

HYSEQ INC
Form S-4/A
December 13, 2002

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As filed with the Securities and Exchange Commission on December 13, 2002

Registration No. 333-101503

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 1
TO
Form S-4
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Hyseq, Inc.

(Exact name of registrant as specified in its charter)

Nevada
*(State or other jurisdiction of
incorporation or organization)*

2835
*(Primary Standard Industrial
Classification Code Number)*

363855489
*(I.R.S. Employer
Identification No.)*

670 Almanor Avenue
Sunnyvale, California 94085
(408) 524-8100
*(Address, including zip code, and telephone number,
including area code, of registrant's principal executive offices)*

Ted W. Love
President and Chief Executive Officer
Hyseq, Inc.
670 Almanor Avenue
Sunnyvale, California 94085
(408) 524-8100
*(Name, address, including zip code, and telephone number,
including area code, of agent for service)*

Copies to:

Alan C. Mendelson, Esq.
Latham & Watkins
135 Commonwealth Drive
Menlo Park, California 94025
(650) 328-4600

Joseph S. Mohr
President and Chief Business Officer
Variagenics, Inc.
60 Hampshire Street
Cambridge, Massachusetts 02139
(617) 588-5300

Lewis J. Geffen, Esq.
Andrew J. Merken, Esq.
Mintz, Levin, Cohn, Ferris, Glovsky and
Popeo, P.C.
One Financial Center
Boston, Massachusetts 02111
(617) 542-6000

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effectiveness of this registration statement and the satisfaction or waiver of all other conditions under the merger agreement described herein.

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

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

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

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 that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

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

Subject to completion, dated December 13, 2002

MERGER PROPOSED YOUR VOTE IS VERY IMPORTANT

Hyseq, Inc. and Variagenics, Inc. have agreed to a combination of the two companies under the terms of a merger agreement. Hyseq and Variagenics are proposing the merger because they believe the merger will benefit the stockholders of both companies by leveraging the companies' assets and management to develop biotherapeutic, pharmacogenomic and molecular diagnostic products and accelerate revenue generation.

When the merger is completed, Variagenics stockholders will be entitled to receive 1.6451 shares of Hyseq common stock for each share of Variagenics common stock that they own. Hyseq and Variagenics estimate that Hyseq will issue approximately 39.7 million shares of Hyseq common stock in the merger and that immediately after the merger Variagenics stockholders will hold approximately 63% of the then-outstanding shares of Hyseq common stock, based on the number of shares of Hyseq and Variagenics common stock outstanding on December 6, 2002. Hyseq common stock is traded on the Nasdaq National Market under the trading symbol HYSQ. On December 12, 2002, Hyseq common stock closed at \$1.02 per share as reported on the Nasdaq National Market. Hyseq stockholders will continue to own their existing shares which will not be affected by the merger.

The merger cannot be completed unless the Variagenics stockholders approve the merger agreement and the Hyseq stockholders approve the issuance of shares of Hyseq common stock in connection with the merger. The obligations of Hyseq and Variagenics to complete the merger are also subject to the satisfaction or waiver of several conditions. More information about Hyseq, Variagenics and the merger is contained in this joint proxy statement/prospectus. **Hyseq and Variagenics encourage you to read this joint proxy statement/prospectus, including the section entitled Risk Factors beginning on page 12 before voting.**

The board of directors of Hyseq has approved the merger agreement and the issuance of shares of Hyseq common stock in connection with the merger. The board of directors of Variagenics has approved the merger agreement. The Hyseq board of directors unanimously recommends that Hyseq stockholders vote **FOR** the proposal to approve the issuance of shares of Hyseq common stock in connection with the merger. The Variagenics board of directors recommends that Variagenics stockholders vote **FOR** the proposal to approve the merger agreement.

Hyseq and Variagenics have each scheduled special meetings in connection with the respective votes required. The dates, times and places of the meetings are as follows:

For Hyseq stockholders:

Date: January 28, 2003
Time: 9:00 a.m. (Pacific Standard Time)
Place: 675 Almanor Avenue,
Sunnyvale, California

For Variagenics stockholders:

Date: January 28, 2003
Time: 9:00 a.m. (Eastern Standard Time)
Place: Mintz, Levin, Cohn, Ferris, Glovsky and
Popeo, P.C.
One Financial Center
Boston, Massachusetts

Your vote is very important. Whether or not you plan to attend your respective company's special meeting, please take the time to vote by marking your votes on the enclosed proxy card, signing and dating the proxy card, and returning it to your respective company in the enclosed envelope.

Sincerely,

TED W. LOVE

Sincerely,

JOSEPH S. MOHR
President and Chief Business Officer

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President and Chief Executive Officer
Hyseq, Inc.

Variagenics, Inc.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities to be issued under this joint proxy statement/ prospectus or determined if this joint proxy statement/ prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

This joint proxy statement/prospectus is dated December 13, 2002, and is first being mailed to Hyseq and Variagenics stockholders on or about December 17, 2002.

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**NOTICE OF SPECIAL MEETING OF STOCKHOLDERS
TO BE HELD ON JANUARY 28, 2003**

To the Stockholders of Hyseq, Inc.:

NOTICE IS HEREBY GIVEN that a Special Meeting of Stockholders of Hyseq, Inc. will be held on January 28, 2003 at 9:00 a.m., local time, at 675 Almanor Ave., Sunnyvale, California for the following purposes:

1. To consider and vote upon a proposal to approve the issuance of shares of Hyseq common stock, par value \$0.001 per share, pursuant to the Agreement and Plan of Merger, dated as of November 9, 2002, by and among Hyseq, Vertical Merger Corp., which is a wholly-owned subsidiary of Hyseq, and Variagenics, Inc.
2. To consider and vote upon a proposal to amend Hyseq's Employee Stock Purchase Plan to increase the number of shares of Hyseq common stock available for issuance under the Plan by 500,000 shares to 750,000 shares.
3. To transact any other business as may properly come before the special meeting or any adjournment or postponement of the special meeting.

Please refer to the attached joint proxy statement/prospectus, which forms a part of this Notice and is incorporated herein by reference, for further information with respect to the business to be transacted at the special meeting.

Stockholders of record at the close of business on December 6, 2002 are entitled to notice of, and to vote at, the special meeting or any adjournment or postponement thereof.

The board of directors of Hyseq unanimously recommends that you vote **FOR** approval of the issuance of Hyseq common stock pursuant to the merger agreement and the amendment to the Hyseq, Inc. Employee Stock Purchase Plan.

Your vote is important. Please sign, date and return the enclosed proxy card as soon as possible to make sure that your shares are represented at the special meeting. To do so, you may complete and return the enclosed proxy card. If you are a stockholder of record of Hyseq common stock, you also may cast your vote in person at the special meeting. If your shares are held in an account at a brokerage firm or bank, you must instruct it on how to vote your shares.

By Order of the Board of Directors,

Li-Hsien Rin-Laures
Secretary

December 13, 2002

Please note that attendance at the special meeting will be limited to stockholders as of the record date, or their authorized representatives, and guests of Hyseq.

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VARIAGENICS, INC.

NOTICE OF SPECIAL MEETING OF STOCKHOLDERS TO BE HELD ON JANUARY 28, 2003

To the Stockholders of Variagenics, Inc.:

NOTICE IS HEREBY GIVEN that a Special Meeting of Stockholders of Variagenics, Inc. will be held on January 28, 2003 at 9:00 a.m., local time, at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, Massachusetts for the following purposes:

1. To consider and vote upon a proposal to approve the Agreement and Plan of Merger, dated as of November 9, 2002, by and among Hyseq, Inc., Vertical Merger Corp., which is a wholly-owned subsidiary of Hyseq, and Variagenics. In the merger contemplated by the merger agreement:

Vertical Merger Corp. will merge with and into Variagenics, with Variagenics surviving the merger as a wholly-owned subsidiary of Hyseq;

each outstanding share of Variagenics common stock will be converted into the right to receive 1.6451 shares of Hyseq common stock; and

promptly after the merger, Variagenics will be merged upstream into Hyseq with Hyseq as the surviving entity.

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

These items of business are described in the attached joint proxy statement/prospectus. Only Variagenics stockholders of record at the close of business on December 11, 2002, the record date for the special meeting, are entitled to notice of and to vote at the special meeting and any adjournments or postponements of the special meeting.

The board of directors of Variagenics recommends that you vote **FOR** approval of the merger agreement. The affirmative vote of the holders of a majority of the shares of Variagenics common stock outstanding as of the record date entitled to vote is required to approve the merger agreement.

Your vote is important. Please sign, date and return the enclosed proxy card as soon as possible to make sure that your shares are represented at the special meeting. To do so, you may complete and return the enclosed proxy card. If you are a stockholder of record of Variagenics common stock, you also may cast your vote in person at the special meeting. If your shares are held in an account at a brokerage firm or bank, you must instruct it on how to vote your shares. If you do not vote or do not instruct your broker or bank how to vote, it will have the same effect as voting against the merger.

Please do not send any certificates representing your Variagenics common stock at this time.

By Order of the Board of Directors,

Joseph S. Mohr
Secretary

December 13, 2002

Please note that attendance at the special meeting will be limited to stockholders as of the record date, or their authorized representatives, and guests of Variagenics.

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ADDITIONAL INFORMATION

This joint proxy statement/prospectus incorporates important business and financial information about Hyseq and Variagenics from other documents that are not included in or delivered with this joint proxy statement/ prospectus. For a listing of the documents incorporated by reference into this joint proxy statement/ prospectus, please see the section entitled "Where You Can Find More Information" beginning on page 168.

Hyseq will provide you with copies of the information relating to Hyseq, without charge, upon written or oral request to:

Hyseq, Inc.
670 Almanor Avenue
Sunnyvale, California 94085
(408) 524-8100
Attn: Investor Relations

In addition, you may obtain copies of the information relating to Hyseq, without charge, by sending an e-mail to ir@hyseq.com. Furthermore, you may obtain copies of some of this information by clicking on the "Information Request" link on the Investor Center web page of the Hyseq web site located at <http://www.hyseq.com/content/168.php>.

Variagenics will provide you with copies of the information relating to Variagenics, without charge, upon written or oral request to:

Variagenics, Inc.
60 Hampshire Street
Cambridge, Massachusetts 02139
(617) 588-5300
Attn: Investor Relations

In addition, you may obtain copies of the information relating to Variagenics, without charge, by sending an e-mail to info@variagenics.com. Furthermore, you may obtain copies of some of this information by making a request through the Variagenics investor relations web site, <http://www.variagenics.com>.

