GENOME THERAPEUTICS CORP
Form S-4/A
December 30, 2003
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As filed with the Securities and Exchange Commission on December 30, 2003

Registration No. 333-111171

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

AMENDMENT NO. 1 TO

FORM S-4

REGISTRATION STATEMENT

Under

THE SECURITIES ACT OF 1933

GENOME THERAPEUTICS CORP.

(Exact Name of Registrant as Specified in Its Certificate of Incorporation)

Massachusetts	**2834**	**04-2297484**
(State or Other Jurisdiction of Incorporation or Organization)	**(Primary Standard Industrial Classification Code Number)**	**(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)

Copies to:

Patrick O Brien, Esq.

Ropes & Gray LLP

One International Place

Boston, Massachusetts 02109

(617) 951-7000

Christopher Dillon, Esq.

Gunderson Dettmer Stough Villeneuve

Franklin & Hachigian, LLP

155 Constitution Drive

Menlo Park, California 94025

(650) 321-2400

Approximate date of commencement of proposed sale to the public: As soon as possible after the effective date of this registration statement and the consummation of the merger described in this registration statement.

If the securities being registered on this form are being offered in connection with the formation of a holding company and there is compliance with General Instruction G, check the following box. ¨

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 number for the same offering. ¨

If this form is a post-effective amendment filed pursuant to Rule 462(d) 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. ¨

CALCULATION OF REGISTRATION FEE

Title of each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee
Common Stock, par value $.10 par value	28,571,405(1)	N/A	$678(2)	$1(3)

(1) Represents the estimated maximum number of shares of common stock of the registrant that may be issued pursuant to Agreement and Plan of Merger and Reorganization, dated as of November 17, 2003, among registrant, Guardian Acquisition, Inc., a wholly-owned subsidiary of registrant, GeneSoft Pharmaceuticals, Inc., and Luke Evnin, as the representative of the stockholders of GeneSoft Pharmaceuticals, Inc.

(2) Estimated solely for the purpose of calculating the registration fee in accordance with Rule 457(f)(2) under the Securities Act of 1933, as amended. Because there is no market for Genesoft s securities and Genesoft has an accumulated capital deficit, the proposed maximum aggregate offering price was calculated as one-third of the par value per share of $0.0001 of (i) the 12,378,931 shares of Genesoft common stock to be exchanged in the merger, (ii) the 2,939,747 shares of Genesoft common stock issuable pursuant to options assumed in the merger and (iii) the 5,025,970 shares of Gensoft common stock issuable pursuant to warrants outstanding immediately prior to the merger, determined as of December 15, 2003.

(3) As the registration fee calculated pursuant to Rule 457(f)(2) would be less than $1, the registrant previously paid the minimum registration fee of $1 on December 15, 2003.

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

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The boards of directors of Genome Therapeutics Corp. and GeneSoft Pharmaceuticals, Inc. have agreed to combine the two companies through a business combination transaction pursuant to which (i) a wholly-owned subsidiary of Genome will first merge with and into Genesoft, with Genesoft surviving as a wholly-owned subsidiary of Genome and (ii) immediately following the foregoing step, the surviving entity will be merged with and into a second wholly-owned subsidiary of Genome. Both steps will occur as part of a single integrated plan.

The boards of directors of Genome and Genesoft believe that the merger between the two companies is advisable and in the best interests of their respective stockholders.

Genome s board of directors recommends that its stockholders vote (i) to approve the issuance of a total of 28,571,405 shares of Genome common stock pursuant to the merger agreement and the issuance of shares of Genome common stock upon the potential conversion of the convertible notes of Genome, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger, (ii) to approve the Amendment to Genome s Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000 shares of common stock and (iii) subject to approval of proposal (i) above, to authorize the Genome board of directors, in the three month period commencing with the date of the approval of this proposal, to issue up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, subject to the terms and conditions described in the attached joint proxy statement/prospectus. **Since the consummation of the merger is conditioned upon the approval or completion of the matters set forth in each of these three proposals, Genome recommends that its stockholders vote in favor of each of the proposals.**

The merger is conditioned, unless such condition is waived by both parties, upon Genome raising additional capital of at least $32 million to fund the combined company. Genome is seeking stockholder approval for the potential issuance and sale of shares in order to satisfy this condition. Genome is seeking approval for the issuance and sale of shares in excess of the number of shares that Genome currently expects will be required to raise the $32 million under the merger agreement so that Genome could raise additional capital to fund the combined company if Genome s board of directors determines that market conditions appear favorable and that such issuance is in the best interests of the company. Genome intends to use any capital raised to support its sales and marketing activities relating to FACTIVE following the merger and to fund clinical trials and other research and development activities of the combined company.

If the merger is completed, each outstanding share of Genesoft common stock will be converted into a right to receive shares of Genome s authorized common stock, unless Genesoft s stockholders exercise appraisal or dissenters rights under the laws of Delaware or California, as applicable. Genome will issue a total of 28,571,405 shares of its common stock (i) in exchange for all shares of capital stock of Genesoft, (ii) as payment of certain interest and related amounts due to Genesoft s note holders and (iii) upon the exercise of Genesoft options and warrants, which will be assumed by Genome. We will determine the number of shares of Genome common stock into which each share of Genesoft common stock will be converted immediately prior to completion of the merger in accordance with formulas specified in the merger agreement and described in the attached joint proxy statement/prospectus.

Genesoft s board of directors recommends that its stockholders vote (i) to adopt and approve the merger agreement and (ii) to amend and restate Genesoft s Seventh Amended and Restated Certificate of Incorporation to eliminate all authorized shares of Genesoft preferred stock if the merger is completed. The amendment and restatement of Genesoft s Seventh Amendment and Restated Certificate of Incorporation is subject to completion of the merger and will not be made if the merger is not completed.

Genome common stock is listed in the Nasdaq National Market under the symbol GENE.

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Your Vote is Very Important. Whether or not you plan to attend your company s stockholders meeting, please take the time to vote on the proposal(s) submitted for your company s meeting by completing and mailing the enclosed proxy card to us. If you sign, date and mail your proxy card without indicating how you wish to vote, your proxy will be counted as a vote in favor of the proposal(s) submitted at your meeting. Failure to return or sign your proxy card will have the effect of a vote against the merger and the related transactions, unless you attend your stockholders meeting and vote in person.

The dates, times and places of the stockholders meetings are as follows:

For Genome s stockholders: February 2, 2004 at 1:00 p.m. local time, at Ropes & Gray LLP, One International Place, 36th floor, Boston, Massachusetts.

For Genesoft s stockholders: February 2, 2004 at 10:00 a.m. local time at Genesoft s offices, 7300 Shoreline Court, South San Francisco, California.

Following this letter you will find a formal notice of the special meeting of each company s stockholders and a joint proxy statement/prospectus. The joint proxy statement/prospectus provides you with detailed information concerning the merger and the related transactions as well as the other proposals to be presented and voted upon at the special meetings of stockholders of Genome and Genesoft. You may also obtain more information about Genome from documents that it has filed with the Securities and Exchange Commission.

Sincerely,

Steven M. Rauscher
Chairman, President and Chief Executive Officer of
Genome Therapeutics Corp.

David B. Singer
Chairman and Chief Executive Officer of
GeneSoft Pharmaceuticals, Inc.

Please give all of the information contained or incorporated by reference in the joint proxy statement/prospectus your careful attention. In particular, you should carefully consider the discussion in the section entitled Risk Factors beginning on page 24 of the joint proxy statement/prospectus. Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the shares to be issued under, or passed upon the adequacy of, this joint proxy statement/prospectus. Any representation to the contrary is a criminal offense.

The accompanying joint proxy statement/prospectus is dated December 30, 2003 and was first mailed to stockholders of Genome and Genesoft on or about December 31, 2003.

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GENOME THERAPEUTICS CORP.

100 Beaver Street

Waltham, Massachusetts 02453

(781) 398-2300

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS

to be held on February 2, 2004

To the Stockholders of Genome Therapeutics Corp.:

A special meeting of stockholders of Genome Therapeutics Corp. will be held on February 2, 2004 at 1:00 p.m., local time, at Ropes & Gray LLP, One International Place, 36th floor, Boston, Massachusetts, for the following purposes:

1. To consider and vote on a proposal to approve (i) the issuance of 28,571,405 shares of Genome common stock pursuant to the Agreement and Plan of Merger and Reorganization, dated as of November 17, 2003, among Genome Therapeutics Corp., Guardian Acquisition, Inc., a wholly-owned subsidiary of Genome Therapeutics Corp., GeneSoft Pharmaceuticals, Inc., and Luke Evnin, as the representative of the Genesoft stockholders and (ii) the issuance of shares of Genome common stock upon the potential conversion of the convertible notes of Genome, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger. A copy of the merger agreement is attached as Annex A to the accompanying joint proxy statement/prospectus.

2. To consider and vote on a proposal to approve the Amendment to the Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000.

3. Subject to approval of proposal 1 above, to consider and vote on a proposal to authorize the Genome board of directors, in light of the limitations imposed by the rules of the Nasdaq Stock Market with respect to the issuance of shares without prior stockholder approval, to issue, in the three month period commencing with the date of the approval of this proposal, in connection with one or more capital raising transactions to finance the combined company, up to 20,000,000 shares of Genome common stock (including pursuant to options, warrants, convertible debt or other securities convertible into common stock), upon such terms as the board of directors shall deem to be in the best interests of Genome, for an aggregate consideration of not more than $50,000,000 and at a price not less than 75% of the market price of Genome common stock at the time of issuance, including issuances of shares to Genome s officers or directors or their affiliates, so long as, in the case of any such issuances of shares to officers or directors or their affiliates, the price and other terms of the transactions are approved by Genome s audit committee or another committee comprised entirely of independent members of Genome s board of directors who do not purchase securities in the transactions.

4. To transact any other business as may properly come before the special meeting and any adjournment or postponement of the special meeting.

Only stockholders of record of Genome Therapeutics Corp. as of the close of business on December 23, 2003 are entitled to notice of, and will be entitled to vote at, the special meeting or any adjournment or postponement thereof. Assuming a quorum is present at the special meeting,

approval of proposals 1 and 3 described above will require a majority of the votes of Genome Therapeutics Corp. common stock properly cast upon each of these proposals at the special meeting. Under the by-laws of Genome Therapeutics Corp., a quorum consists of a majority in interest of all stock issued and outstanding and entitled to vote at the meeting. Approval of proposal 2 described above will require the affirmative vote of a majority of the shares of Genome Therapeutics Corp. common stock outstanding as of the record date and entitled to vote on the proposal at the special meeting.

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We invite you to attend the special meeting because it is important that your shares be represented at the meeting. Whether or not you plan to attend the special meeting, please sign, date and return the enclosed proxy card in the accompanying postage-paid envelope. Please note that, by delivering a proxy to vote at the special meeting, you are also granting a proxy to vote at any adjournments or postponements of the special meeting of Genome Therapeutics Corp. If you attend the meeting, you may vote in person, which will revoke a signed proxy if you have already sent one in. You may also revoke your proxy at any time before the meeting in the manner described in the accompanying joint proxy statement/prospectus.

