mr. Singer served as Chief Executive Officer and Director of Genesoft from September 1998 to February 2004 and served as Chairman from September 1998 to February 2004.

(9) Dr. Rutter joined the Company s board following the completion of its merger with Genesoft in February 2004. Dr. Rutter was a member of the Board of Directors of Genesoft from January 1999 through February 2004.

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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 transactions).

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).

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);

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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 later of February 6, 2006 or two years from the date that the Company or any affiliate of the Company last owned any of the Genome notes or such shorter period of time as all the shares offered by this prospectus have been sold 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. 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.

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LEGAL MATTERS

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

EXPERTS

The consolidated financial statements of Genome Therapeutics Corp. at December 31, 2003 and 2002, and for each of the two years in the period ended December 31, 2003, appearing in this Prospectus and Registration Statement have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The financial statements of GeneSoft Pharmaceuticals, Inc. (a development stage company) at December 31, 2001 and 2002, and for each of the three years in the period ended December 31, 2002, incorporated by reference in this prospectus and elsewhere in this registration statement have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the ability of GeneSoft Pharmaceuticals, Inc. to continue as a going concern as described in Note 1 to the financial statements), and are incorporated by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

Our consolidated financial statements for the year ended December 31, 2001 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 the Securities Market Certain of our financial statements have been audited by Arthur Andersen LLP, and the ability to recover damages from Arthur Andersen may be limited. contained in the Risk Factors.

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INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with them, which means that we can disclose important information by referring to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. 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. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the filing of a post-effective amendment that indicates that all securities covered by this prospectus have been sold or which deregisters all securities remaining unsold:

(a) Our Annual Report on Form 10-K for the fiscal year ended December 31, 2003.

(b) Our Current Reports on Form 8-K as filed on January 9, 2004.

(c) Our Current Report on Form 8-K/A as filed on January 30, 2004.

(d) Our Current Report on Form 8-K as filed on February 2, 2004.

(e) Our Current Report on Form 8-K as filed on February 3, 2004.

(f) Our Current Report on Form 8-K as filed on February 10, 2004.

(g) 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.

We will provide to you, without charge, upon your written or oral request, a copy of any or all of the documents that we incorporate 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 Christopher Taylor, Investor Relations, Genome Therapeutics Corp., 100 Beaver Street, Waltham, Massachusetts 02453, telephone number (781) 398-2300.

WHERE YOU CAN FIND MORE INFORMATION

You should rely only on the information contained in this prospectus. We have not authorized any person to provide you different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the cover. 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 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.

9,102,511 Shares of

Common Stock

PROSPECTUS

March , 2004

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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	$ 6781.35
Printing and engraving expenses	1,000.00
Accountant s fees and expenses	5,000.00
Legal fees and expenses	20,000.00
Miscellaneous expenses	2,218.65
Total	$ 35,000.00

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.

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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)
5.1.	Opinion of Ropes & Gray LLP (3)
10.1.	Note Amendment and Exchange Agreement dated as of November 17, 2003 among GeneSoft Pharmaceuticals, Inc., Genome Therapeutics Corp. and the holders listed on the signature pages thereto (2)
10.2.	Registration Rights Agreement dated November 17, 2003 by and between Genome Therapeutics Corp. and the holders listed therein (2)
23.1	Consent of Ropes & Gray LLP (included in Opinion filed as Exhibit 5.1)
23.2.	Consent of Ernst & Young LLP, on Genome Therapeutics Corp. (3)
23.3	Consent of Ernst & Young LLP, on GeneSoft Pharmaceuticals, Inc. (3)
24.1.	Power of Attorney (included on the signature page of this registration statement)

(1) Incorporated by reference to our Registration Statement on Form S-3 (File No. 333-00127).

(2) Incorporated by reference to our Registration Statement on Form S-4 (File No. 333-111171).

(3) 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

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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 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

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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 registration statement on Form S-3 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Waltham, The Commonwealth of Massachusetts, on March 5, 2004.

GENOME THERAPEUTICS CORP.

/s/ STEVEN M. RAUSCHER

Name: Steven M. Rauscher

Title: President, Director and

Chief Executive Officer

Each person whose signature appears below hereby constitutes and appoints Steven M. Rauscher and Stephen Cohen, and each of them singly, his true and lawful attorneys-in-fact and agents with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign this registration statement on Form S-3 and any and all amendments (including post-effective amendments) to said registration statement on Form S-3 and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement on Form S-3 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, President and Chief Executive Officer (Principal Executive Officer)	March 5, 2004
/s/ STEPHEN COHEN Stephen Cohen	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 5, 2004
/s/ DAVID B. SINGER David B. Singer	Director and Chairman of the Board	March 5, 2004

/s/ Luke Evnin	Director	March 5, 2004
Luke Evnin.		
/s/ Robert J. Hennessey	Director	March 5, 2004
Robert J. Hennessey		
/s/ Vernon R. Loucks, Jr.	Director	March 5, 2004
Vernon R. Loucks, Jr.		
/s/ Norbert G. Riedel	Director	March 5, 2004
Norbert G. Riedel, Ph.D.		
/s/ William S. Reardon	Director	March 5, 2004
William S. Reardon		
/s/ William Rutter	Director	March 5, 2004
William Rutter		
/s/ David K. Stone	Director	March 5, 2004
David K. Stone		

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