In order for you to receive timely delivery of the documents in advance of the Hyseq and Variagenics special meetings, Hyseq or Variagenics should receive your request no later than January 21, 2003.

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CHAPTER ONE THE MERGER

QUESTIONS AND ANSWERS ABOUT THE MERGER

Q: Why am I receiving this joint proxy statement/prospectus?

A: Hyseq and Variagenics have agreed to the acquisition of Variagenics by Hyseq under the terms of a merger agreement that is described in this joint proxy statement/ prospectus. A copy of the merger agreement is attached to this joint proxy statement/prospectus as Annex A.

In order to complete the merger, Hyseq stockholders must vote to approve the issuance of shares of Hyseq common stock in connection with the merger and Variagenics stockholders must vote to approve the merger agreement.

Hyseq and Variagenics will hold separate meetings of their respective stockholders to obtain these approvals. This joint proxy statement/prospectus contains important information about the merger and the special meetings of the respective stockholders of each of Hyseq and Variagenics, and you should read it carefully. The enclosed voting materials allow you to vote your shares without attending your special meeting.

Your vote is important. Hyseq and Variagenics encourage you to vote as soon as possible.

Q: Why are Hyseq and Variagenics proposing the merger?

A: Hyseq and Variagenics believe that the merger will provide substantial strategic and financial benefits to the stockholders of both companies. Hyseq and Variagenics believe that the combination will create a stronger and more competitive biotechnology company that is capable of creating more stockholder value than either Hyseq or Variagenics could on its own. Hyseq and Variagenics are proposing the merger because they believe it will benefit the stockholders of both companies by leveraging the companies' assets and management to develop biotherapeutic and molecular diagnostic products and accelerate revenue generation. To review the reasons for the merger in greater detail, see pages 32 and 34.

Q: What will happen in the merger?

A: A wholly-owned subsidiary of Hyseq will merge with and into Variagenics, following which Variagenics will merge with and into Hyseq (sometimes referred to in this joint proxy statement/ prospectus as the "Transaction"). Immediately after the merger, the former Variagenics stockholders, in the aggregate, will own approximately 63% of the then-outstanding shares of Hyseq common stock.

Q: What will I receive for my shares?

A: As a result of the merger, Variagenics will cease to exist, and Variagenics stockholders will be entitled to receive 1.6451 shares of Hyseq common stock for each share of Variagenics common stock they own, with cash in lieu of any fractional shares of Hyseq common stock. Based on the number of shares of Hyseq and Variagenics common stock outstanding on December 6, 2002, Hyseq and Variagenics estimate that Hyseq will issue approximately 39.7 million shares of Hyseq common stock in the merger.

Example: If you currently own 100 shares of Variagenics common stock, then as a result of the merger you will be entitled to receive 164 shares of Hyseq common stock.

Q: Where and when are the special meetings?

A: The Hyseq special meeting will take place at 675 Almanor Ave., Sunnyvale, California, on January 28, 2003, at 9:00 a.m., local time.

The Variagenics special meeting will take place at the offices of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, Massachusetts, on January 28, 2003 at 9:00 a.m., local time.

Q: What vote of Hyseq stockholders is required to approve the issuance of Hyseq common stock in the merger?

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A: The affirmative vote of the holders of a majority of the shares of Hyseq common stock present or represented by proxy and voting at the Hyseq special meeting is required to approve the issuance of Hyseq common stock to the Variagenics stockholders in the merger. As of December 6, 2002, the record date for the special meeting of Hyseq stockholders, directors and executive officers of Hyseq beneficially owning and entitled to vote 3,621,573 shares of Hyseq common stock, representing approxi-

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mately 15.7% of the outstanding shares of Hyseq common stock, have agreed to vote all of these shares in favor of approval of the merger.

Q: What vote of Variagenics stockholders is required to approve the merger agreement?

A: The affirmative vote of the holders of a majority of the outstanding shares of Variagenics common stock entitled to vote is required to approve the merger agreement. As of December 11, 2002, the record date for the special meeting of Variagenics stockholders, directors and current executive officers of Variagenics beneficially owning and entitled to vote 3,515,143 shares of Variagenics common stock, representing approximately 14.6% of the outstanding shares of Variagenics common stock, have agreed to vote all of these shares in favor of approval of the merger agreement.

Q: How does my company's board of directors recommend that I vote?

A: The Hyseq board of directors unanimously recommends that Hyseq stockholders vote **FOR** the proposal to approve the issuance of shares of Hyseq common stock to the Variagenics stockholders in the merger. For a more complete description of the recommendation of the Hyseq board of directors, see page 148.

The Variagenics board of directors recommends that Variagenics stockholders vote **FOR** the proposal to approve the merger agreement. For a more complete description of the recommendation of the Variagenics board of directors, see page 151.

Q: What do I do now?

A: Carefully read and consider the information contained in this joint proxy statement/ prospectus, including its annexes. There are several ways your shares can be represented at your special meeting. You can attend your special meeting in person or you can indicate on the enclosed proxy card how you want to vote and return it in the accompanying pre-addressed postage paid envelope. If you sign and send in your proxy but do not indicate how you want to vote, your proxy will be counted as a vote cast in favor of the applicable proposals.

Q: How do I cast my vote?

A: If you are a holder of record, you may vote in person at your special meeting or by submitting a proxy for your special meeting. You can submit your proxy by completing, signing, dating and returning the enclosed proxy card in the accompanying pre-addressed postage paid envelope. You may also submit your proxy by telephone or through the Internet. Information for voting by telephone or through the Internet is set forth in the enclosed proxy card instructions. To review how to submit your proxy, see pages 151 and 152.

Q: If my broker holds my shares in street name, will my broker vote my shares?

A: If you hold your shares in a stock brokerage account or if your shares are held by a bank or nominee (i.e., in street name), you must provide the record holder of your shares with instructions on how to vote your shares. Please refer to the voting instruction card used by your broker or nominee to see if you may submit voting instructions by telephone.

Q: Can I change my vote after I have delivered my proxy?

A: Yes. You can change your vote at any time before your proxy is voted at your stockholders meeting. You can do this in one of three ways:
you can send a signed notice of revocation;

you can grant a new, valid proxy; or

if you are a holder of record, you can attend your special meeting and vote in person; however, your attendance alone will not revoke your proxy.

If you choose either of the first two methods, you must submit your notice of revocation or your new proxy to the respective Secretary of Hyseq or Variagenics, as appropriate, before the applicable special meeting. However, if your shares are held in a street name account at a brokerage firm or bank, you should contact your brokerage firm or bank to change your vote.

Q: What will happen if I abstain from voting or fail to vote?

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A: In the case of Variagenics stockholders, the failure to cast your vote will have the same effect as voting against the merger agreement.

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In the case of Hyseq stockholders, the failure to cast your vote will not have any impact on the proposal to issue shares of Hyseq common stock in connection with the merger.

Q: Should I send in my Variagenics stock certificates now?

A: No. After the merger is completed, you will receive written instructions from the exchange agent on how to exchange your Variagenics stock certificates for Hyseq stock certificates. **Please do not send in your Variagenics stock certificates with your proxy.**

Q: What should I do if I receive more than one set of voting materials?

A: You may receive more than one set of voting materials, including multiple copies of this joint proxy statement/prospectus and multiple proxy cards or voting instruction cards. For example, if you hold your shares in more than one brokerage account, you will receive a separate voting instruction card for each brokerage account in which you hold shares. If you are a holder of record and your shares are registered in more than one name, you will receive more than one proxy card. In addition, if you are a stockholder of Hyseq and a stockholder of Variagenics, you will receive one or more separate proxy cards or voting instruction cards for each company. Please complete, sign, date and return each proxy card and voting instruction card that you receive.

Q: When do you expect the merger to be completed?

A: Hyseq and Variagenics are working to complete the merger as quickly as practicable. They currently expect to complete the merger in the first quarter of 2003. However, they cannot predict the exact timing of the completion of the merger.

Q: What rights do I have to seek a valuation of my shares?

A: Neither Hyseq stockholders nor Variagenics stockholders will have appraisal rights in connection with the proposals to be voted on.

Q: What are the expected United States federal income tax consequences of the Transaction?

A: The Transaction has been structured to qualify as a reorganization for U.S. federal income tax purposes, and Hyseq and Variagenics are required to receive opinions from their respective counsel to the effect that the Transaction will so qualify. Assuming that the Transaction so qualifies, then, in general, Variagenics stockholders will not recognize gain or loss for U.S. federal income tax purposes as a result of the Transaction, except that Variagenics stockholders will recognize gain or loss with respect to any cash they receive in lieu of a fractional share of Hyseq common stock upon completion of the Transaction.

Q: Who can help answer my questions?

A: If you have any questions about the merger or how to submit your proxy, or if you need additional copies of this joint proxy statement/prospectus or the enclosed proxy card or voting instructions, you should contact:

if you are a Hyseq stockholder:

MacKenzie Partners, Inc.
105 Madison Avenue
New York, New York 10016
(212) 929-5500

if you are a Variagenics stockholder:

D.F. King & Co.
77 Water Street
New York, New York 10005
(212) 269-5550

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SUMMARY

*The following is a summary of information contained in this joint proxy statement/prospectus. This summary may not contain all of the information about the merger that is important to you. For a more complete description of the merger, Hyseq and Variagenics encourage you to read carefully this entire joint proxy statement/prospectus, including the attached annexes. In addition, they encourage you to read the information incorporated by reference into this joint proxy statement/prospectus, which includes important business and financial information about Hyseq and Variagenics which each has filed with the Securities and Exchange Commission, or the SEC. 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 More Information*.*

The Companies

Hyseq, Inc.

670 Almanor Avenue
Sunnyvale, California 94085
(408) 524-8100

Hyseq is a company engaged in research and development of novel biopharmaceutical protein-based products for the treatment of human disease from its collection of proprietary genes discovered using its high-throughput signature-by-hybridization platform. Hyseq is researching several product candidates to treat a variety of serious diseases and medical conditions and is developing alfineprase, a clot-dissolving protein, in collaboration with Amgen, Inc.