BY THE ORDER OF THE BOARD OF DIRECTORS,

Steven M. Rauscher

Chairman, President and Chief Executive Officer

Waltham, Massachusetts

December 30, 2003

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THE MERGER

The merger is structured as a reverse triangular merger followed by a subsequent merger into a wholly-owned subsidiary of Genome as illustrated below. Both of these steps, which are intended to qualify as a tax-free reorganization under Section 368(a) of the Internal Revenue Code, will occur as part of a single integrated plan.

(1) Guardian Acquisition, Inc., a wholly-owned subsidiary of Genome Therapeutics Corp., merges with and into GeneSoft Pharmaceuticals, Inc., with GeneSoft Pharmaceuticals, Inc. surviving as a wholly-owned subsidiary of Genome Therapeutics Corp.

(2) The surviving entity from step (1) merges with and into Guardian Holdings, LLC, a wholly-owned subsidiary of Genome Therapeutics Corp.

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GENESOFT PHARMACEUTICALS, INC.

7300 Shoreline Court

South San Francisco, California 94080

650-837-1800

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS

to be held on February 2, 2004

To the Stockholders of GeneSoft Pharmaceuticals, Inc.:

A special meeting of stockholders of GeneSoft Pharmaceuticals, Inc. will be held on February 2, 2004, at 10:00 a.m., local time, at Genesoft s offices, 7300 Shoreline Court, South San Francisco, California, for the following purposes:

1. To consider and vote on a proposal to adopt and approve the Agreement and Plan of Merger and Reorganization, dated as of November 17, 2003, among Genome Therapeutics Corp., a Massachusetts corporation, Guardian Acquisition, Inc., a Delaware corporation and a wholly-owned subsidiary of Genome Therapeutics Corp., GeneSoft Pharmaceuticals, Inc., a Delaware corporation, and Luke Evnin, as the representative of the Genesoft stockholders.

2. To consider and vote on a proposal to amend and restate GeneSoft Pharmaceuticals, Inc. s Seventh Amended and Restated Certificate of Incorporation to eliminate any authorized shares of GeneSoft Pharmaceuticals, Inc. preferred stock if, and only if, the merger is completed.

3. To transact any other business as may properly come before the special meeting and any adjournment or postponement of the special meeting.

Only stockholders of record of GeneSoft Pharmaceuticals, Inc. as of the close of business on December 23, 2003 are entitled to notice of, and will be entitled to vote at, the special meeting or any adjournment or postponement thereof. Approval of the merger agreement and the transactions contemplated by the merger agreement requires the affirmative vote of the holders of a majority of the shares of GeneSoft Pharmaceuticals, Inc. common stock outstanding as of the record date. Approval of the amendment and restatement of the Seventh Amended and Restated Certificate of Incorporation of GeneSoft Pharmaceuticals, Inc. requires the affirmative vote of the holders of a majority of the shares of GeneSoft Pharmaceuticals, Inc. common stock outstanding as of the record date. The amendment and restatement of Genesoft s Seventh Amendment and Restated Certificate of Incorporation is subject to completion of the merger and will not be made if the merger is not completed.

Your vote is important. To ensure that your shares are represented at the special meeting, you are urged to complete, date and sign the enclosed proxy card and mail it promptly in the postage-prepaid envelope provided, whether or not you plan to attend the special meeting in person. You may revoke your proxy in the manner described in the accompanying joint proxy statement/prospectus at any time before it has been voted at the special meeting of GeneSoft Pharmaceuticals, Inc. If you attend the special meeting, you may vote in

person even if you returned a proxy.

BY ORDER OF THE BOARD OF DIRECTORS,

David B. Singer

Chairman and Chief Executive Officer

South San Francisco, California

December 30, 2003

Please do not send your stock certificates at this time. If the merger is completed, you will be sent instructions regarding the surrender of your stock certificates.

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ADDITIONAL INFORMATION

This joint proxy statement/prospectus incorporates important business and financial information about Genome from other documents that are not included in or delivered with this document. We have listed the documents containing this information on page 147. This information is available to you without charge upon your written or oral request. You can obtain those documents relating to Genome which are incorporated by reference in this joint proxy statement/prospectus by requesting them in writing or by telephone at the following address and telephone number:

GENOME THERAPEUTICS CORP.

100 Beaver Street

Waltham, Massachusetts 02453

(781) 398-2300

If you would like to request documents, you must do so by January 22, 2004 in order to receive them before the special meeting of your company s stockholders. You will not be charged for any of these documents that you request.

For additional information regarding where you can find information about Genome and Genesoft, please see the section entitled Where You Can Find Additional Information beginning on page 147 of this joint proxy statement/prospectus. The information contained in this joint proxy statement/prospectus with respect to Genome was provided by Genome and the information contained in this joint proxy statement/prospectus with respect to Genesoft was provided by Genesoft.

SPECIAL NOTE REGARDING REFERENCES

References in this document to *www.genomecorp.com, www.genesoft.com*, any variations of the foregoing, or any other uniform resource locator, or URL, are inactive textual references only. The information on Genome s web site, Genesoft s web site or any other web site is not incorporated by reference into this document and should not be considered to be a part of this document.

NOTE ON TRADEMARKS

The following trademarks are the properties of the specified holders: FACTIVE® is the property of LG Life Sciences, Ltd., Nanobinder® is the property of Genesoft, Levaquin® is the property of Ortho-McNeil Pharmaceutical, Inc., Tequin® is the property of Bristol-Myers Squibb Company, Cipro® and Avelox® are both the property of Bayer Corporation, Biaxin® is the property of Abbott Laboratories, Zithromax® is the property of Pfizer Inc., Augmentin® is the property of GlaxoSmithKline, Ketek® is the property of Aventis Pharmaceuticals and Vanconin® is the property of Eli Lilly and Company. Unless otherwise indicated, trademarks or service marks appearing in this joint proxy statement/prospectus are the property of their respective holders.

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QUESTIONS AND ANSWERS ABOUT THE MERGER

Q: Why are Genome and Genesoft proposing the merger? (See pages 63 and 71)

A: Genome and Genesoft believe the merger will strengthen the outlook for both companies. Genome Therapeutics is a biopharmaceutical company focused on the discovery, development and commercialization of pharmaceutical products for specialty markets. Genesoft is a specialty pharmaceutical company focused on the discovery and development of novel anti-infective agents.

Genome is proposing the merger because it will enable Genome to realize its goal of becoming a biopharmaceutical company with an FDA approved anti-infective product (FACTIVE) with the potential to significantly increase Genome s revenue stream, permitting Genome to build a sales and marketing force that will benefit Ramoplanin, Genome s current lead product candidate, and future product candidates of the combined company. Genesoft is proposing the merger because it will provide additional expertise and resources necessary to successfully launch FACTIVE, Genesoft s FDA approved anti-infective product, in the U.S. and provide a broader portfolio of product candidates, including Ramoplanin.

Overall, both Genome and Genesoft believe the merger will provide added value to their respective stockholders. Achieving these anticipated benefits, however, is subject to risk and uncertainty, including the risks discussed in Risk Factors beginning on page 24.

Q: What will I, as a holder of Genesoft common stock or options or warrants to purchase Genesoft common stock, receive in the merger? (See page 83)

A: If you are a holder of Genesoft common stock, you will receive a number of shares of Genome common stock equal to the common exchange ratio for each share of Genesoft common stock you own. The common exchange ratio is determined by:

deducting the shares of Genome common stock to be issued to the holders of Genesoft s promissory notes as payment of accrued interest and related amounts from the total of 28,571,405 shares of Genome common stock issuable in the merger and

dividing that remaining number of Genome shares by the fully-diluted number of shares of Genesoft common stock outstanding on the closing date (the fully diluted number of shares assumes the conversion or exercise in full of all Genesoft options and warrants).

The exact exchange ratio between Genesoft and Genome common stock will depend on when the closing of the merger occurs, which will determine how much interest has accrued on the Genesoft promissory notes, as well as the price at which the accrued interest and other related amounts due under the Genesoft promissory notes are converted into Genome common stock. The interest and other related amounts will be converted into Genome common stock at a price of $2.84 per share, unless the price per share of Genome common stock expected to be issued in the capital raising transaction to raise up to $50 million to finance the combined company is less than $2.84, in which case that lesser per share price will become the conversion price.

Each holder of an option or warrant to purchase shares of Genesoft common stock that does not terminate by its terms upon or prior to the merger will receive an option or warrant to purchase a number of shares of Genome common stock equal to the product of the number of Genesoft shares for which such option or warrant was exercisable multiplied by the common exchange ratio. For information on the terms of exercise for such options and warrants to acquire Genome common stock, please see The Merger and Related Transactions The Merger Agreement Conversion of Genesoft Stock.

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The following chart shows the approximate common exchange ratio that would be used to determine the per share consideration to be received by Genesoft stockholders assuming different possible closing dates and prices of shares sold in the financing:

		Merger Closing Date			
		February 2, 2004	**February 28, 2004**	**March 31, 2004**	**April 30, 2004**
	Prices of $2.84 or higher	1.189	1.188	1.186	1.184
Closing	$2.66	1.173	1.171	1.170	1.168
Financing	$2.48	1.154	1.153	1.151	1.149
Price	$2.30	1.133	1.131	1.129	1.127
	$2.12	1.108	1.106	1.103	1.101

Each Genesoft stockholder will receive 80% of the merger consideration otherwise due to it upon closing of the merger. The remainder will be placed in escrow, pursuant to the escrow agreement attached to this joint proxy statement/prospectus as Annex B, to cover potential indemnity claims and any payments relating to those claims by Genome under the merger agreement. An additional 400,000 shares of Genome common stock issuable to the Genesoft stockholders in the merger will be placed in escrow to fund potential issuances of equity (including options) to a senior clinical development officer that may be hired by the combined company following the merger. The shares to be placed in escrow will be deducted from the shares of Genome common stock to be received by the Genesoft stockholders on a pro rata basis. If a holder of a Genesoft option assumed by Genome pursuant to the merger agreement exercises any portion of the holder s option prior to the termination of the escrow fund, the holder will contribute a portion of the shares of Genome common stock issued upon exercise to the escrow fund in accordance with the terms of the escrow agreement. Subject to any claims made by Genome or its affiliates, officers, directors or employees, up to half of the indemnity escrow amount will be released from escrow one year after closing of the merger and the remainder will be released 18 months after closing. Adoption and approval of the merger agreement by Genesoft s stockholders will constitute approval by such stockholders of the indemnification obligations set forth in the merger agreement, the terms of the escrow agreement and the authority of the stockholders representative established by the merger agreement.

Q: What will happen to Genesoft as a result of the merger? (See page 83)

A: In the initial merger, Guardian Acquisition, Inc., a wholly-owned subsidiary of Genome, will be merged into Genesoft. Immediately thereafter, Genesoft will be merged into a second wholly-owned subsidiary of Genome in the second-step merger. As a result of the initial merger, the separate corporate existence of Guardian will cease, and Genesoft will continue as the surviving corporation of the initial merger and as a wholly-owned subsidiary of Genome. As a result of the second-step merger, the separate corporate existence of Genesoft will cease, and the second acquisition subsidiary, which is a Delaware limited liability company, will continue as the surviving company of the second-step merger and be wholly-owned by Genome.

Q: Will Genesoft stockholders be able to trade the Genome common stock that they receive in the merger? (See page 98)

A: Yes. The Genome common stock issued in the merger will be registered under the Securities Act and will be listed on the Nasdaq National Market under the symbol GENE. All shares of Genome common stock that you receive in the merger or upon exercise of Genesoft options or warrants assumed by Genome in the merger will be freely transferable unless you are deemed to be an affiliate of Genesoft at the time of the special meetings or your shares are subject to contractual transfer restrictions. Shares of Genome common stock received by persons deemed to be affiliates of Genesoft may only be sold in compliance with Rule 145 under the Securities Act or as otherwise permitted under the Securities Act.

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Q: When do Genesoft and Genome expect to complete the merger?

A: Genesoft and Genome expect to complete the merger when all of the conditions to completion of the merger contained in the merger agreement have been satisfied or waived. The stockholders of Genesoft must approve (i) the merger and the related transactions and (ii) the amendment and restatement of Genesoft s Seventh Amended and Restated Certificate of Incorporation at their special stockholders meeting. The stockholders of Genome must vote for the proposals (i) to approve the issuance of a total of 28,571,405 shares of Genome common stock pursuant to the merger agreement and the issuance of shares of Genome common stock upon the potential conversion of the convertible notes of Genome, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger, (ii) to approve the Amendment to Genome s Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000 shares of common stock and (iii) subject to approval of proposal (i) above, to authorize the Genome board of directors, in the three month period commencing with the date of the approval of this proposal, to issue up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, subject to the terms and conditions described in this joint proxy statement/prospectus.

Genesoft and Genome are working toward satisfying these conditions and completing the merger as soon as practicable. Genesoft and Genome currently anticipate they will complete the merger in the first quarter of 2004 following the respective special meetings of Genesoft s and Genome s stockholders, assuming their stockholders approve the merger and related transactions, Genome is able to successfully raise a minimum of $32 million to fund the combined company, unless waived by both parties, and the other merger conditions are satisfied or waived. However, because the merger is subject to some conditions which are beyond Genesoft s and Genome s control, the exact timing cannot be predicted.

Q: What happens if the merger is not completed? (See page 95)

A: If the merger is not completed, each of Genome and Genesoft will continue as independent companies. In addition, as a result of some termination events described in the merger agreement, Genome or Genesoft may be required to pay the other party a termination fee of $3,044,063.90 for certain termination events, and to reimburse the other for out-of-pocket expenses up to $1,000,000.00, including legal, accounting, investment banking, printing and other fees, related to this transaction if the merger is not completed. For a more complete discussion of requirements relating to payments of fees and expenses by each of Genome and Genesoft see the section entitled The Merger and Related Transactions The Merger Agreement Termination Fees in this joint proxy statement/prospectus.

Q: What vote is required to approve the merger and the related transactions? (See pages 45 and 52)

A: Approval of the merger agreement and the transactions contemplated by the merger agreement and approval of the amendment and restatement of the Seventh Amended and Restated Certificate of Incorporation of Genesoft each requires the affirmative vote of the holders of a majority of the shares of Genesoft common stock outstanding as of the record date.

Approval of the issuance of Genome common stock to the Genesoft stockholders pursuant to the merger agreement and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes to be exchanged for Genesoft promissory notes in connection with the merger, and approval of the issuance of up to 20,000,000 shares in connection with the capital raising transactions to finance the combined company, will each require a majority of the votes of Genome common stock properly cast upon this proposal at the special meeting. Approval of the increase in authorized Genome shares will require the affirmative vote of a majority of the shares of Genome common stock outstanding as of the record date and entitled to vote on the proposal at the special meeting.

The boards of directors of Genesoft and Genome have approved the merger agreement, the merger and the transactions contemplated by the merger agreement.

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Q: How do I vote on the merger? (See pages 47 and 53)

A: First, please review the information contained or incorporated by reference in this joint proxy statement/prospectus, including the annexes, as it contains important information about Genome, Genesoft and the merger. It also contains important information about what each of the boards of directors of Genome and Genesoft, respectively, considered in evaluating the merger. Next, complete and sign the enclosed proxy card, and then mail it in the enclosed return envelope (addressed to Genesoft if you are a Genesoft stockholder or to Genome, c/o Equiserve Trust Company, if you are a Genome stockholder) as soon as possible so that your shares can be voted at your company s special meeting of stockholders at which, (a) in the case of Genesoft, the merger and the related transactions and the amendment and restatement of Genesoft s Seventh Amended and Restated Certificate of Incorporation will be presented and voted upon or, (b) in the case of Genome, the increase in Genome authorized shares, the issuance of Genome common stock to the security holders of Genesoft in the merger and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes to be exchanged for Genesoft promissory notes in connection with the merger, and the issuance of up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, will be presented and voted upon. You may also attend the special meeting of your company in person and vote at the special meeting instead of submitting a proxy.

Q: What happens if I don t indicate how to vote my proxy? (See pages 47 and 53)

A: If you sign and send in your proxy, but do not include instructions on how to vote your properly signed proxy card, your shares will be voted (a) FOR the adoption and approval of the merger and the related transactions and the amendment and restatement of Genesoft s Seventh Amended and Restated Certificate of Incorporation, if you are a Genesoft stockholder, or (b) FOR the increase in Genome authorized shares, the issuance of Genome common stock to the security holders of Genesoft in the merger and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes to be exchanged for Genesoft promissory notes in connection with the merger, and the issuance of up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, if you are a Genome stockholder.

Q: What happens if I don t return a proxy card? (See pages 46 and 53)

A: Not returning your proxy card will have the same effect as voting (a) against adoption and approval of the merger agreement and approval of the merger and the amendment and restatement of Genesoft s Seventh Amended and Restated Certificate of Incorporation, if you are a Genesoft stockholder, and (b) against the increase in Genome authorized shares, the issuance of Genome common stock to the security holders of Genesoft in the merger and the issuance of up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, if you are Genome stockholder.

Q: Can I change my vote after I have mailed my signed proxy card? (See pages 47 and 53)

A: Yes. You can change your vote at any time before your proxy is voted at the special meeting of your company s stockholders. You can do this in one of three ways:

first, you can send a written notice stating that you would like to revoke your proxy to the appropriate address below;

second, you can complete and submit a later-dated proxy card to the appropriate address below; or

third, you can attend the special meeting of Genome or Genesoft, as appropriate, and vote in person. Your attendance at the special meeting alone will not revoke your proxy. You must vote at the special meeting in order to revoke your previously submitted proxy.

You should send any notice of revocation or your completed new proxy card, as the case may be, to:

For Genome Stockholders:

Genome Therapeutics Corp.

100 Beaver Street

Waltham, MA 02453

Attn: Stephen Cohen

Chief Financial Officer

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For Genesoft Stockholders:

GeneSoft Pharmaceuticals, Inc.

7300 Shoreline Court

South San Francisco, CA 94080

Attn: Asha Rajagopal

Director of Finance

Q: If my broker holds my Genome shares in street name, will my broker vote these shares for me? (See page 47)

A: No. Your broker will not be able to vote your shares without instructions from you. If you do not provide your broker with voting instructions, your shares may be considered present at the special meeting for purposes of determining a quorum, but will not be considered to have been voted in favor of the increase in Genome authorized shares and the issuance of Genome common stock to the security holders of Genesoft in the merger and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes to be exchanged for Genesoft promissory notes in connection with the merger. As a result, failure to provide your broker with voting instructions will have the effect of a vote against the increase in Genome authorized shares, the issuance of Genome common stock to the security holders of Genesoft and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes to be exchanged for Genesoft promissory notes in connection with the merger, and the issuance of up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company. If you have instructed a broker to vote your shares and wish to change your vote, you must follow the directions received from your broker to change those instructions.

Q: Should I send my Genesoft stock certificates now? (See page 85)

A: No. If the merger is completed, Genome will send you written instructions for exchanging your Genesoft stock certificates for Genome stock certificates. Please do not send in your stock certificates with your proxy. If you send your stock certificates to Genome, Genome assumes no risk of loss.

Q: What do I need to do now?

A: After carefully reading and considering the information contained in this document, please complete and sign your proxy card and return it in the enclosed, postage-paid envelope as soon as possible so that your shares may be represented at your special meeting.

Q: Am I entitled to appraisal rights in connection with the merger? (See pages 47, 54 and 56)

A: Appraisal and dissenters rights are available to Genesoft stockholders under the respective laws of Delaware and California, as applicable, in connection with the merger. Appraisal or dissenters rights are not available to Genome stockholders.

Q: Are there any risks I should consider in deciding whether to vote for the merger?

A: Yes. In the section entitled Risk Factors beginning on page 24 of this joint proxy statement/prospectus, Genome and Genesoft have described a number of risk factors that you should consider.

Q: What are the tax consequences to a Genesoft stockholder of the merger? (See page 96)

A: It is the opinion of Genesoft and Genome s respective legal counsel that, based on facts and representations provided to such counsel and assumptions stated in the opinions, the merger will qualify as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code. As a consequence of the merger

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qualifying as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code, we expect that the exchange of shares of Genesoft common stock by the stockholders of Genesoft for shares of Genome common stock will not cause a Genesoft stockholder to recognize gain or loss for United States federal income tax purposes. A Genesoft stockholder will recognize gain or loss with respect to cash received upon proper exercise of its appraisal rights pursuant to the merger. These opinions will not bind the Internal Revenue Service, which could take a different view. The tax consequences to a Genesoft stockholder will depend on the facts of such holder s particular situation. Therefore, we urge each Genesoft stockholder to consult with its own tax advisor to determine the particular tax consequences of the merger to it. To review the tax consequences in greater detail, see the section entitled The Merger and Related Transactions Material United States Federal Income Tax Consequences of the Merger beginning on page 96 of this joint proxy statement/prospectus.

Q: Where can I find more information about the companies and who can help answer my questions about the proposals?

A: You can find more information about Genome and Genesoft from various sources described under Where You Can Find Additional Information on page 147.

If you have any questions about the proposals presented in this joint proxy statement/prospectus, you should contact:

For Genome Stockholders:

Genome Therapeutics Corp.

100 Beaver Street

Waltham, MA 02453

Attn: Christopher Taylor

Senior Director of Investor Relations

(781) 398-2300

For Genesoft Stockholders:

GeneSoft Pharmaceuticals, Inc.