Vertical Merger Corp. is a newly-formed, wholly-owned subsidiary of Hyseq that was formed solely for the purpose of effecting the merger. Vertical Merger Corp. has not conducted and will not conduct any business during any period of its existence.

Variagenics, Inc.

60 Hampshire Street
Cambridge, Massachusetts 02139
(617) 588-5300

Variagenics is a leader in the development and commercialization of technologies related to pharmacogenomics, the study of the correlation between an individual's genetic differences, or genetic variability, and his or her specific response to a drug. Variagenics develops molecular diagnostic tests by identifying genetic markers associated with response to cancer therapies, with the goal of optimizing patient care. Variagenics analyzes genetic variation, including single nucleotide polymorphisms (SNPs), haplotypes, loss of heterozygosity and expression levels in normal and tumor cells. Variagenics is developing molecular diagnostic tests through both biopharmaceutical collaborations and its own internal research programs.

The Merger (see page 28)

Hyseq and Variagenics have agreed to the combination of Hyseq and Variagenics under the terms of the merger agreement that is described in this joint proxy statement/prospectus. They have attached the merger agreement as Annex A to this joint proxy statement/prospectus. They encourage you to read the merger agreement in its entirety.

Under the terms of the merger agreement, Vertical Merger Corp. will merge with and into Variagenics, following which Variagenics will merge with and into Hyseq. Hyseq and Variagenics anticipate that shortly after the completion of the merger, the combined company will change its name to a new name that has not yet been determined. As a result of the merger, Variagenics will cease to exist. If you are a Variagenics stockholder, upon completion of the merger each of your shares of Variagenics common stock will be converted into a right to receive 1.6451 shares of Hyseq common stock. Hyseq and Variagenics sometimes refer to the shares to be paid to the Variagenics stockholders by Hyseq as the merger consideration. Hyseq stockholders will continue to own their existing shares which will not be affected by the merger.

Recommendations of the Hyseq and Variagenics Boards of Directors (see pages 148 and 151)

Hyseq

The Hyseq board of directors believes that the merger is fair to and in the best interests of Hyseq and its stockholders, and that the amendment to the Hyseq, Inc. Employee Stock Purchase Plan is in the best interest of Hyseq and its stockholders, and unanimously recommends that Hyseq stockholders

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vote **FOR** approval of the issuance of Hyseq common stock in the merger and the amendment of the Hyseq, Inc. Employee Stock Purchase Plan.

Variagenics

The Variagenics board of directors believes that the merger agreement and the transactions contemplated by the merger agreement, including the merger, are fair to and in the best interests of Variagenics and its stockholders, and recommends that Variagenics stockholders vote **FOR** approval of the merger agreement.

Stockholders and Stockholders Entitled to Vote; Vote Required (see pages 148 and 151)

Hyseq Stockholders

You can vote at the Hyseq special meeting if you owned Hyseq common stock at the close of business on December 6, 2002, the record date for the Hyseq special meeting. On that date, there were 23,042,922 shares of Hyseq common stock outstanding and entitled to vote. You can cast one vote for each share of Hyseq common stock that you owned on that date. Approval of the issuance of shares of Hyseq common stock in connection with the merger and approval of the amendment to the Hyseq, Inc. Employee Stock Purchase Plan each requires the affirmative vote of the holders of a majority of the shares of Hyseq common stock present or represented by proxy and voting at the Hyseq special meeting.

Variagenics Stockholders

You can vote at the Variagenics special meeting if you owned Variagenics common stock at the close of business on December 11, 2002, the record date for the Variagenics special meeting. On that date, there were 24,156,274 shares of Variagenics common stock outstanding and entitled to vote. You can cast one vote for each share of Variagenics common stock that you owned on that date. Approval of the merger agreement requires the affirmative vote of the holders of a majority of the outstanding shares of Variagenics common stock entitled to vote.

Stockholder Voting Agreements (see page 74)

Hyseq

Hyseq has entered into stockholder voting agreements with certain directors and current executive officers of Variagenics, pursuant to which these individuals agreed, among other things, to vote all of the shares of Variagenics common stock beneficially owned by them in favor of the approval of the merger agreement. As of the record date, these individuals beneficially owned and were entitled to vote 3,515,143 shares of Variagenics common stock, representing approximately 14.6% of the outstanding shares of Variagenics common stock on that date.

Variagenics

Variagenics has entered into stockholder voting agreements with the directors and certain executive officers of Hyseq, pursuant to which these individuals agreed, among other things, to vote all of the shares of Hyseq common stock beneficially owned by them in favor of the approval of the issuance of Hyseq common stock in connection with the merger. As of the record date, these individuals beneficially owned and were entitled to vote 3,621,573 shares of Hyseq common stock, representing approximately 15.7% of the outstanding shares of Hyseq common stock on that date.

Opinions of Financial Advisors (see pages 38 and 43)

Hyseq

On November 9, 2002, Banc of America Securities LLC, financial advisor to Hyseq, delivered its oral opinion to the Hyseq board of directors, which was subsequently confirmed by delivery of a written opinion dated November 9, 2002, that, as of that date, and based upon and subject to the considerations described in its opinion and based upon such other matters as Banc of America Securities considered relevant, the merger consideration to be paid by Hyseq for each outstanding share of Variagenics common stock pursuant to the merger agreement was fair from a financial point of view to Hyseq. The full text of Banc of America Securities' written opinion is attached to this joint proxy

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statement/prospectus as Annex C. Hyseq and Variagenics encourage you to read this opinion carefully in its entirety for a description of the procedures followed, assumptions made, matters considered and limitations on the review undertaken. Banc of America Securities' opinion is directed to the Hyseq board of directors and does not constitute a recommendation to any stockholder as to any matters relating to the merger.

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Variagenics

On November 8, 2002, SG Cowen Securities Corporation, financial advisor to Variagenics, delivered to the Variagenics board of directors its oral opinion, which was subsequently confirmed by delivery of a written opinion dated November 8, 2002, that, as of that date, and based upon and subject to the factors and assumptions set forth in the opinion, the merger consideration pursuant to the merger agreement was fair, from a financial point of view, to holders of shares of Variagenics common stock. The full text of SG Cowen's written opinion is attached to this joint proxy statement/prospectus as Annex D. Hyseq and Variagenics encourage you to read this opinion carefully in its entirety for a description of the procedures followed, assumptions made, matters considered and limitations on the review undertaken. SG Cowen's opinion is directed to the Variagenics board of directors and does not constitute a recommendation to any stockholder as to any matters relating to the merger.

Ownership of the Combined Company after the Merger

Based on the number of shares of Variagenics common stock outstanding on December 6, 2002, Hyseq expects to issue approximately 39.7 million shares of Hyseq common stock in the merger. Based on the number of shares of Hyseq and Variagenics common stock outstanding on December 6, 2002, after completion of the merger, former Variagenics stockholders will own approximately 63% of the then-outstanding shares of Hyseq common stock.

Share Ownership of Directors and Executive Officers of Hyseq and Variagenics

At the close of business on the record date for the Hyseq special meeting, directors and executive officers of Hyseq and their affiliates beneficially owned and were entitled to vote approximately 3,621,573 shares of Hyseq common stock, collectively representing approximately 15.7% of the 23,042,922 shares of Hyseq common stock outstanding on that date.

At the close of business on the record date for the Variagenics special meeting, directors and current executive officers of Variagenics and their affiliates beneficially owned and were entitled to vote approximately 3,800,723 shares of Variagenics common stock, collectively representing approximately 15.7% of the 24,156,274 shares of Variagenics common stock outstanding on that date.

Interests of Directors and Executive Officers of Hyseq in the Merger (see page 55)

When considering the Hyseq board of directors' recommendation that the Hyseq stockholders vote in favor of the issuance of shares in connection with the merger, Hyseq stockholders should be aware that some directors and executive officers of Hyseq may have interests in the merger that may be different from, or in addition to, the interests of Hyseq stockholders.

The Hyseq board of directors knew about these additional interests, and considered them, among other matters, when it approved the merger agreement.

Interests of Directors and Executive Officers of Variagenics in the Merger (see page 56)

When considering the Variagenics board of directors' recommendation that the Variagenics stockholders vote in favor of the approval of the merger agreement, Variagenics stockholders should be aware that some directors and executive officers of Variagenics may have interests in the merger that may be different from, or in addition to, the interests of Variagenics stockholders.

The Variagenics board of directors knew about these additional interests, and considered them, among other matters, when it approved the merger agreement.

Listing of Hyseq Common Stock and Delisting and Deregistration of Variagenics Common Stock (see page 54)

Application will be made to have the Hyseq common stock issued in the merger approved for listing on the Nasdaq National Market, where Hyseq common stock currently is traded under the symbol HYSQ. If the merger is completed, Variagenics common stock will no longer be listed on the Nasdaq National Market and will be deregistered under the Securities Exchange Act of 1934, and Variagenics will no longer file

periodic reports with the SEC.

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Appraisal Rights (see page 63)

Neither Hyseq stockholders nor Variagenics stockholders will have appraisal rights in connection with the proposals to be voted on.

Conditions to Completion of the Merger (see page 69)

In order to complete the merger Hyseq and Variagenics must satisfy the conditions described on pages 69 and 70, including the following:

Variagenics stockholders must adopt the merger agreement;

Hyseq's stockholders must approve the issuance of Hyseq shares in the merger;

The registration statement of which this joint proxy statement/prospectus is a part must not be the subject of any stop order or related proceedings;

Hyseq and Variagenics must receive legal opinions that the Transaction will be a reorganization for U.S. federal income tax purposes; and

the shares of Hyseq common stock issuable in the merger must be approved for listing on the Nasdaq National Market.

No Solicitation by Variagenics or Hyseq

(see page 66)

The merger agreement contains detailed provisions prohibiting Hyseq and Variagenics from seeking an alternative transaction with another party. These no solicitation provisions prohibit Hyseq and Variagenics, as well as their officers, directors, subsidiaries and representatives from taking any action to solicit an acquisition proposal from another party. The merger agreement does not, however, prohibit any party or its respective board of directors from considering, and potentially recommending, an unsolicited bona fide written superior proposal under certain circumstances.

Termination of the Merger Agreement

(see page 71)

Hyseq and Variagenics can jointly agree to terminate the merger agreement at any given time. Either company may also terminate the merger agreement if the merger is not completed by May 31, 2003 and under other circumstances described on pages 71 to 73.