7300 Shoreline Court

South San Francisco, CA 94080

Attn: Asha Rajagopal

Director of Finance

(650) 837-1800

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SUMMARY

The following is a summary of the information contained in this joint proxy statement/prospectus. This summary may not contain all of the information that is important to you. You should carefully read this entire joint proxy statement/prospectus and the other documents referred to for a more complete understanding of the merger and related transactions. In particular, you should read the section entitled Risk Factors and the annexes attached to this joint proxy statement/prospectus, including the merger agreement, which is attached to this joint proxy statement/prospectus as Annex A. We have included page references in parentheses to direct you to a more complete description of the topics presented in this summary. In addition, important business and financial information concerning Genome is incorporated by reference into this joint proxy statement/prospectus. You may obtain the information incorporated by reference into this joint proxy statement/prospectus without charge by following the instructions in the section entitled Where You Can Find Additional Information beginning on page 147 of this joint proxy statement/prospectus.

The Companies

GENOME THERAPEUTICS CORP.

100 Beaver Street

Waltham, Massachusetts 02453

www.genomecorp.com

Genome is a biopharmaceutical company focused on the discovery, development and commercialization of pharmaceutical products.

Genome has nine established product development programs. Genome is managing the development and commercialization of its lead product candidate, Ramoplanin, in the United States and Canada. This product is in a Phase III clinical trial for the prevention of bloodstream infections caused by vancomycin-resistant enterococci (VRE) and a Phase II trial for the treatment of patients with *Clostridium difficile*-associated diarrhea (CDAD). The company has seven product discovery and development alliances with pharmaceutical companies including Amgen, AstraZeneca, bioMérieux, Schering-Plough and Wyeth. Genome s biopharmaceutical product candidates are all currently in discovery or development phases and are neither approved by the FDA nor available for commercial sale.

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

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

For more information on the business of Genome, please refer to Genome s Annual Report on Form 10-K for the fiscal year ended December 31, 2002 and Form 10-Q for the quarterly period ended September 27, 2003. Please refer to the section of this joint proxy statement/prospectus entitled Where You Can Find Additional Information on page 147 to find out where you can obtain copies of Genome s Annual Report as well as the other documents Genome files with the Securities and Exchange Commission.

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GENESOFT PHARMACEUTICALS, INC.

7300 Shoreline Court

South San Francisco, CA 94080

www.genesoft.com

Genesoft is an emerging pharmaceutical company based in South San Francisco, California, that has a FDA-approved anti-infective product and a portfolio of product development programs. Genesoft s lead product is FACTIVE (gemifloxacin mesylate), an orally administered, broad-spectrum fluoroquinolone antibiotic to which the company has an exclusive license to develop and market in North America, 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. FACTIVE was approved for sale in the United States on April 4, 2003 by the FDA. Following the completion of the proposed merger with Genome, the combined company currently intends to launch the product in the second half of 2004.

The address for Genesoft s executive offices is 7300 Shoreline Court, South San Francisco, California 94080 and its telephone number is (650) 837-1800.

For more information on the business of Genesoft, please refer to the section of this joint proxy statement/prospectus entitled Information About Genesoft beginning on page 110.

Voting Requirements for the Merger and Other Matters (See pages 45 and 52)

Assuming a quorum is present at the special meeting, the affirmative vote of the holders of a majority of the votes of Genome common stock properly cast at the special meeting will be required (i) to approve the issuance of a total of 28,571,405 shares of Genome common stock to the Genesoft security holders pursuant to the merger agreement and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger and (ii) subject to approval of proposal (i) above, to authorize the board of directors, in the three month period commencing with the date of the approval of this proposal, to issue up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, subject to the terms and conditions described in this joint proxy statement/prospectus. The affirmative vote of a majority of the Genome shares outstanding as of the record date and entitled to vote on the proposal at the special meeting will be required to approve the Amendment to the Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000 shares. Holders of Genome common stock will be entitled to cast one vote per share of Genome common stock owned as of December 23, 2003, the record date for the Genome special meeting of stockholders at which the proposals will be presented and voted upon.

The affirmative vote of the holders of a majority of the outstanding shares of Genesoft common stock as of the record date will be required (i) to approve the merger agreement and the transactions contemplated by the merger agreement and (ii) to approve the amendment and restatement of the Seventh Amended and Restated Certificate of Incorporation of Genesoft. Holders of Genesoft common stock will be entitled to cast one vote per share of Genesoft common stock owned as of December 23, 2003, the record date for the Genesoft special meeting of stockholders at which the proposals will be presented and voted upon.

Share Ownership of Genome Directors and Officers (See page 46)

As of the close of business on the record date for the special meeting of Genome stockholders at which the proposals described in this joint proxy statement/prospectus will be presented and voted upon, directors and officers of Genome (and their respective affiliates) collectively owned approximately 0.4% of the outstanding shares of Genome common stock entitled to vote at the special meeting.

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This does not include 1,794,871 shares of Genome common stock issuable upon the exercise of presently exercisable options which these directors and officers hold. If all of these stock options were exercised prior to the record date for the special meeting, the directors and executive officers of Genome (and their respective affiliates) would collectively beneficially own approximately 5.8% of the outstanding shares of Genome common stock entitled to vote at the special meeting.

The directors and executive officers of Genome have entered into a voting agreement with Genesoft, pursuant to which each such person has agreed to vote the shares owned beneficially by such person in favor of the merger and the related transactions. See Voting Agreements below.

Share Ownership of Genesoft Directors and Officers (See page 53)

As of the close of business on the record date for the special meeting of Genesoft stockholders at which the merger agreement will be presented and voted upon, directors and officers of Genesoft (and their respective affiliates) collectively owned approximately 29.3% of the outstanding shares of Genesoft common stock entitled to vote at the special meeting on the merger agreement.

Each of the directors and executive officers of Genesoft has entered into voting agreements with Genome, pursuant to which each such person has agreed to vote the shares owned beneficially by such person in favor of the merger and the related transactions. See Voting Agreements below.

Interests of Directors and Executive Officers of Genome in the Merger (See page 80)

Genome s stockholders should be aware that some Genome executive officers and directors may have interests in the merger that may be different from, or in addition to, their interests as stockholders of Genome in considering the recommendation of the Genome board of directors that Genome s stockholders vote in favor of the proposals (i) to approve the issuance of a total of 28,571,405 shares of Genome common stock pursuant to the merger agreement and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger and (ii) to approve the Amendment to the Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000 shares and (iii) subject to approval of proposal (i) above, to authorize the board of directors, in the three month period commencing with the date of the approval of this proposal, to issue up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, subject to the terms and conditions described in this joint proxy statement/prospectus.

Genome s board of directors was aware of, and considered, these interests among other matters during its deliberations on the merits of the proposals specified above and in making its recommendation to Genome s stockholders that they vote for each of the proposals specified above.

Interests of Directors and Executive Officers of Genesoft in the Merger (See page 81)

In considering the recommendation of Genesoft s board of directors that Genesoft stockholders vote in favor of approval of the merger agreement, Genesoft stockholders should be aware that some Genesoft executive officers and directors may have interests in the merger that

may be different from, or in addition to, their interests as stockholders of Genesoft.

Genesoft s board of directors was aware of, and considered, these interests among other matters during its deliberations on the merits of the merger and related transactions and in making its recommendation to Genesoft s stockholders that they vote for the merger and related transactions.

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Board Recommendations to Stockholders and Reasons for the Merger

Recommendation of Genome s Board of Directors (See page 48)

After careful consideration, Genome s board of directors determined that the merger is advisable, is in the best interests of Genome s stockholders, and is on terms that are fair to the stockholders of Genome. **Accordingly, Genome s board of directors approved the merger and the related transactions and recommends that its stockholders vote FOR the proposals (i) to approve the issuance of a total of 28,571,405 shares of Genome common stock pursuant to the merger agreement and the issuance of Genome common stock upon the potential conversion of the Genome convertible notes, in an aggregate principal amount of $22,309,647, to be exchanged for Genesoft promissory notes in connection with the merger, (ii) to approve the Amendment to the Articles of Organization to increase the number of shares of Genome common stock the company is authorized to issue from 50,000,000 to 175,000,000 shares and (iii) subject to approval of proposal (i) above, to authorize the board of directors, in the three month period commencing with the date of the approval of this proposal, to issue up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company, subject to the terms and conditions described in this joint proxy statement/prospectus. Since the consummation of the merger is conditioned upon the approval or completion of the matters set forth in each of these three proposals, Genome recommends that its stockholders vote in favor of each of the proposals.**

Genome s Reasons for the Merger (See page 71)

In reaching its decision to approve the merger agreement and the transactions contemplated by the merger agreement, Genome s board of directors consulted with management of Genome, as well as its financial and legal advisors, and considered a number of potential benefits and factors pertaining to the merger, including the following:

- the merger will enable Genome to realize its goal of becoming a biopharmaceutical company with an FDA approved anti-infective product (FACTIVE);
- potential revenue stream from FACTIVE will allow Genome to build a sales and marketing infrastructure that will benefit Ramoplanin, Genome s current lead product candidate, and future product candidates;
- the merger will help position Genome as a key participant in the commercialization of anti-infective therapeutics;
- the merger will increase the visibility of Genome and provide a stronger portfolio of products to serve as the basis for raising additional capital for the company; and
- the merger will significantly enhance Genome s clinical development staff, intellectual property and technical resources.

Genome s board of directors also identified a number of potentially negative factors, including the following:

- the risk that the potential benefits of the merger might not be realized;

the risk that FACTIVE might not launch in the second half of 2004, causing a delay in the realization of potential revenue;

the risk that FACTIVE may not attain commercial acceptance and generate the level of revenues expected;

the challenges and risks involved in combining the businesses of two geographically distant companies;

the effect of the announcement on Genome s share price;

the risk of diverting management s focus and resources from other strategic opportunities and from operational matters while working to complete and implement the merger;

the risk that Genome will not be able to raise a minimum of $32 million of capital, which is a condition to the closing unless both parties agree to waive this condition;

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- the risk that LG Life Sciences will not be able to supply FACTIVE in a timely manner, or maintain its manufacturing facilities in accordance with regulatory requirements;

- the risk that the merger would not be completed; and

- the other risks described under Risk Factors beginning on page 24.

Recommendation of Genesoft s Board of Directors (See page 57)

After careful consideration, Genesoft s board of directors has determined that the merger is advisable, in the best interests of Genesoft stockholders and on terms that are fair to the stockholders of Genesoft. **Accordingly, Genesoft s board of directors has approved the merger and the related transactions and recommends that stockholders vote FOR the proposals to (i) adopt and approve the merger agreement and (ii) to amend and restate Genesoft s Seventh Amended and Restated Certificate of Incorporation to eliminate all authorized shares of Genesoft preferred stock if, and only if, the merger is completed.**

Genesoft s Reasons for the Merger (See page 63)

In reaching its decision to approve the merger agreement and the transactions contemplated by the merger agreement, Genesoft s board of directors consulted with management of Genesoft, as well as its financial and legal advisors, and considered a number of potential benefits and factors pertaining to the merger, including the following:

- the strategic fit of Genesoft s and Genome s respective core anti-infective product portfolios and the increased number of potential products of the combined company;

- the proposed merger would substantially increase Genesoft s immediate capital resources and the combined company is expected to have greater leverage in obtaining financing for its operations;

- the difficulty in (and the related cost of) obtaining additional financing for Genesoft as a stand-alone enterprise and Genesoft s management s assessment of possible strategic alternatives; and

- the amount and nature of the merger consideration to be received by the Genesoft stockholders.