Termination Fees and Expenses (see pages 71 through 73)

The merger agreement provides that, in several circumstances, Hyseq or Variagenics may be required to pay a termination fee in the amount of \$1,750,000, or the expenses of the other party up to an amount equal to \$750,000, each as described on pages 71 to 73).

Variagenics Stock Options and Warrants; Variagenics Employee Stock Purchase Plan

(see pages 61 and 62)

At the effective time, each option or warrant to purchase shares of Variagenics common stock outstanding immediately before the effective time of the merger will be assumed by Hyseq and converted into and become a right to purchase shares of Hyseq common stock. Each option or warrant assumed by Hyseq will be exercisable for the number of shares of Hyseq common stock equal to the number of shares of Variagenics common stock issuable upon exercise of the option or warrant multiplied by 1.6451, rounded down to the nearest whole share. The per share exercise price for each option or warrant will be the exercise price of each Variagenics option or warrant divided by 1.6451, rounded up to the

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nearest whole cent. Any restrictions on the exercise of any options or warrants shall continue and the term, vesting schedule and other provisions of each option or warrant, as applicable, shall remain unchanged.

Each outstanding purchase right under the Variagenics 2000 Employee Stock Purchase Plan will be exercised for the purchase of shares of Variagenics common stock at a price per share determined by the Employee Stock Purchase Plan on the date immediately prior to the completion of the merger. The Employee Stock Purchase Plan will be terminated immediately prior to the effective time of the merger.

Material United States Federal Income Tax Consequences of the Merger

(see page 51)

Hyseq and Variagenics expect the Transaction to be treated as a tax-free reorganization for U.S. federal income tax purposes, and Hyseq and Variagenics are required to receive opinions from

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their respective counsel to the effect that the Transaction will so qualify. If these opinions are not rendered, Hyseq and Variagenics will not consummate the merger unless further stockholder approval is obtained with appropriate disclosure. Assuming that the Transaction qualifies as a tax-free reorganization, then, in general, Variagenics stockholders will not recognize any gain or loss on the exchange of their shares of Variagenics common stock for shares of Hyseq common stock pursuant to the Transaction, except for gain or loss on fractional shares of Hyseq common stock for which cash is received. No gain or loss will be recognized by Hyseq, Variagenics or Hyseq stockholders as a result of the Transaction.

Tax matters are very complicated, and the tax consequences of the Transaction to you will depend on the facts of your own situation. For a more complete description of the tax consequences of the Transaction, see *The Merger* Material United States Federal Income Tax Consequences of the Transaction on page 51. Hyseq and Variagenics encourage you to consult your own tax advisor for a full understanding of the tax consequences of the Transaction to you.

Accounting Treatment (see page 53)

Hyseq will account for the merger under the purchase method of accounting for business combinations under accounting principles generally accepted in the United States of America.

The determination of accounting acquirer in a business combination in accordance with Statement of Financial Accounting Standards No. 141 requires consideration of multiple factors, including voting rights, any significant minority voting rights, governance and senior management of the combined enterprise, as well as any premium that was paid. Given the composition of the board of directors and senior management of the combined company, as well as the premium paid by Hyseq, Hyseq was determined to be the accounting acquirer.

Regulatory Approvals (see page 51)

Neither Hyseq nor Variagenics is aware of any material federal or state regulatory requirements or approvals required for completion of the merger.

Table of Contents**Summary Selected Historical Financial Data**

The following information is provided to aid you in your analysis of the financial aspects of the merger. This information was derived from the audited financial statements of Hyseq and Variagenics for the years ended December 31, 1997 through December 31, 2001, respectively, and the unaudited quarterly financial statements of Hyseq and Variagenics for the nine months ended September 30, 2002 and 2001, respectively. This information is only a summary, and you should read it together with the historical financial statements and related notes contained in the annual reports and other information filed with the SEC and incorporated by reference into this joint proxy statement/prospectus. See [Where You Can Find More Information](#).

Hyseq, Inc.**Summary Selected Historical Financial Data****(In thousands, except per share amounts)**

	Nine Months Ended September 30,		Fiscal Year Ended December 31,				
	2002	2001	2001	2000	1999	1998	1997
Statements of Operations							
Data(1)(2):							
Contract revenues	\$ 22,915	\$ 17,522	\$ 24,590	\$ 15,604	\$ 6,397	\$ 9,590	\$ 6,199
Operating expenses:							
Research and development	40,885	31,532	46,506	29,018	18,157	19,207	9,430
General and administrative	9,102	9,805	13,452	9,315	8,101	9,495	4,854
Restructuring	610	825	825				
Loss before minority interest	(28,580)	(25,115)	(36,765)	(22,253)	(18,547)	(16,369)	(6,537)
Loss attributable to minority interest	112		293				
Net loss	(28,468)	(25,115)	(36,472)	(22,253)	(18,547)	(16,369)	(6,537)
Basic and diluted net loss per share	(1.34)	(1.64)	(2.26)	(1.65)	(1.43)	(1.27)	(0.86)
Weighted average shares used in computing basic and diluted net loss per share	21,197	15,351	16,158	13,449	13,004	12,839	7,589
Cash dividends per share							
Balance Sheet Data(1)(2):							
Cash, cash equivalents	\$ 4,272	\$ 16,534	\$ 12,329	\$ 2,699	\$ 13,675	\$ 21,555	\$ 23,204
Short and long-term marketable securities					16,962	24,880	33,930
Working capital	(3,151)	8,094	(1,717)	(2,577)	22,077	42,345	56,824
Total assets	32,143	39,823	39,904	21,288	45,364	57,914	66,950
Noncurrent portion of capital lease and loan Obligations	1,289	2,911	2,228	4,722	5,221	4,479	613
Note payable	4,000		4,000				
Other non-current liabilities			125				
Minority interest			112				
Stockholders' equity	11,690	24,680	15,421	8,362	29,222	47,576	62,937

- (1) Factors that affected the comparability of information between 2000 and 2001 were Hyseq's private placement in August of 2001 in which an aggregate of 3,040,734 shares of Hyseq common stock and warrants to purchase an aggregate of 1,520,368 shares of Hyseq common stock were sold for net proceeds of approximately \$20.7 million, and the conversion of its loan from Dr. George B. Rathmann's first line of credit into 2,237,637 shares of Hyseq common stock in March 2001.

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- (2) Factors that affected the comparability of information between the nine months ended September 30, 2001 and the nine months ended September 30, 2002 were Hyseq's private placement in August of 2001 in which an aggregate of 3,040,734 shares of Hyseq common stock and warrants to purchase an aggregate of 1,520,368 shares of Hyseq common stock were sold for net proceeds of approximately \$20.7 million, the conversion of its loan from Dr. Rathmann's first line of credit into 2,237,637 shares of Hyseq common stock in March 2001, and Hyseq's private placement in April of 2002 in which an aggregate of 3,575,691 shares of Hyseq common stock and warrants to purchase an aggregate of approximately 893,927 shares of Hyseq common stock were sold for net proceeds of approximately \$14.3 million.

Table of Contents**Variagenics, Inc.****Summary Selected Historical Financial Data**

(In thousands, except per share amounts)

	Nine Months Ended September 30,		Fiscal Year Ended December 31,				
	2002	2001	2001	2000	1999	1998	1997
Statements of Operations Data:							
Research and development collaborations and other	\$ 592	\$ 2,381	\$ 2,773	\$ 2,254	\$ 399	\$	\$
Product sales	450	210	210				
Total revenue	1,042	2,591	2,983	2,254	399		
Operating expenses:							
Cost of product sales	236	186	186				
Research and development(1)	16,792	12,894	19,868	11,836	8,602	5,071	2,908
General and administrative(1)	9,187	9,052	12,449	11,339	6,945	3,176	2,059
Restructure and related charges	1,974						
Net loss	(26,200)	(15,894)	(25,303)	(17,800)	(16,728)	(8,145)	(4,789)
Dividends on redeemable convertible preferred stock				(22,106)	(1,437)		(153)
Net loss attributable to common stockholders	(26,200)	(15,894)	(25,303)	(39,906)	(18,165)	(8,145)	(4,942)
Basic and diluted net loss per share	(1.11)	(0.68)	(1.09)	(3.69)	(29.96)	(16.13)	(13.48)
Weighted average shares used in computing basic and diluted net loss per share	23,688	23,272	23,295	10,816	606	505	367
Cash dividends per share							
Balance Sheet Data:							
Cash, cash equivalents and short and long-term marketable securities	\$ 60,783	\$ 85,218	\$ 80,029	\$ 99,025	\$ 4,328	\$ 734	\$ 6,994
Working capital	52,456	83,550	69,709	88,181	2,799	(3,771)	6,591
Total assets	69,630	95,687	90,932	106,244	9,403	5,249	8,177
Long-term obligations, less current portion	1,348	2,563	2,515	880	977	868	
Redeemable convertible preferred stock					29,094	16,804	16,804
Stockholders equity	62,583	89,431	82,983	101,282	(22,390)	(17,403)	(9,285)

(1) Non-cash equity compensation included in R&D and G&A expense, above:

Research and development	\$2,180	\$1,417	\$2,926	\$2,950	\$1,949	\$	\$
General and administrative	3,123	2,426	3,876	5,616	1,051		

Table of Contents**Summary Unaudited Pro Forma Condensed Combining Financial Data**

The table below presents selected financial data from the Hyseq and Variagenics unaudited pro forma condensed combining statements of operations for the nine months ended September 30, 2002 and the year ended December 31, 2001 and the unaudited pro forma condensed combining balance sheet as of September 30, 2002 included in this joint proxy statement/ prospectus. The unaudited pro forma condensed combining statements of operations are presented as if the merger had occurred on January 1, 2001 and January 1, 2002, respectively. The unaudited pro forma condensed combining balance sheet presents the combined financial position of Hyseq and Variagenics as of September 30, 2002 assuming that the merger had occurred as of that date. The unaudited pro forma condensed combining financial data is based on the estimates and assumptions set forth in the notes to such statements, which are preliminary and have been made solely for the purposes of developing such pro forma information. The unaudited pro forma condensed combining financial data is not necessarily indicative of the financial position or operating results that would have been achieved had the merger been consummated as of the dates indicated, nor is it necessarily indicative of future financial position or operating results. This information should be read in conjunction with the unaudited pro forma condensed combining financial statements and related notes and the historical financial statements and related notes of Hyseq and Variagenics included in or incorporated by reference into this joint proxy statement/ prospectus.

	Nine Months Ended September 30, 2002	Year Ended December 31, 2001
(In thousands, except per share data)		
Statement of Operations Data:		
Total revenues	\$ 23,957	\$ 27,573
Net income	\$ (53,156)	\$ (59,939)
Earnings per share	\$ (0.88)	\$ (1.10)
Shares used in calculation of earnings per share	60,166	54,480

	Pro Forma Combined As of September 30, 2002
(In thousands)	
Balance Sheet Data:	
Total assets	\$96,133
Long-term debt	6,637
Working capital	45,405
Stockholders' equity	64,733

Table of Contents**Comparative Per Share Information**

The following table presents (a) the unaudited loss per share and book value per share data for each of Hyseq and Variagenics on a historical basis, (b) the unaudited loss per share and book value per share data for the combined company on a pro forma basis and (c) the unaudited loss per share and book value per share data for Variagenics on an equivalent pro forma basis. The unaudited pro forma combined financial data is not necessarily indicative of the financial position had the merger occurred on December 31, 2001 or September 30, 2002, respectively, or operating results that would have been achieved had the merger been in effect as of the beginning of the periods presented, and should not be construed as representative of future financial position or operating results. The pro forma combined loss, pro forma stockholders equity and the pro forma number of shares of Hyseq common stock outstanding used in determining the amounts presented below have been derived from unaudited pro forma condensed combining financial statements included in this joint proxy statement/ prospectus.

This information is only a summary and should be read in conjunction with the selected historical financial data of Hyseq and Variagenics, the Hyseq and Variagenics unaudited pro forma condensed combining financial statements, and the separate historical financial statements of Hyseq and Variagenics and related notes included in or incorporated by reference into this joint proxy statement/ prospectus.

	Hyseq	
	As of And For the Nine Months Ended September 30, 2002	As of And For the Year Ended December 31, 2001
Historical per common share data:		
Loss per share	\$ (1.34)	\$ (2.26)
Net book value per share(1)	\$ 0.51	\$ 0.80

	Variagenics	
	Nine Months Ended September 30, 2002	Year Ended December 31, 2001
Historical per common share data:		
Loss per share	\$ (1.11)	\$ (1.09)
Net book value per share(1)	\$ 2.60	\$ 3.55

	Combined	
	Nine Months Ended September 30, 2002	Year Ended December 31, 2001
Pro forma combined per common share data:		
Loss per share	\$ (0.88)	\$ (1.10)
Loss per equivalent Variagenics share(2)	\$ (1.46)	\$ (1.82)
Net book value per combined company's share	\$ 1.03	
Pro forma net book value per equivalent Variagenics share(1)(2)	\$ 1.70	

- (1) The historical net book value per share of Hyseq common stock and Variagenics common stock is computed by dividing common stockholders' equity at period end by the number of shares of common stock outstanding at the respective period end. The pro forma net book value per share of the combined company's common stock is computed by dividing the pro forma common stockholders' equity by the pro forma number of shares of Hyseq common stock outstanding at the respective period end, assuming the merger had occurred as of that date.

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- (2) The equivalent pro forma combined per share data of Variagenics common stock is calculated by multiplying the pro forma combined amounts by the exchange ratio of 1.6451 for each share of Hyseq common stock.

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Table of Contents**Comparative Per Share Market Price Data**

Hyseq common stock trades on the Nasdaq National Market under the symbol HYSQ. Variagenics common stock began trading on the Nasdaq National Market under the symbol VGNX on July 21, 2000. There was no public market for Variagenics common stock prior to that date. The table below sets forth, for the periods indicated, the high and low per share sales prices for Hyseq common stock and Variagenics common stock as reported on the Nasdaq National Market:

	Hyseq Common Stock		Variagenics Common Stock	
	High	Low	High	Low
Fiscal Year 2000				
First quarter	\$ 139.50	\$ 12.44	\$	\$
Second quarter	46.88	17.00		
Third quarter	53.25	30.25	30.25	18.19
Fourth quarter	37.00	11.25	23.00	6.75
Fiscal Year 2001				
First quarter	\$ 16.44	\$ 7.50	\$ 12.06	\$ 3.69
Second quarter	18.00	7.50	6.60	3.50
Third quarter	11.35	5.20	4.04	2.20
Fourth quarter	10.22	5.94	3.30	2.22
Fiscal Year 2002				
First quarter	\$ 9.00	\$ 5.32	\$ 3.55	\$ 2.35
Second quarter	5.33	1.70	2.50	1.07
Third quarter	2.84	1.35	1.40	0.77
Fourth quarter (through December 12, 2002)	1.90	0.85	1.81	0.63

On November 8, 2002, the last trading day before the merger was announced, the closing price of Hyseq common stock on the Nasdaq National Market was \$1.35 per share and the closing price of Variagenics common stock on the Nasdaq National Market was \$0.96 per share. Based on the exchange ratio (i.e., 1.6451 shares of Hyseq common stock for each outstanding share of Variagenics common stock) and the closing price of Hyseq common stock on November 8, 2002, the pro forma equivalent per share value of Variagenics common stock on November 8, 2002 was approximately \$2.22 per share. On December 12, 2002, the last trading day prior to the date of this joint proxy statement/prospectus, the closing price of Hyseq common stock on the Nasdaq National Market was \$1.02, the closing price of Variagenics common stock on the Nasdaq National Market was \$1.49 and the pro forma equivalent per share value of Variagenics common stock, based on the closing price of Hyseq common stock on the Nasdaq National Market, was approximately \$1.68 per share. Neither Hyseq nor Variagenics has ever declared or paid cash dividends on its common stock.

The market value of the shares of Hyseq common stock that will be issued in exchange for shares of Variagenics common stock upon the completion of the merger will not be known at the time Variagenics stockholders vote to adopt the merger agreement, or at the time Hyseq stockholders vote on the adoption of the merger agreement and the issuance of shares of Hyseq common stock in the merger, because the merger will not be completed by then.

The above table shows only historical comparisons. Because the market prices of Hyseq common stock and Variagenics common stock will likely fluctuate prior to completion of the merger, these comparisons may not provide meaningful information to Hyseq stockholders in determining whether to approve the issuance of shares of Hyseq common stock in the merger or to Variagenics stockholders in determining whether to adopt the merger agreement. Hyseq and Variagenics stockholders are encouraged to obtain current market quotations for Hyseq and Variagenics common stock and to review carefully the other information contained in this joint proxy statement/prospectus or incorporated by reference into this joint proxy statement/prospectus in considering whether to approve their respective proposal(s). See the section entitled Where You Can Find More Information.

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RISK FACTORS

The merger involves a high degree of risk for Hyseq and Variagenics stockholders. Variagenics stockholders will be choosing to invest in Hyseq common stock by voting in favor of adoption of the merger agreement. An investment in shares of Hyseq common stock involves a high degree of risk. In addition to the other information included in this joint proxy statement/prospectus, including the matters addressed in

Cautionary Statement Concerning Forward-Looking Statements, you should carefully consider the following risks before deciding whether to vote for adoption of the merger agreement, in the case of Variagenics stockholders, or for the issuance of shares of Hyseq common stock in the merger and the amendment to the Employee Stock Purchase Plan, in the case of Hyseq stockholders. In addition, you should read and consider the risks associated with each of the businesses of Hyseq and Variagenics because these risks will also affect the combined company. These risks can be found in Hyseq's Annual Report on Form 10-K for the year ended December 31, 2001 and in its Quarterly Reports for the quarters ended March 31, 2002, June 30, 2002 and September 30, 2002, and in Variagenics' Annual Report on Form 10-K for the year ended December 31, 2001. Each of these reports is filed with the SEC and incorporated by reference into this joint proxy statement/prospectus. Additional risks and uncertainties not presently known to Hyseq and Variagenics or that are not currently believed to be important to you also may adversely affect the merger and the combined company following the merger.

Risks Related to the Merger

The exchange ratio is fixed and does not give effect to possible fluctuations in the value of Hyseq common stock to be received in the merger.

In the merger, Variagenics stockholders will be entitled to receive 1.6451 shares of Hyseq common stock for each share of Variagenics common stock they own. As a result of Variagenics stockholders receiving the merger consideration in shares of Hyseq common stock, the value of the merger consideration to be received by Variagenics stockholders will depend on the market price of Hyseq common stock at the time the merger is completed. The market price of Hyseq common stock at the closing of the merger may vary from its market prices at the date of this joint proxy statement/prospectus and at the date of the Hyseq and Variagenics special meetings. These variations may be caused by a number of factors, including changes in the businesses, operations or prospects of Hyseq or Variagenics, the timing of the merger and general market and economic conditions. The merger consideration will not be adjusted for any increase or decrease in the market price of Hyseq common stock or Variagenics common stock. Accordingly, if the market value of Hyseq common stock declines prior to the time the merger is completed, the value of the merger consideration to be received by Variagenics stockholders will decline. In addition, because the date that the merger is completed may be later than the date of the special meetings, Hyseq and Variagenics stockholders may not know the exact value of the Hyseq common stock that will be issued in connection with the merger at the time they vote on the merger proposals. Hyseq and Variagenics encourage you to obtain current market quotations for Hyseq and Variagenics shares before you vote your shares.

The issuance of shares of Hyseq common stock to Variagenics stockholders in the merger will substantially reduce the percentage interests of Hyseq stockholders.

If the merger is completed, approximately 39,739,486 shares of Hyseq common stock will be issued to Variagenics stockholders, based on the number of shares of Variagenics common stock outstanding on December 6, 2002, and former Variagenics stockholders will own approximately 63% of the combined company. The issuance of approximately 39,739,486 shares of Hyseq common stock to Variagenics stockholders will cause a significant reduction in the relative percentage interests of current Hyseq stockholders in earnings, voting, liquidation value and book and market value. The issuance of additional shares of Hyseq common stock in future transactions could also reduce the percentage interests of former Variagenics and Hyseq stockholders in the combined company.

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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 Variagenics with the business of Hyseq. The combined company's success in realizing these benefits and the timing of this realization depends upon the successful integration of the operations of Variagenics. 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 include, among others:

consolidating research and development operations;

retaining key employees;

consolidating corporate and administrative infrastructures;

preserving the research and development and other important relationships of Hyseq and Variagenics;

integrating and managing the technology of two companies;

using Variagenics' liquid capital assets efficiently to develop the business of the combined company;

minimizing the diversion of management's attention from ongoing business concerns; and

coordinating geographically separate organizations.