Genesoft s board of directors also identified a number of potential negative factors pertaining to the merger, including the following:

- the risk that the transaction might not be completed in a timely matter or at all and, if not completed, the difficulty as a stand-alone company in being able to raise sufficient funds to meet its obligations;

- the risk that the potential benefits of the merger may not be realized;

the risk of management and employee disruption associated with the merger, including the risk that key personnel may decide not to continue employment with Genome after the merger;

terms of the merger agreement and related agreements that limit the ability of Genesoft and its representatives to pursue alternative transactions; and

the other risks described under Risk Factors beginning on page 24.

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Opinion of Genome s Financial Advisor (See page 73)

In deciding to approve the merger, the Genome board of directors received an opinion from its financial advisor, Harris Nesbitt Corp., that, based upon and subject to the factors and assumptions set forth in the opinion, as of November 10, 2003, the aggregate stock consideration to be issued by Genome to Genesoft s security holders in the merger and the related transactions was fair, from a financial point of view, to Genome.

The full text of the Harris Nesbitt Corp. written opinion which sets forth the assumptions made, matters considered and limitations on the review undertaken is attached to this joint proxy statement/prospectus as Annex C. We encourage you to read the opinion carefully in its entirety as well as the section of this joint proxy statement/prospectus entitled The Merger and Related Transactions Opinion of Genome s Financial Advisor. The opinion of Harris Nesbitt Corp. does not constitute a recommendation as to how any holder of Genome or Genesoft common stock should vote on the merger.

Opinion of Genesoft s Financial Advisor (See page 65)

In deciding to approve the merger, the Genesoft board of directors considered the opinion of Merrill Lynch, Pierce, Fenner & Smith Incorporated, its financial advisor in connection with the merger, that, as of November 12, 2003 and subject to the factors and assumptions set forth in the opinion, the common exchange ratio was fair, from a financial point of view, to the holders of Genesoft shares, other than Genome and its affiliates. The Merrill Lynch opinion does not address any other aspect of the merger, including the merits of the underlying decision by Genesoft to engage in the merger, and does not constitute a recommendation to any stockholder as to how such stockholder should vote on the proposed merger or any matter related thereto.

The full text of the Merrill Lynch written opinion, which sets forth the assumptions made, matters considered, and qualifications and limitations on the review undertaken by Merrill Lynch, is included in this joint proxy statement/prospectus as Annex D. We encourage you to read the opinion, as well as the section of this joint proxy statement/prospectus entitled The Merger and Related Transactions Opinion of Genesoft s Financial Advisor, carefully and in its entirety.

Voting Agreements (See page 92)

The directors and executive officers of Genome, who collectively have voting control over approximately 0.4% of the outstanding shares of Genome, have entered into voting agreements with Genesoft, pursuant to which each such person has agreed to vote the shares of Genome common stock beneficially owned by such person in favor of the increase in Genome s authorized shares and the issuance of Genome common stock to the Genesoft stockholders pursuant to the merger agreement, in favor of any other matter relating to consummation of the transactions contemplated by the merger agreement and against any other merger or similar transaction involving Genome.

Certain directors, executive officers and stockholders of Genesoft, who collectively have voting control over approximately 63% of the outstanding shares of Genesoft, have entered into similar voting agreements with Genome to vote the shares of Genesoft common stock beneficially owned by such person in favor of the merger agreement, in favor of any other matter relating to consummation of the transactions contemplated by the merger agreement and against any other merger or similar transaction involving Genesoft. The percentage of shares subject to these agreements will be reduced if Genesoft s board of directors changes its recommendations in favor of the merger agreement due to a superior proposal.

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Structure and Effects of the Merger (See page 83)

In the initial merger, Guardian Acquisition, a wholly-owned subsidiary of Genome, will be merged into Genesoft. Immediately thereafter, Genesoft will be merged into a second wholly-owned subsidiary of Genome in the second-step merger. As a result of the initial merger, the separate corporate existence of Guardian Acquisition will cease, and Genesoft will continue as the surviving corporation of the initial merger and as a wholly-owned subsidiary of Genome. As a result of the second-step merger, the separate corporate existence of Genesoft will cease, and the second acquisition subsidiary, which is a Delaware limited liability company, will continue as the surviving company of the second-step merger and be wholly-owned by Genome.

At the effective time of the merger, each share of Genesoft common stock will be cancelled and terminated and will be automatically converted into the right to receive the number of shares of Genome common stock equal to the common exchange ratio as described in The Merger The Merger Agreement Conversion of Genesoft Stock.

Indemnification (See page 92)

If the merger agreement is approved and the merger occurs, all holders of Genesoft capital stock who have not perfected dissenters rights under Delaware or California law will be deemed to have agreed, subject to the limitations described below, to indemnify Genome and its affiliates, officers, directors and employees against losses due to:

- any inaccuracy or breach of any representation or warranty of Genesoft contained in the merger agreement or any certificate required to be delivered in connection with the merger agreement;
- any breach of, non-compliance with or non-fulfillment of any covenant or agreement made by Genesoft in the merger agreement or any certificate required to be delivered in connection with the merger agreement;
- any fraudulent action, and any violation of any criminal law by Genesoft; or
- any claim by a holder or former holder of Genesoft s equity interests or any other person seeking to assert, or based upon: (i) ownership or rights of ownership to any shares of capital stock of Genesoft; (ii) any rights of a stockholder of Genesoft, including any option, preemptive rights, rights to notice or to vote or any appraisal rights under the applicable provisions of the DGCL; (iii) any rights under the organizational documents of Genesoft; (iv) any claim that his, her or its equity interests were wrongfully repurchased, canceled, terminated or otherwise limited by Genesoft; or (v) any claim in connection with the issuance of any equity interests or otherwise, regardless of whether an action, suit or proceeding can or has been made against Genesoft.

Genome s right to indemnification is limited to the merger consideration placed in escrow pursuant to the escrow agreement attached to this joint proxy statement/prospectus as Annex B (and described on page 99), representing 20% of the Genome common stock that would otherwise be due to Genesoft stockholders in the merger. Genome is entitled to indemnification after all losses exceed $676,458.64 in the aggregate, and then for losses in excess of such amount. Subject to any claims made by Genome or its affiliates, officers, directors or employees and any payments related to those claims, up to half of the escrow amount will be released from escrow one year after closing of the merger and the remainder will be released 18 months after closing.

Genome has agreed to indemnify Genesoft s stockholders against losses due to:

any inaccuracy or breach of any representation or warranty of Genome contained in the merger agreement or any certificate required to be delivered in connection with the merger agreement;

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any breach of, non-compliance with or non-fulfillment of any covenant or agreement made by Genome in the merger agreement or any certificate required to be delivered in connection with the merger agreement; or

any fraudulent action and any violation of any criminal law by Genome.

The aggregate indemnification obligations of Genome will not exceed $13,529,172.87 and indemnification is available only when Genesoft losses exceed $676,458.64 in the aggregate, and then only for losses in excess of such amount.

Completion and Effectiveness of the Merger

The closing of the merger will take place as promptly as practicable following satisfaction or waiver of the closing conditions set forth in the merger agreement, including, without limitation, the condition that Genome raise a minimum of $32 million to finance the combined company (unless waived by both parties). Although Genome and Genesoft are working toward satisfying these conditions and completing the merger in the first quarter of 2004, the exact timing cannot be predicted as the merger is subject to specified conditions, some of which are beyond Genome s and Genesoft s control.

Assuming that the other conditions to completion of the merger have been satisfied or waived, the merger will become effective at the time specified in the certificates of merger filed with the Secretary of the State of Delaware with respect to the merger.

Conditions to Completion of the Merger (See page 90)

Genome s and Genesoft s obligations to complete the merger are subject, unless waived by Genome, Genesoft or both parties, as applicable, to specified conditions described under The Merger and Related Transactions The Merger Agreement Conditions to Completion of the Merger.

Management After the Merger (See page 132)

Upon consummation of the merger, the combined company will be led by a board of directors consisting of: Luke Evnin, Ph.D., Managing Director of MPM Asset Management, Robert J. Hennessey, former Chairman and CEO of Genome, Vernon R. Loucks, Jr., former Chairman and CEO of Baxter International, Steven Rauscher, President and CEO of the combined company, William S. Reardon, former partner at PricewaterhouseCoopers, Norbert G. Riedel, Ph.D., Corporate Vice President and Chief Scientific Officer at Baxter International, William Rutter, Ph.D., Professor Emeritus of Biochemistry at the University of California, San Francisco and Founder of Chiron, David B. Singer, Chairman of the Board of the combined company, and David K. Stone, Managing Director of Flagship Ventures.

The executive officers of the combined company will consist of the following: Steven Rauscher as Chief Executive Officer and President, Stephen Cohen as Senior Vice President and Chief Financial Officer and Martin Williams as Senior Vice President of Corporate Development and Marketing.

Genesoft and Genome are Prohibited from Soliciting Other Offers (See page 89)

Each of Genesoft and Genome has agreed that, while the merger is pending, it will not solicit, initiate or encourage, or, except with respect to an unsolicited superior offer as described in The Merger The Merger Agreement, engage in discussions with any third parties regarding certain types of extraordinary transactions, such as a merger, consolidation or other similar transaction involving it.

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Termination of the Merger Agreement and Payment of Termination Fee (See pages 94 and 95)

Genome and Genesoft may terminate the merger agreement by mutual agreement and under other circumstances specified in the merger agreement. Genome and Genesoft have agreed that if the merger agreement is terminated under certain circumstances described under The Merger and Related Transactions The Merger Agreement Termination Fees, Genome or Genesoft will pay the other party s transaction expenses of up to $1,000,000 and an additional $3,044,063.90 if Genome or Genesoft, as the case may be, enters into (or announces its intention to enter into) an agreement to consummate a competing merger or acquisition transaction within 12 months of terminating the merger agreement.

Material United States Federal Income Tax Consequences of the Merger (See page 96)

Genome and Genesoft have structured the merger to qualify as a reorganization under the Internal Revenue Code. It is the intention of Genome and Genesoft that no gain or loss will generally be recognized by Genesoft stockholders for federal income tax purposes on the exchange of shares of Genesoft common stock solely for shares of Genome common stock.

Tax matters are very complicated, and the tax consequences of the merger to the Genesoft stockholders will depend on the facts of each Genesoft stockholder s own situation. Each Genesoft stockholder should consult his, her or its tax advisor for a full understanding of the tax consequences of the merger.

Accounting Treatment of the Merger (See page 98)

The merger will be accounted for as a purchase by Genome under accounting principles generally accepted in the United States.

Regulatory Approvals Required to Complete the Merger (See page 98)

Neither Genome nor Genesoft is aware of any material governmental or regulatory approval required for completion of the merger, other than compliance with applicable corporate laws of The Commonwealth of Massachusetts and the State of Delaware and federal and state securities laws.

Appraisal Rights (See pages 47, 54 and 56)

Appraisal rights are available to Genesoft stockholders under the respective laws of Delaware and California in connection with the merger. Appraisal rights are not available to Genome stockholders.

Restrictions on the Ability to Sell Genome Common Stock Received in the Merger (See page 98)

All shares of Genome common stock that Genesoft stockholders receive in the merger will be freely transferable unless a Genesoft stockholder is deemed to be an affiliate of Genesoft at the time of the special meetings or such shares are subject to contractual restrictions. Shares of Genome common stock received by persons deemed to be affiliates of Genesoft may only be sold in compliance with Rule 145 under the Securities Act or as otherwise permitted under the Securities Act.

Listing of Genome Common Stock (See page 145)

The shares of Genome common stock are listed on the Nasdaq National Market under the symbol GENE.

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GENOME SUMMARY SELECTED CONSOLIDATED FINANCIAL DATA

The following summary selected consolidated statement of operations data for each of the three fiscal years ended December 31, 2000, 2001 and 2002 and the summary selected consolidated balance sheet data as of December 31, 2001 and 2002 set forth below, are derived from the historical audited consolidated financial statements included in Genome s Annual Report on Form 10-K for the year ended December 31, 2002. The financial statements for the year ended December 31, 2002 have been audited by Ernst & Young LLP, independent auditors. The financial statements for the two years ended December 31, 2001 have been audited by other independent auditors. The data should be read in conjunction with the consolidated financial statements, related notes, and other financial information incorporated by reference herein. The summary selected consolidated statement of operations data for the fiscal years ended December 31, 1998 and 1999, and the summary selected consolidated balance sheet data as of December 31, 1998, 1999 and 2000 are derived from Genome s historical audited consolidated financial statements.

Genome derived the summary selected consolidated balance sheet and statement of operations data as of and for the nine months ended September 28, 2002 and September 27, 2003, respectively, from its unaudited condensed consolidated financial statements. These statements include, in the opinion of management, all normal and recurring adjustments that are necessary for a fair statement of results in accordance with generally accepted accounting principles. The operating results for the nine months ended September 27, 2003 are not necessarily indicative of the results that may be expected for the year ending December 31, 2003. It is important that you read the following summary historical data along with the historical consolidated financial statements and related notes in Genome s Annual Report on Form 10-K for the year ended December 31, 2002 and Genome s quarterly reports on Form 10-Q filed with the Securities and Exchange Commission, which are incorporated by reference into this joint proxy statement/prospectus, and other Genome documents to which we refer. See Where You Can Find Additional Information on page 147.

	Year Ended December 31,					Nine Months Ended	
	1998	1999	2000	2001	2002	Sept. 28, 2002	Sept. 27, 2003
	(in thousands, except per share amounts)					(Unaudited)	
Statement of Operations Data:							
Revenues:							
Biopharmaceutical	$ 18,135	$ 18,162	$ 11,851	$ 18,438	$ 7,716	$ 6,206	$ 5,519
Genomics services	3,913	6,666	13,594	17,302	15,271	10,943	1,799
Total revenues	22,048	24,828	25,445	35,740	22,987	17,149	7,318
Net loss	$ (12,968)	$ (3,940)	$ (5,847)	$ (10,090)	$ (34,017)	$ (25,175)	$ (28,455)
Net loss per common share, basic and diluted	$ (0.71)	$ (0.21)	$ (0.27)	$ (0.45)	$ (1.48)	$ (1.10)	$ (1.16)
Weighted average common shares outstanding, basic and diluted	18,290	18,627	21,377	22,572	22,921	22,881	24,581

	December 31,					Sept. 28,	Sept. 27,
	1998	1999	2000	2001	2002	2002	2003
	(in thousands)					(Unaudited)	
Balance Sheet Data:							
Cash and cash equivalents, restricted cash, warrant and long and short-term marketable securities	$ 30,819	$ 26,778	$ 73,010	$ 67,341	$ 50,866	$ 58,381	$ 25,786
Working capital	19,750	19,447	51,601	44,156	36,511	43,607	15,174
Total assets	48,921	45,443	90,251	82,740	65,845	72,936	30,739
Total liabilities	21,364	16,596	17,564	16,008	30,428	28,863	11,393

Stockholders equity	27,557	28,847	72,687	66,732	35,417	44,073	19,346

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GENESOFT SUMMARY SELECTED FINANCIAL DATA

The following summary financial data should be read in conjunction with the Genesoft Management s Discussion and Analysis of Financial Condition and Results of Operations section included later in this joint proxy statement/prospectus, and Genesoft s financial statements and related notes included in the back of this joint proxy statement/prospectus. Genesoft has derived the statements of operations data for the years ended December 31, 2000, 2001 and 2002 from its audited financial statements which are included in this joint proxy statement/prospectus. Genesoft has derived the statements of operations and balance sheet data as of and for the nine months ended September 30, 2002 and 2003 from its unaudited financial statements which are also included in this joint proxy statement/prospectus. These unaudited statements include, in the opinion of management, all normal and recurring adjustments that are necessary for a fair statement of results in accordance with generally accepted accounting principles.

	Year Ended December 31,					Nine Months Ended	
	1998	1999	2000	2001	2002	Sept. 30, 2002	Sept. 30 2003
	(in thousands, except per share amounts)					(Unaudited)	
Statement of Operations Data:							
Total revenues	$	$ 2,520	$ 4,187	$ 2,059	$ 5,402	$	$ 3,072
Net loss	(770)	(2,987)	(7,921)	(18,321)	(25,569)	(18,368)	(19,796)
Basic and diluted net loss per common share	$ (1.03)	$ (2.92)	$ (8.27)	$ (15.69)	$ (12.81)	$ (14.04)	$ (1.69)
Weighted average shares used in computing basic and diluted net loss per common share	745	1,024	957	1,168	1,996	1,308	11,729

	December 31,					Sept. 30,	Sept. 30
	1998	1999	2000	2001	2002	2002	2003
	(in thousands)					(Unaudited)	
Balance Sheet Data:							
Cash and cash equivalents, short-term investments and restricted cash	$ 3,195	$ 12,405	$ 29,379	$ 24,714	$ 5,951	$ 7,225	$ 7,826
Working capital (net capital deficiency)	2,703	12,056	22,644	18,208	(3,076)	715	(20,993)
Total assets	3,406	14,037	35,918	40,162	19,432	20,539	25,799
Total liabilities	548	1,200	6,202	7,498	11,983	6,270	32,924
Stockholders equity (net capital deficiency)	2,858	12,837	29,716	32,664	7,448	14,269	(7,125)

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SELECTED COMBINED COMPANY

UNAUDITED PRO FORMA FINANCIAL INFORMATION

The following selected unaudited pro forma condensed combined financial information has been derived from and should be read in conjunction with the Unaudited Pro Forma Condensed Combined Financial Information and related notes included in this joint proxy statement/prospectus on page 102. This information is based on the historical balance sheets and related historical statements of operations of Genome and the historical balance sheets and related historical statements of operations of Genesoft, using the purchase method of accounting for business combinations under accounting principles generally accepted in the United States. This information is for illustrative purposes only. The companies may have performed differently had they always been combined. You should not rely on the selected unaudited pro forma condensed combined financial information as being indicative of the historical results that would have been achieved had the companies always been combined or the future results that the combined company will experience after the merger. For the interim period, Genome s nine months ended September 27, 2003 was combined with Genesoft s nine months ended September 30, 2003.

	Pro Forma Year Ended December 31, 2002	Pro Forma Nine Months Ended September 27, 2003
Statement of Operations Data:		
Total revenues	$ 28,389	$ 10,390
Net loss	(67,265)	(54,011)
Net loss per share, basic and diluted	(1.39)	(1.08)
Shares used in computing net loss per share, basic and diluted	48,397	50,057
Balance Sheet Data:		
Cash and cash equivalents, restricted cash and long and short-term marketable securities		$ 23,915
Working capital (net capital deficiency)		(17,820)
Total assets		139,916
Total liabilities		46,620
Stockholders equity		93,296

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COMPARATIVE HISTORICAL AND PRO FORMA PER SHARE DATA

The following table sets forth certain historical per share data of Genome and Genesoft and combined per share data on an unaudited pro forma basis after giving effect to the merger using the purchase method of accounting. For purposes of the table below, Genome has estimated that 25,476,176 shares of Genome common stock will be issued to existing Genesoft common stockholders and promissory note holders at the closing of the merger and the remainder of the 28,571,405 shares of Genome common stock to be issued in the merger will be reserved for issuance upon the exercise of Genesoft options and warrants assumed in the merger.

The following data should be read in connection with the separate historical financial statements of Genesoft included in this joint proxy statement/prospectus and the separate historical financial statements of Genome incorporated by reference in this joint proxy statement/prospectus, as well as the unaudited pro forma condensed combined financial information included in this joint proxy statement/prospectus. The unaudited pro forma combined per share data do not necessarily indicate the operating results that would have been achieved had the merger been completed as of the beginning of the earliest period presented and should not be taken as representative of future operations. The results may have been different if the companies had always been consolidated.

	Year Ended December 31, 2002	Nine Months Ended September 2003[2]
Genome Historical:		
Basic and diluted net loss per share	$ (1.48)	$ (1.16)
Book value per common share	1.54	.74
Genesoft Historical:		
Basic and diluted net loss per share	(12.81)	(1.69)
Book value per common share	0.69	(0.58)
Pro Forma Combined:		
Basic and diluted net loss per share	(1.39)	(1.08)
Book value per common share		1.81
Equivalent Pro Forma Combined[1]:		
Basic and diluted net loss per share	(1.65)	(1.28)
Book value per common share		2.15

[1] The equivalent pro forma combined represents the pro forma combined amount multiplied by the estimated exchange ratio of 1.189. See Unaudited Pro Forma Combined Financial Statements of Genome and Genesoft.

[2] Information as of September 27, 2003 in the case of Genome and September 30, 2003 in the case of Genesoft. For the pro forma calculations, Genome s nine months ended September 27, 2003 were combined with Genesoft s nine months ended September 30, 2003.

No options or warrants outstanding are included in the calculation of diluted loss per share because their impact would have been anti-dilutive to loss per share for each period presented. Neither Genome nor Genesoft has paid a cash dividend to its stockholders.