Hyseq and Variagenics cannot assure you that the integration of Variagenics with Hyseq will result in the realization of the full benefits anticipated by them to result from the merger.

Hyseq and Variagenics may suffer negative consequences if the merger is not completed.

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

the provision in the merger agreement which provides that under specified circumstances either Hyseq or Variagenics could be required to pay the other a termination fee of \$1.75 million incurred in connection with the merger;

the market price of Hyseq common stock and/or Variagenics 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, and a decline to a market price of below \$1.00 per share for a period of thirty consecutive trading days may cause the Nasdaq Stock Market to take action to have the common stock delisted from the Nasdaq National Market for failure to comply with its minimum listing requirements;

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

benefits that Hyseq and Variagenics 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 Hyseq and Variagenics to regain their financial and market position if the merger does not occur;

if the merger is terminated and Variagenics' board of directors seeks another merger or business combination, Variagenics stockholders cannot be certain that Variagenics will be able to find a partner willing to pay an equivalent or more attractive price than the price to be paid by Hyseq in the merger;

Hyseq will have insufficient working capital and may be unable to obtain additional funding on terms acceptable to Hyseq, or at all;

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

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.

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

Some of the directors of Hyseq and Variagenics who recommend that you vote in favor of the merger and the officers of Hyseq and Variagenics 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 Hyseq in the Merger and Interests of Directors and Executive Officers of Variagenics in the Merger.

Some third-party agreements of Hyseq and Variagenics have change of control or termination provisions.

Some of the agreements that Hyseq and Variagenics have with third parties have change of control or termination provisions that may be triggered by the merger, but have not yet been waived. The completion of the merger is not conditioned upon Hyseq or Variagenics receiving waivers from any third parties and neither Hyseq nor Variagenics may terminate the merger agreement for failure of the other party to receive a third-party waiver to an agreement with a change of control or termination provision. Hyseq has agreed to use commercially reasonable efforts to obtain waivers from some of the third parties.

Risks Related to the Combined Company

Hyseq's stock price has been volatile, is likely to continue to be volatile and could decline substantially.

The price of Hyseq common stock has been, and is likely to continue to be, highly volatile, including after the merger. That price could fluctuate significantly for the following reasons:

volatility and uncertainty in the capital markets in general;

fluctuations in results of operations;

sales of Hyseq common stock by existing holders;

loss of key personnel;

economic and other external factors;

announcements by governmental agencies that may have, or may be perceived to have, an impact on potential products;

changes in earnings estimates;

changes in accounting principles;

lack of trading volume in Hyseq common stock;

fluctuations within the biotechnology sector;

announcements by competitors; and

other factors not within Hyseq's control.

In addition, the stock market in general, and the market for biotechnology and other life science stocks in particular, has historically been subject to extreme price and volume fluctuations. This volatility has had a

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significant effect on the market prices of securities issued by many companies for reasons unrelated to the operating performance of these companies and may have an adverse effect on the market price for Hyseq common stock, including after the merger.

In the past, following periods of volatility in the market price of a company's securities, class action securities litigation has often been instituted against such a company. Any such litigation instigated against Hyseq could result in substantial costs and a diversion of management's attention and resources, which could significantly harm the combined company's business, financial condition and operating results.

The Hyseq common stock is at risk of being delisted from the Nasdaq National Market, and, if delisted, investors may find it more difficult to sell Hyseq common stock.

The Hyseq common stock is listed on the Nasdaq National Market, which has minimum quantitative listing criteria that are required to be maintained. Two of these criteria are a minimum stock price of \$1.00 per share and minimum stockholders' equity of \$10 million. For the period commencing on January 1, 2002 through December 12, 2002, the high and low closing sales price of Hyseq common stock as reported by the Nasdaq National Market was \$9.00 and \$0.85, respectively, and from November 12, 2002 through November 27, 2002, Hyseq common stock closed below \$1.00. As of September 30, 2002, Hyseq had stockholders' equity of \$11.7 million. If the price of Hyseq common stock dips below \$1.00 per share in the future, or if Hyseq does not continue to satisfy the \$10.0 million stockholders' equity requirement and the other applicable continued listing requirements, the Hyseq common stock may be delisted from the Nasdaq National Market. If this were to happen, it would be more difficult to purchase or sell Hyseq common stock or obtain accurate quotations as to the price of the securities, and the price of the Hyseq common stock could suffer a material decline. In addition, any delisting could have a materially adverse affect on Hyseq's access to the capital markets and its ability to raise capital through alternative financing sources on terms acceptable to Hyseq or at all.

Neither Hyseq nor Variagenics has achieved profitability and both have recent and anticipated continuing losses.

For the years ended December 31, 2001, 2000 and 1999, Hyseq had net losses of \$36.5 million, \$22.3 million and \$18.5 million, respectively. As of September 30, 2002, Hyseq had an accumulated deficit of \$136.9 million. For the years ended December 31, 2001, 2000 and 1999, Variagenics had net losses of \$25.3 million, \$17.8 million and \$16.7 million, respectively. As of September 30, 2002, Variagenics had an accumulated deficit of \$104.2 million.

The process of developing Hyseq's therapeutic protein candidates and Variagenics' molecular diagnostic products will require significant additional research and development, preclinical testing, clinical trials and regulatory approvals. These activities, together with general administrative and other expenses, are expected to result in operating losses for the foreseeable future. The combined company may never generate profits and as a result, the trading price of Hyseq common stock could decline. Moreover, utilization of the combined company's net operating loss carryforwards and credits may be subject to an annual limitation due to the change in ownership provisions of the Internal Revenue Code of 1986 and similar state law provisions. It is possible that this Transaction, when considered in connection with other transactions, may result in a change in ownership for purposes of these provisions.

The combined company will have a relatively short operating history.

Hyseq and Variagenics each have short operating histories. Hyseq commenced operations in the fourth quarter of 1994 with an initial business focused on gene discovery using its signature by hybridization platform, and applications of its sequencing-by-hybridization technology, including the HyChip system. In 1998, Hyseq began to transition its business strategy from gene discovery to research and development of potential therapeutic protein candidates. Variagenics commenced operations in 1992 and is still in the early stage of commercializing its products and services. As companies with relatively short operating histories,

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Hyseq and Variagenics both face risks and uncertainties frequently encountered by companies in new and rapidly evolving markets, including:

the implementation and successful execution of business strategy and sales and marketing initiatives;

retention of current customers and collaborators and attraction of new customers and collaborators;

the ability to respond effectively to competitive and technological developments related to their technologies, products and services;

the ability to attract, retain and motivate qualified personnel; and

effectively managing their anticipated growth.

If the combined company fails to address these risks and uncertainties successfully, its business, results of operations, financial condition and prospects will be materially adversely affected.

The combined company may need to raise additional capital and such capital may be unavailable to the combined company when it needs it or may not be available on acceptable terms.

The combined company expects to have enough cash to fund its operations through 2004. However, unanticipated expenses, or unanticipated opportunities that require financial commitments, could give rise to requirements for additional financing sooner than the combined company expects. Financing may be unavailable when the combined company needs it or may not be available on acceptable terms. The unavailability of financing may require the combined company to delay, scale back or eliminate expenditures for its research, development and marketing activities necessary to commercialize the combined company's potential biopharmaceutical products. The combined company may also be required to grant rights to third parties to develop and market product candidates that the combined company would prefer to develop and market itself. If the combined company was required to grant such rights, the ultimate value of these product candidates to the combined company would be reduced.

If the combined company is unable to obtain additional financing when it needs it, the perception in the capital markets that it may not be able to raise the amount of financing it desires, or on terms favorable to it, may have a negative effect on the trading price of Hyseq common stock. Additional equity financings could result in significant dilution of current stockholders' equity interests. If sufficient capital is not available, the combined company will delay, reduce the scope of, eliminate or divest one or more of its subsidiaries or its discovery, research or development programs. Any such action could significantly harm the combined company's business, financial condition and results of operations.

The combined company's future capital requirements and the adequacy of its currently available funds will depend on many factors, including, among others, the following:

continued scientific progress in the combined company's research and development programs, including progress in its research and preclinical studies on its potential therapeutic protein candidates;

the cost involved in any facilities expansion to support research and development of its potential therapeutic protein candidates;

the combined company's ability and the ability of its subsidiary Callida to attract additional financing on favorable terms;

the magnitude and scope of its research and development programs, including development of potential therapeutic protein candidates, potential molecular diagnostic tests and Callida technology and applications;

the combined company's ability to maintain, and the financial commitments involved in, its existing collaborative and licensing arrangements;

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the combined company's ability to establish new corporate relationships with other biotechnology and pharmaceutical companies to share costs and expertise of identifying and developing product candidates;

the cost of prosecuting and enforcing its intellectual property rights;

the cost of manufacturing material for preclinical, clinical and commercial purposes;

progress in its clinical studies of alfimeprase;

the time and cost involved in obtaining regulatory approvals;

the combined company's need to develop, acquire or license new technologies or products;

competing technological and market developments;

future funding commitments to the combined company's subsidiary Callida, and its ability to borrow funds from Affymetrix to fund its commitment, under the terms of the Affymetrix settlement;

the combined company's ability to use Hyseq common stock to repay its outstanding note to Affymetrix and its line of credit with Dr. Rathmann;

legal and Nasdaq restrictions that impede the combined company's ability to raise funds from private placements of Hyseq common stock;

future funding commitments to its collaborators;

general conditions in the financial markets and in the biotech sector;

the uncertain condition of the capital markets; and

other factors not within the combined company's control.

Development of the combined company's products will take years; its products will require approval before they can be sold.

Because substantially all of the combined company's potential products will be in research, or preclinical or clinical development, revenues from sales of any products will not occur for at least the next several years, if at all. It is uncertain whether any of the combined company's products will be safe and effective or that regulatory approvals will be obtained. In addition, any products that the combined company develops may not be economical to manufacture on a commercial scale. Even if the combined company develops a product that becomes available for commercial sale, there is no certainty that consumers will accept the product. The combined company cannot predict whether it will be able to develop and commercialize any of Hyseq's protein candidates or Variagenics' molecular diagnostic products successfully. If it is unable to do so, the combined company's business, results of operations and financial condition will be materially adversely affected.