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COMPARATIVE PER SHARE

MARKET PRICE DATA AND DIVIDEND INFORMATION

	GENE*	
Calendar Quarters	**High**	**Low**
2001:		
First Quarter	11.120	5.500
Second Quarter	16.850	4.940
Third Quarter	13.850	4.690
Fourth Quarter	8.270	5.520
2002:		
First Quarter	7.050	5.000
Second Quarter	5.640	2.200
Third Quarter	2.100	1.340
Fourth Quarter	2.330	1.030
2003:		
First Quarter	2.070	1.280
Second Quarter	3.750	1.450
Third Quarter	3.430	2.410
Fourth Quarter (through December 29, 2003)	3.320	2.630

* Based on closing price.

Recent Closing Prices

The following table shows the closing prices per share of Genome common stock as reported on the Nasdaq National Market on (1) November 17, 2003, the business day preceding the public announcement that Genome and Genesoft had entered into the merger agreement, and (2) December 29, 2003, the last full trading day for which closing prices were available at the time of the printing of this joint proxy statement/prospectus.

The following table also includes the equivalent price per share of Genesoft common stock on those dates. This equivalent per share price reflects the value of the Genome common stock Genesoft stockholders would receive for each share of Genesoft common stock if the merger was completed on either of these dates. These amounts are estimates based on the number of outstanding shares of Genesoft common stock on the date of this joint proxy statement/prospectus, and may change at the completion of the merger as a result of those factors described in the section of this joint proxy statement/ prospectus entitled The Merger and Related Transactions The Merger Agreement Conversion of Genesoft Stock.

	Genome Common Stock	Genesoft Equivalent Price Per Share
November 17, 2003	$ 2.85	$ 3.39[(1)]

December 29, 2003	$ 2.97	$ 3.53[1]

[1] Assumes that the merger closes on February 2, 2004 and the price at which shares are sold in the transaction to fund the combined company is at least $2.84 per share. The actual number of shares of Genome common stock issued to the holders of Genesoft s promissory notes will vary based on a variety of factors described in The Merger and Related Transactions The Merger Agreement Conversion of Genesoft Stock.

Because the market price of Genome common stock may increase or decrease before the completion of the merger, you are urged to obtain current market quotations.

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As of the date of this joint proxy statement/prospectus, there were approximately 1053 stockholders of record of Genome who held an aggregate of 31,477,889 shares of Genome common stock.

As of the date of this joint proxy statement/prospectus, there were approximately 160 stockholders of record of Genesoft who held an aggregate of 12,378,931 shares of Genesoft common stock.

Dividend Policy

Except as set forth below, neither Genome nor Genesoft has ever declared or paid dividends on its common stock in the past, and neither company intends to pay such dividends in the foreseeable future. Any determination to pay dividends after consummation of the merger will be at the discretion of the combined company s board of directors and will depend on the combined company s financial condition, results of operations, capital requirements and other factors the combined company s board of directors deems relevant.

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CAUTIONARY STATEMENTS

REGARDING FORWARD-LOOKING STATEMENTS IN THIS

JOINT PROXY STATEMENT/PROSPECTUS

This joint proxy statement/prospectus and the documents incorporated by reference into this joint proxy statement/prospectus contain forward-looking statements about the merger, Genome and Genesoft within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements represent the judgment of the managements of Genome and Genesoft, as the case may be, regarding future events. Forward-looking statements typically are identified by use of terms such as may, will, should, plan, expect, intend, anticipate, estimate, and similar words, although some forward-looking stat expressed differently. Genome, Genesoft or the combined company do not plan to update these forward-looking statements. You should be aware that actual results could differ materially from those contained in the forward-looking statements due to a number of risks affecting the business of Genome, Genesoft or the combined company.

Although each company believes that its plans, intentions and expectations as reflected in or suggested by these forward-looking statements are reasonable, it can give no assurance that these plans, intentions or expectations will be achieved. Genome stockholders and Genesoft stockholders are cautioned that all forward-looking statements involve risks and uncertainties and actual results may differ materially from those discussed as a result of various risk factors described in the section entitled Risk Factors . Listed below and discussed elsewhere in this joint proxy statement/prospectus are some important risks, uncertainties and contingencies which could cause each company s actual results, performances or achievements to be materially different from the forward-looking statements made in this joint proxy statement/prospectus, particularly if the merger is not completed. These risks, uncertainties and contingencies include, but are not limited to, the following:

- the ability of the combined company to launch and successfully commercialize FACTIVE in the U.S.;
- the ability of the combined company to obtain regulatory approval to commercialize FACTIVE in Europe and other foreign markets;
- the ability of the combined company to successfully complete required clinical trials of Ramoplanin, to obtain regulatory approval to commercialize Ramoplanin and to commercialize Ramoplanin;
- the satisfaction or waiver of the conditions to closing of the merger, including receipt of stockholder approvals;
- the ability of the combined company to raise sufficient capital to fund its programs following the merger;
- the expected closing date of the merger;
- the risk that the merger will not close;
- the risk that the merger will not qualify as a reorganization under the provisions of Section 368(a) of the Internal Revenue Code for United States federal income tax purposes;
- the risk that Genome will not integrate the acquired business successfully;

the risk that Genome will incur unanticipated costs to integrate and restructure the acquired business;

fluctuations in the trading price and volume of Genome common stock;

competitive factors, such as price competition from other products and competition from other comparable companies; and

the cost of complying with current and future governmental regulations.

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In addition, events may occur in the future that Genome or Genesoft are not able to accurately predict or control and that may cause actual results to differ materially from the expectations described in these forward-looking statements.

In evaluating the merger and the related transactions, you should carefully consider the discussion of risks and uncertainties discussed in the section entitled Risk Factors and the risk factors set forth in Exhibit 99.1 to Genome s Quarterly Report on Form 10-Q for the quarter ended September 27, 2003 and those set forth in other filings that the company may make with the Securities and Exchange Commission from time to time.

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RISK FACTORS

In addition to the other information contained or incorporated by reference in this joint proxy statement/prospectus, (i) Genesoft stockholders should carefully consider the following factors in voting on whether to approve the merger and the related transactions and the resulting investment in Genome common stock and (ii) Genome stockholders should carefully consider the following factors in voting on whether to approve the issuance of shares of Genome common stock to Genesoft security holders, including issuances to the Genesoft note holders upon potential conversion of the Genome convertible notes that they will obtain in the merger, the amendment to Genome s articles of organization increasing Genome s authorized common stock, and the issuance of up to 20,000,000 shares of Genome common stock in order to raise capital to finance the combined company. In addition, you should keep the following risk factors in mind when you read forward-looking statements in this joint proxy statement/prospectus. Please refer to the section entitled Cautionary Statements Regarding Forward-Looking Statements in this Joint Proxy Statement/Prospectus beginning on page 22 of this joint proxy statement/prospectus.

Risks Related to the Merger Transaction

The issuance of 28,571,405 shares of Genome common stock to Genesoft security holders in the merger will substantially reduce the percentage interests of Genome security holders.

If the merger is completed, 28,571,405 shares of Genome common stock will be issued to current Genesoft security holders, including shares of Genome common stock to be issued upon the exercise of Genesoft options and warrants that Genome will assume. As of November 30, 2003, Genome had 31,451,099 shares of its common stock outstanding, outstanding options exercisable into 4,086,634 shares of its common stock, outstanding warrants exercisable into 3,221,250 shares of common stock or a total of 38,758,983 shares of common stock on a fully diluted basis. The issuance of the 28,571,405 shares of Genome common stock to current Genesoft stockholders will cause a significant reduction in the relative percentage interests of current Genome stockholders in earnings, voting, liquidation value and book and market value.

The issuance of at least $32 million and up to $50 million of securities of Genome to finance the combined company will substantially reduce the percentage interests of both Genome and Genesoft stockholders in the combined company.

As a condition to the closing of the merger, Genome must raise a minimum of $32 million of capital to finance the combined company, unless both parties agree to waive this condition. Genome intends to sell its securities in order to raise the capital. If Genome s board of directors determines that market conditions appear favorable for the issuance of additional securities by Genome and that such issuance is in the best interests of the company, Genome could sell up to a total of $50 million of its securities. The type of security to be sold and price at which it will be sold are subject to market conditions and negotiations with investors. The securities may be sold at a discount to the market price at the time of sale. The issuance of the securities to finance the combined company will cause a significant reduction in the relative percentage interests of Genome stockholders and Genesoft stockholders in the earnings, voting power, liquidation value and book and market value of the combined company.

Because the number of shares of Genome common stock to be issued in the merger is fixed, Genome stockholders are exposed to the risk that the market price of Genome common stock could increase and Genesoft stockholders are exposed to the risk that the market price of Genome common stock could decrease.

Under the merger agreement, 28,571,405 shares of Genome common stock will be issued to current Genesoft security holders, including shares of Genome common stock to be issued upon the exercise of Genesoft options and warrants that Genome will assume and shares to be issued to the holders of Genesoft s promissory notes as payment of accrued interest and related amounts. The number of shares to be issued is fixed and will not be adjusted if the price of Genome common stock increases or decreases prior to the completion of the merger. The price of Genome common stock at the closing of the merger might vary from its price on the date of this joint proxy statement/prospectus and on the dates of the Genome and Genesoft stockholders special meetings.

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These prices might vary because of changes in the business, operations or prospects of Genome or Genesoft, market assessments of the likelihood that the merger will be completed, the timing of the completion of the merger, the prospects of post-merger operations, regulatory considerations, general market and economic conditions and other factors. Because the date that the merger is completed may be later than the dates of the Genome and Genesoft stockholders respective special meetings, the price of Genome common stock on such dates might not be indicative of its price on the date the merger is completed. As a result, the market value of the shares of Genome common stock that Genome will be required to issue to former Genesoft security holders upon completion of the merger might be greater or lesser than the value attributed to Genesoft s business and assets at the time the merger agreement was entered into and/or the date it is approved by Genome or Genesoft stockholders. We urge you to obtain current market quotations for Genome common stock, and to be aware that the price of Genome common stock might change dramatically after the Genome and Genesoft stockholders special meetings.

The assumption by Genome of approximately $24 million of debt of Genesoft at the closing will substantially increase its leverage and, to the extent that a portion of this debt is subsequently converted into Genome common stock, will substantially reduce the percentage interests of both Genome and Genesoft stockholders in the combined company.

Upon the closing of the merger, Genome will assume approximately $24 million of debt of Genesoft. Genome will pay approximately $1.7 million of this debt at closing. The remainder of the debt consists of promissory notes of Genesoft that Genome will exchange with holders of such notes for convertible promissory notes of Genome, 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 Genome common stock during the five-year period, the subsequent payment of these notes at maturity may require Genome to expend a significant portion of its 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 convertible notes of Genome to be issued at the closing of the merger will be convertible into shares of Genome common stock at the holder s election at any time after the closing of the merger at a price per share equal to one hundred and ten percent of the average closing price of Genome common stock for the five trading days preceding the closing date of the merger, subject to subsequent adjustment. In addition, following the one year anniversary of the closing of the merger, the combined company will have the right to force conversion if the price of Genome 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 Genome stockholders and Genesoft stockholders in the earnings, voting power, liquidation value and book and market value of the combined company.