Neither Hyseq nor Variagenics has products in the commercial markets. The combined company will be unable to apply for regulatory approval of its potential products until additional research and development and testing have been performed. It is uncertain whether the combined company, or its strategic partners, will be permitted to undertake clinical testing of its potential products, or continue clinical testing of alfimeprase, and if the combined company is successful in initiating clinical trials, it may experience delays in conducting them. The clinical trials may not demonstrate the safety and efficacy of the combined company's potential products, and the combined company may encounter unacceptable side effects or other problems in the clinical trials. Should this occur, the combined company may have to delay or discontinue development of the potential product that causes the problem. After a successful clinical trial, the combined company cannot market products in the United States until regulatory approval is received. Even if the combined company is able to gain regulatory approval of its products after successful clinical trials and then commercialize and sell those products, the combined company may be unable to manufacture enough products to maintain its business, which could have a negative impact on its financial condition and the trading price of its common stock.

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The success of the combined company's business will depend on patents and other proprietary information.

Hyseq currently has patents that cover some of its technological discoveries and patent applications that it expects to cover some of its gene, protein and technological discoveries. Hyseq has seventeen issued patents relating to its gene and protein discoveries. Variagenics currently has patents and patents pending which cover or describe, respectively, single nucleotide polymorphisms and their application to pharmacogenetic studies, genotyping and haplotyping methods, and allele specific inhibitors. Variagenics owns or has rights to 26 issued U.S. patents relating to these methods. The combined company will continue to apply for patents for its discoveries. Hyseq and Variagenics cannot assure you that any of the combined company's applications will issue as patents, or that any patent issued to the combined company will not be challenged, invalidated, circumvented or held unenforceable by way of an interference proceeding or litigation. The patent positions of biotechnology companies involve complex legal and factual questions. Even though the combined company will own patents, it is uncertain whether:

the patents would be challenged;

protection against competitors will be provided by such patents; or

competitors will not independently develop similar products or design around the patents.

Hyseq seeks patents on:

full-length gene sequences;

partial gene sequences;

proteins produced by those genes;

antibodies to those proteins;

diagnostic and therapeutic methods involving such genes, proteins or antibodies; and

processes, devices and other technology that enhance the ability to develop and/or manufacture gene-based products.

Variagenics seeks patents on:

single nucleotide polymorphisms;

methods for identification of single nucleotide polymorphisms;

methods for genotyping and haplotyping;

diagnostic methods to select optimal therapeutic regimens based upon genetic and/or epigenetic assay methods;

diagnostic methods to stratify clinical trial subjects based on genotypes;

diagnostic methods to identify the basis of genetic variation of disease; and

allele specific inhibition of genes that have undergone loss of heterozygosity.

To obtain a patent on a novel gene, the combined company will need to identify a utility for the novel gene or the encoded protein it seeks to protect by patent law. Identifying a utility may require significant research and development with respect to which the combined company may incur a substantial expense and invest a significant amount of time. To obtain a patent on a pharmacogenetic method or technology relating to pharmacogenomics, the combined company may require enablement and utility data to secure a patent. Acquisition of such data may require significant research and development with respect to which the combined company may incur a substantial expense and invest a significant amount of time.

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Patent applications describing and seeking patent protection of methods, compositions, or processes relating to proprietary inventions involving human therapeutics or pharmacogenomics could require the

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combined company to generate data, which may involve substantial costs. Finally, the timing of the grant of a patent cannot be predicted.

Hyseq and Variagenics have relied and the combined company will also rely on trade secret protection for its confidential and proprietary information. Although the combined company's policy will be to enforce security measures to protect its assets, trade secrets are difficult to protect. The combined company expects to require all employees to enter into confidentiality agreements. However:

competitors may independently develop substantially equivalent proprietary information and techniques;

competitors may otherwise gain access to the combined company's trade secrets;

persons with whom Hyseq or Variagenics has or the combined company will have confidentiality agreements may disclose trade secrets;
or

the combined company may be unable to protect its trade secrets meaningfully.

Certain of the patent applications describing Hyseq's and Variagenics' proprietary methods are filed only in the United States. Even where Hyseq or Variagenics has filed its patent applications internationally, for some cases and in certain countries, it has chosen and the combined company may choose not to maintain foreign patent protection through failure to enter national phase or failure to pay maintenance annuities.

The combined company may be required to obtain licenses to patents or other proprietary rights of others in order to conduct research, development, or commercialization of some or all its programs. These required licenses may not, however, be made available on terms acceptable to the combined company. If the combined company does not obtain these licenses, it may encounter delays in product market introductions, incur substantial costs while it attempts to design around existing patents or not be able to develop, manufacture or sell products. Any of these obstacles could significantly harm the combined company's business, financial condition and operating results. Further, if the combined company does obtain these licenses, the agreed terms may necessitate reevaluation of the potential commercialization of any one of the combined company's programs.

The combined company will lack manufacturing experience and intends to rely initially on contract manufacturers.

The combined company will not have significant manufacturing facilities. The combined company will be dependent on contract research and manufacturing organizations, and will be subject to the risks of finalizing contractual arrangements, transferring technology and maintaining relationships with such organizations in order to file an Investigational New Drug application, or IND, with the Food and Drug Administration, or FDA, and proceed with clinical trials for any of its potential therapeutic protein candidates. The combined company will be dependent on third-party contract research organizations to conduct certain research, including good laboratory practices toxicology studies in order to gather the data necessary to file an IND with the FDA for any of its potential therapeutic protein candidates. Hyseq's potential therapeutic protein candidates have never been manufactured on a commercial scale. Third-party manufacturers may not be able to manufacture such proteins at a cost or in quantities necessary to make them commercially viable. In addition, if any of the potential therapeutic protein candidates enter the clinical trial phase, initially the combined company will be dependent on third-party contract manufacturers to produce the volume of current good manufacturing practices materials needed to complete such trials. The combined company will need to enter into contractual relationships with these or other organizations in order to (i) complete the good laboratory practices, or GLP, toxicology and other studies necessary to file an IND with the FDA, and (ii) produce a sufficient volume of current good manufacturing practices, or cGMP, material in order to conduct clinical trials of its potential therapeutic protein candidates. The combined company cannot be certain that it will be able to do so on a timely basis or that it will be able to obtain sufficient quantities of material on commercially reasonable terms. In addition, the failure of any of these relationships with third-party contract organizations may result in a delay of the combined company's filing for an IND, or its progress through the clinical trial phase. Any significant delay or interruption would have a material adverse effect on

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the combined company's ability to file an IND with the FDA and/or proceed with the clinical trial phase for any of its potential therapeutic protein candidates.

Moreover, contract manufacturers that the combined company may use must continually adhere to current cGMP regulations enforced by the FDA through a facilities inspection program. If the facilities of such manufacturers cannot pass a pre-approval plant inspection, the FDA premarket approval of the combined company's products will not be granted.

The combined company will be dependent upon collaborative arrangements.

The combined company will focus on new collaborative arrangements where the combined company would share costs of identifying, developing and marketing product candidates. There can be no assurance that the combined company will be able to negotiate new collaboration arrangements of this type on acceptable terms, or at all.

The success of the combined company's business will be dependent, in significant part, upon its ability to enter into multiple collaboration arrangements and to manage effectively the numerous issues that arise from such collaborations. Management of the combined company's relationships with its collaboration partners will require:

the combined company's management team to devote a significant amount of time and effort to the management of these relationships;

effective allocation of the combined company's resources to multiple projects; and

an ability to obtain and retain management, scientific and other personnel.

The combined company's need, including the need of its direct and indirect subsidiaries, to manage simultaneously a number of collaboration arrangements may not be successful, and the failure to manage effectively such collaborations would significantly harm the combined company's business, financial condition and results of operations.

The combined company will be dependent on key personnel.

The success of the combined company's business will be highly dependent on the principal members of its scientific and management staff, including its chairman and senior management team. The loss of the services of any such individual might significantly delay or prevent the combined company from achieving its scientific or business objectives. Competition among biotechnology and biopharmaceutical companies for qualified employees is intense. The ability to retain and attract qualified individuals is critical to the combined company's success. The combined company may not be able to attract and retain qualified employees currently or in the future on acceptable terms, or at all. The failure to do so would significantly harm the combined company's business, financial condition and results of operations.

The combined company must attract and retain qualified employees and consultants.

The combined company's success will depend on its ability to retain its key executive officers and scientific staff to develop its potential products and formulate its research and development strategy. The combined company will have programs in place to retain personnel, including programs to create a positive work environment and competitive compensation packages. Because competition for employees in the combined company's field is intense, however, it may be unable to retain its existing personnel or attract additional qualified employees. The combined company's success also depends on the continued availability of outside scientific collaborators to perform research and develop processes to advance and augment its internal research efforts. Competition for collaborators is intense. If the combined company does not attract and retain qualified personnel and scientific collaborators, and if it experiences turnover or difficulties recruiting new employees, its research and development programs could be delayed and the combined could experience difficulties in generating sufficient revenue to maintain its business.

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FDA regulatory approval of the combined company's products will be uncertain; the combined company will face heavy government regulation.

Products such as those that may be proposed to be developed by the combined company or its collaboration partners, typically will be subject to an extensive regulatory process by federal, state and local governmental authorities, including the FDA, and comparable agencies in other countries before the combined company may market and sell such products. In order to obtain regulatory approval of a drug product, the combined company or its collaboration partners must demonstrate to the satisfaction of the applicable regulatory agency, among other things, that such product is safe and effective for its intended uses. In addition, the combined company will need to show that the manufacturing facilities used to produce the products are in compliance with cGMP requirements. In the event the combined company or its collaboration partners, develop products classified as drugs, the combined company and its collaboration partners will be required to obtain appropriate approvals as well.

The process of obtaining FDA and other required regulatory approvals and clearances is lengthy and will require the combined company to expend substantial capital and resources. The combined company may not ultimately be able to obtain the necessary approvals and clearances. Moreover, if and when the combined company's products do obtain such approval or clearances, the marketing, distribution and manufacture of such products would remain subject to extensive ongoing regulatory requirements. Failure to comply with applicable regulatory requirements can result in:

warning letters;

finest;

civil penalties;

recall or seizure of products;

total or partial suspension of production;

refusal of the government to grant approvals, premarket clearance or premarket approval; or

withdrawal of approvals and criminal prosecution.