Upon the consummation of the merger, Genome will be required to pay $8 million to LG Life Sciences, Ltd. under Genesoft s License and Option Agreement with LG Life Sciences for FACTIVE, which will diminish the combined company s financial resources.

Upon the closing of the merger, Genome will be required to pay $8 million to LG Life Sciences as a milestone payment under Genesoft s License and Option Agreement with LG for FACTIVE. This payment will consume a substantial portion of the combined company s available cash at closing and, depending upon how much capital has been raised at that point, may limit the combined company s ability to pursue additional development or commercialization programs.

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The combined company may not realize all of the anticipated benefits of the merger.

The success of the merger will depend, in part, on the ability of the combined company to realize the anticipated synergies, cost savings and growth opportunities from integrating the business of Genome with the business of Genesoft. The combined company s success in realizing these benefits and the timing of this realization depends upon the successful integration of the operations of Genesoft. The 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;
- 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.

Genome and Genesoft cannot assure you that the integration of Genesoft with Genome will result in the realization of the full benefits anticipated by them to result from the merger. In addition, if Genome fails to raise the full $32 million that it is required to raise as a condition to the closing of the merger and the parties, in any event, choose to close the merger, the combined company may not have sufficient capital to fully implement its strategies which may cause a delay in the launch of FACTIVE and could prevent the company from realizing the anticipated benefits of the merger.

Genome and Genesoft may suffer negative consequences if the merger is not completed.

If the merger is not completed for any reason, Genome and/or Genesoft will be subject to a number of material risks, including:

- the provision in the merger agreement which provides that under specified circumstances either Genome or Genesoft could be required to pay the other a termination fee of approximately $3 million, plus up to $1 million of expenses incurred in connection with the merger;

the market price of Genome common stock may decline to the extent that the current market price of such shares reflects a market assumption that the merger will be completed, or for other reasons;

costs related to the merger, such as legal and accounting fees, must be paid even if the merger is not completed;

benefits that Genome and Genesoft expect to realize from the merger would not be realized;

the diversion of management attention from the day-to-day business of the companies and the unavoidable disruption to their employees during the period before completion of the merger may make it difficult for Genome and Genesoft to regain their financial position and strategic focus if the merger does not occur;

if the merger is terminated, Genesoft s stockholders cannot be certain that Genesoft will be able (i), if Genesoft s board of directors seeks another merger or business combination, to find a partner willing to pay an equivalent or more attractive price than the price to be paid by Genome in the merger or (ii) to raise sufficient financing to pay its obligations and continue the operation of its business;

employees important to the success of either company as a stand-alone company may have left in anticipation of the merger; and

business opportunities important to either company as a stand-alone company may have been terminated or not pursued by either that company or third parties in anticipation of the merger.

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If the merger does not close, Genome may not be able to obtain repayment of the $6.2 million bridge loan made to Genesoft.

At the time of the signing of the merger agreement, Genome made a bridge loan of $6.2 million to Genesoft pursuant to a promissory note issued by Genesoft, which is repayable within 60 days of an event of default (as defined in the note) or termination of the merger agreement, unless the merger agreement is terminated by Genesoft due to a failure of Genome to obtain the stockholder vote necessary to approve the merger, in which case it is repayable within 180 days of termination. However, if the note becomes repayable, it is uncertain whether Genome will be able to obtain repayment due to Genesoft s lack of liquid assets, and even if Genome is able to obtain repayment, Genome may be required to expend additional resources and time to foreclose on assets of Genesoft.

The cash resources of the combined company could be materially depleted if a substantial number of Genesoft stockholders exercise their dissenters rights under California law or appraisal rights under Delaware law.

Holders of Genesoft capital stock who dissent and do not consent to the approval and adoption of the merger agreement may be entitled to certain dissenters rights under the California Corporations Code and to appraisal rights under Delaware General Corporation Law, or DGCL, in connection with the merger. If the merger is consummated, a holder of record of Genesoft stock who complies with the statutory procedures will be entitled to have those shares appraised by the Delaware Court of Chancery under Section 262 of the DGCL and to receive payment for the fair value of those shares instead of the consideration provided for in the merger agreement. Similarly, under Chapter 13 of the California Corporations Code, a holder of Genesoft common stock who complies with the statutory procedures will be entitled to have its shares converted into the right to receive from Genesoft such consideration as may be determined to be due under the statute. These rights are described under The Special Meeting of Genesoft Stockholders Appraisal Rights Under Delaware General Corporation Law and The Special Meeting of Genesoft Stockholders Dissenters Rights Under California Corporations Code of this joint proxy statement/prospectus. If a substantial number of Genesoft stockholders exercise their dissenters rights under California law or appraisal rights under Delaware law, as the case may be, the combined company may be required to make substantial payments in cash to these stockholders, thereby materially depleting the cash resources of the combined company.

Directors and officers of Genome and Genesoft have potential conflicts of interest that may have influenced them to recommend the merger.

Some of the directors of Genome and Genesoft who recommend that you vote in favor of the merger and the officers of Genome and Genesoft who provided information to their board of directors relating to the merger have employment, indemnification and severance benefit arrangements and rights to acceleration of stock options that provide them with interests in the merger that may differ from yours. The receipt of compensation or other benefits in the merger may have influenced these directors in making their recommendation that you vote in favor of the transactions called for by the merger agreement and these officers in making recommendations to their board of directors relating to the merger. See The Merger Interests of Directors and Executive Officers of Genome in the Merger and Interests of Directors and Executive Officers of Genesoft in the Merger.

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Risks Related to the Business of our Combined Company

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

Genome had a net loss of approximately $28,455,000 for the nine months ended September 27, 2003 and as of September 27, 2003, Genome had an accumulated deficit of approximately $154,231,000. Genome had a net loss of approximately $34,017,000 for the fiscal year ended December 31, 2002, and, as of December 31, 2002, Genome had an accumulated deficit of approximately $125,775,000. For the fiscal year ended December 31, 2001, Genome had a net loss of approximately $10,090,000, and for the fiscal year ended December 31, 2000, Genome had a net loss of approximately $5,847,000. The losses have resulted primarily from costs incurred in research and development, including Genome s clinical trials, and from general and administrative costs associated with Genome s operations. These costs have exceeded Genome s revenues which to date have been generated principally from collaborations, government grants and sequencing services.

Genesoft had a net loss of approximately $19,796,000 for the nine months ended September 30, 2003 and as of September 30, 2003, Genesoft had an accumulated deficit of approximately $75,364,000. 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 our combined company will incur additional losses in the year following the merger and in future years and cannot predict when, if ever, our combined company will achieve profitability. These losses are expected to increase following the consummation of the merger as our combined company significantly increases its expenditures in the sales and marketing area to prepare for the commercial launch of FACTIVE. Our combined company also plans to continue to expand its research and development and clinical trial activities. In addition, our partners product development efforts which utilize our genomic discoveries are at an early stage and, accordingly, we do not expect our losses to be substantially mitigated by revenues from milestone payments or royalties under those agreements for a number of years, if ever.

We will need to raise additional funds in the future.

As described above, we need to raise a minimum of $32 million as a condition to the closing of the merger, unless this condition is waived by both parties. If we raise that money, we believe that those new funds along with our existing cash and marketable securities together with borrowings under equipment financing arrangements and anticipated cash flow from operations would be sufficient to support our current plans for the combined company for approximately 12 months following the closing of the merger. We expect to need to raise additional capital over the course of the twelve months following the closing of the merger for our combined company. In particular, we will need additional funds to support our sales and marketing activities, and fund clinical trials and other research and development activities of our combined company. We may seek funding through additional public or private equity offerings, debt financings or agreements with customers. Our ability to raise additional capital, however, will be heavily influenced by the investment market for biotechnology companies and the progress of the FACTIVE and Ramoplanin commercial and clinical development programs over that period. Additional financing may not be available when needed, or, if available, may not be available on favorable terms. If our combined company cannot obtain adequate financing on acceptable terms when such financing is required, its business will be adversely affected.

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

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

The business of our combined company will be very dependent on the commercial success of FACTIVE.

FACTIVE will be the only commercial product of our combined company upon the closing of the merger and we expect it will account for substantially all of the revenues of our combined company for at least the next several years. FACTIVE has 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 will depend upon its 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 is not commercially successful, our combined company 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 for marketing in April 2003, it required, as a post-marketing study commitment, that Genesoft conduct a prospective, randomized study comparing FACTIVE (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. The results of this trial, as well as other safety information arising out of the marketing of the product, could restrict our ability to commercialize FACTIVE.

Our combined company will need to develop marketing and sales capabilities to successfully commercialize FACTIVE and our other product candidates.

FACTIVE will be the first FDA approved product of our combined company. Accordingly, following the closing of the merger, our combined company will have very limited marketing and sales experience. Our combined company will need to develop a marketing and sales staff to successfully commercialize FACTIVE and our other product candidates, including Ramoplanin. In order to launch FACTIVE in the second half of 2004, our combined company 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. Our combined company may be unable to build such a sales force, the cost of establishing such a sales force may exceed any product revenues, or the marketing and sales efforts of our combined company 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 our combined company from successfully launching FACTIVE in 2004, which would materially adversely affect the business and results of operations of our combined company.

Our combined company will depend on third parties to manufacture our product candidates, including FACTIVE and Ramoplanin.

Our combined company will not have the internal capability to manufacture commercial quantities of pharmaceutical products under the FDA s current Good Manufacturing Practices. Genesoft has entered into an agreement with LG Life Sciences to manufacture bulk quantities of FACTIVE. Genome has entered into an

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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 our combined company expects 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.

Genesoft expects to purchase its requirements for the final drug product from LG Life Sciences for 2004, which final drug product will be tableted and packaged for LG Life Sciences by SB Pharmco at its manufacturing facility in Puerto Rico. This arrangement with SB Pharmco is expected to conclude by the end of 2004. Genesoft is in discussions with a new secondary manufacturer to assume these responsibilities for subsequent periods. Genesoft may be unable, however, to successfully complete these arrangements. If our combined company is unable to obtain an agreement with a qualified finish and fill contractor to provide services by the end of 2004, the commercialization of FACTIVE could be delayed and our business may be 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.

We cannot be certain that LG Life Sciences, Vicuron or future manufacturers will be able to deliver commercial quantities of product candidates to our combined company 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, our combined company would incur substantial costs and delay in the commercialization of FACTIVE. If our combined company is 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. Our combined company may not be able to enter into alternative supply arrangements at commercially acceptable rates, if at all. Also, if our combined company changes the source or location of supply or modifies 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 our combined company 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 our combined company decides to manufacture products, it would be subject to the regulatory requirements described above. In addition, our combined company would require substantial additional capital and would be subject to delays or difficulties encountered in manufacturing pharmaceutical products. No matter who manufactures the products, our combined company will be subject to continuing obligations regarding the submission of safety reports and other post-market information.

Our combined company cannot expand the indications for which it will market FACTIVE unless it receives FDA approval for each ad