The combined company will also be subject to numerous federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, the environment and the use and disposal of hazardous substances used in connection with discovery, research and development work, including radioactive compounds and infectious disease agents. In addition, the combined company will be unable to predict the extent of government regulations or the impact of new governmental regulations that might significantly harm the discovery, development, production and marketing of the combined company's products. The combined company may be required to incur significant costs to comply with current or future laws or regulations and the combined company may be adversely affected by the cost of such compliance.

If the combined company markets molecular diagnostic products outside the United States, such products will be subject to foreign regulatory requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement. Such requirements vary from country to country and are becoming more restrictive throughout the European Community. The process of obtaining foreign regulatory approvals can be lengthy and require the expenditure of substantial capital and resources. The combined company or its collaboration partners may not be successful in obtaining the necessary approvals.

Any delay or failure by Hyseq and Variagenics or their collaboration partners to obtain regulatory approvals for their products:

would adversely affect their ability to generate product and royalty revenues;

could impose significant additional costs on them or their collaboration partners;

could diminish competitive advantages that the combined company may attain; and

would adversely affect the marketing of their products.

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The combined company will face intense competition.

The genomics, pharmacogenomics and biopharmaceutical industries are intensely competitive. The combined company's strategy as a biopharmaceutical company will be to find the genes of the human genome that are most likely to be involved in a disease condition and to focus on identifying product candidates from the proteins produced by genes. There are a finite number of genes in the human genome, virtually all of which have been or will soon be identified. The combined company's competitors will include major pharmaceutical, biotechnology and diagnostic firms, not-for-profit entities and United States and foreign government-financed programs, many of which have substantially greater research and product development capabilities and financial, scientific, marketing and human resources than the combined company will. As a result, they may succeed in identifying genes and determining their functions or developing products earlier than the combined company or its current or future collaboration partners will. They also may obtain patents and regulatory approvals for such products more rapidly than the combined company or its collaboration partners, or develop products that are more effective than those proposed to be developed by the combined company or its collaboration partners. Further, any potential products based on genes the combined company may identify ultimately will face competition from other companies developing gene-based products as well as from companies developing other forms of treatment for diseases which may be caused by, or related to, the genes the combined company identifies.

In addition, the technologies of the combined company, including pharmacogenomic technologies, have undergone and are expected to continue to undergo rapid and significant change. The combined company's competitors may make rapid technological developments which may result in products or technologies becoming obsolete, before the combined company could recover the expenses incurred. The introduction of less expensive or more effective drug discovery and development technologies, including technologies that may be unrelated to genomics, may also make the combined company's products and services obsolete. The combined company may not be able to make the necessary enhancements to its technology to compete successfully with newly emerging technologies.

Many of the companies developing competing products have significantly greater financial resources than the combined company will have. Many such companies also have greater expertise than the combined company or its collaboration partners will have in discovery, research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and marketing. Other smaller companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Academic institutions, government agencies and other public and private research organizations may also conduct research, seek patent protection and establish collaborative arrangements for discovery, research, clinical development and marketing of products similar to the combined company's products. These companies and institutions may compete with the combined company in recruiting and retaining qualified scientific and management personnel as well as in acquiring technologies complementary to the combined company's programs. The combined company will face competition with respect to:

product efficacy and safety;

the timing and scope of regulatory approvals;

availability of resources;

reimbursement coverage; and

price and patent position, including potentially dominant patent positions of others.

There can be no assurance that research and development by others will not render the products that the combined company may develop obsolete or uneconomical, or result in treatments, cures or diagnostics superior to any therapy or diagnostic developed by the combined company or that any therapy the combined company develops will be preferred to any existing or newly developed technologies. While Hyseq and Variagenics believe that the combined company's technology will provide a significant competitive advantage, any one of the combined company's competitors may discover and establish a patent position in one or more genes which the combined company designates as a product candidate, before the combined company does.

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The combined company will lack marketing experience for biopharmaceuticals and pharmacogenomic products.

The combined company will have no sales, marketing or distribution capability. For the foreseeable future, the combined company intends to rely primarily on collaboration partners or licensees, if any, to market its products. Such collaboration partners, however, may not have effective sales forces and distribution systems. If the combined company is unable to maintain or establish such relationships and is required to market any of its products directly, the combined company will have to develop its own marketing and sales force with the appropriate technical expertise and with supporting distribution capabilities. The combined company may not be able to maintain or establish such relationships with third parties or develop in-house sales and distribution capabilities. To the extent that the combined company may depend on its collaboration partners or third parties for marketing and distribution, any revenues the combined company receives will depend upon the efforts of such collaboration partners or third parties. Such efforts may not be successful, and the combined company will not be able to control the amount and timing of resources that such collaboration partners or third parties devote to its products.

The combined company's products may not be accepted in the marketplace.

Even if they are approved for marketing, products the combined company develops may never achieve market acceptance. The combined company's products, if successfully developed, will compete with a number of traditional drugs and therapies manufactured and marketed by major pharmaceutical and other biotechnology companies. The combined company's products will also compete with new products currently under development by such companies and others. The degree of market acceptance of any products developed by the combined company, alone, or in conjunction with its collaboration partners, will depend on a number of factors, including:

the establishment and demonstration of the clinical efficacy and safety of the products;

the products' potential advantage over alternative treatment methods; and

reimbursement policies of government and third-party payors.

Physicians, patients or the medical community in general may not accept and utilize any of the products that the combined company alone, or in conjunction with its collaboration partners, develop. The lack of such market acceptance would significantly harm the combined company's business, financial condition and results of operations.

The combined company may develop molecular diagnostic testing products in the future. The combined company's success in diagnostics will depend in large part upon its ability to obtain customers and upon the ability of these customers to market genetic tests performed with its technology properly. Genetic tests may be difficult to interpret and may lead to misinformation or misdiagnosis. Ethical concerns about genetic testing may adversely affect market acceptance of the combined company's technology for diagnostic applications. Impaired market acceptance of its technology could significantly harm the combined company's business, financial condition and operating results.

The combined company may face uncertainty with respect to pricing, third-party reimbursements and health care reform.

The combined company's ability to collect significant royalties from its products may depend on the combined company's ability, and the ability of its collaboration partners or customers, to obtain adequate levels of reimbursement from third-party payors such as:

government health administration authorities;

private health insurers;

health maintenance organizations;

pharmacy benefit management companies; and

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other health care related organizations.

Currently, third-party payors are increasingly challenging the prices charged for medical products and services, and the overall availability of third-party reimbursement is limited and uncertain for genetic predisposition tests. Third-party payors may deny their insured reimbursement if they determine that a prescribed device or diagnostic test (i) has not received appropriate clearances from the FDA or other government regulators, (ii) is not used in accordance with cost-effective treatment methods as determined by the third-party payor, or (iii) is experimental, unnecessary or inappropriate. If third-party payors routinely deny reimbursement, the combined company may not be able to market its products effectively. The combined company will also face the risk that it will have to offer its diagnostic products at prices lower than anticipated as a result of the current trend in the United States towards managed health care through health maintenance organizations. Prices could be driven down by health maintenance organizations which control or significantly influence purchases of health care services and products. Legislative proposals to reform health care or reduce government insurance programs could also adversely affect prices of the combined company's products. The cost containment measures that health care providers are instituting and the results of potential health care reforms may prevent the combined company from maintaining prices for its products that are sufficient for it to realize profits and may otherwise significantly harm the combined company's business, financial condition and operating results.

The combined company faces product liability exposure and potential unavailability of insurance.

The combined company risks financial exposure to product liability claims in the event that the use of products developed by the combined company or its collaboration partners, if any, result in personal injury. The combined company may experience losses due to product liability claims in the future. The combined company will have limited product liability insurance coverage. Such coverage, however, may not be adequate or may not continue to be available to the combined company in sufficient amounts or at an acceptable cost, or at all. The combined company may not be able to obtain commercially reasonable product liability insurance for any product approved for marketing. A product liability claim or other claim, product recalls, as well as any claims for uninsured liabilities or in excess of insured liabilities, may significantly harm the combined company's business, financial condition and results of operations.

The combined company will use hazardous materials, chemicals and patient samples in its business and any disputes relating to improper handling, storage or disposal of these materials could be time consuming and costly.

The combined company's research and development, production and service activities will involve the controlled use of hazardous or radioactive materials, chemicals, including oxidizing and reducing reagents, and patient tissue and blood samples. The combined company will be subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and certain waste products. The combined company could be liable for accidental contamination or discharge or any resultant injury from hazardous materials, conveyance, processing, and storage of and data on patient samples. If the combined company fails to comply with applicable laws or regulations, it could be required to pay penalties or be held liable for any damages that result and this liability could exceed its financial resources. Further, future changes to environmental health and safety laws could cause the combined company to incur additional expense or restrict its operations.

In addition, the combined company's collaborators may be working with these types of hazardous materials, including viruses and hazardous chemicals, in connection with the combined company's collaborations. In the event of a lawsuit or investigation, the combined company could be held responsible for any injury caused to persons or property by exposure to, or release of, these patient samples that may contain viruses and hazardous materials. The cost of this liability could exceed the combined company's resources.

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Risk of Natural Disasters and Power Blackouts

Hyseq's facilities are located in Sunnyvale, California. In the event that a fire or other natural disaster (such as an earthquake) disrupts the combined company's research or development efforts, the combined company's business, financial condition and operating results could be materially, adversely affected. Some of the combined company's landlords maintain earthquake coverage for its facilities. Although the combined company will maintain personal property and business interruption coverage, it will not maintain earthquake coverage for personal property or resulting business interruption.

Variagenics is a defendant in a class action suit and defending this litigation could hurt the combined company's business.

Variagenics and certain underwriters are defendants in a securities class action lawsuit relating to the failure to disclose additional and excessive commissions purportedly solicited by and paid to underwriters named in the lawsuit in exchange for allocating shares of Variagenics stock to preferred customers and alleged agreements among the underwriters named in the lawsuit and preferred customers tying the allocation of initial public offering shares to agreements to make additional aftermarket purchases at pre-determined prices. Variagenics has been defending, and the combined company will be obligated to continue to defend, against this litigation, if such litigation is not completed or settled by the time the merger closes. Variagenics defense, and ultimately the combined company's defense, of this lawsuit could result in substantial costs and a diversion of management's attention and resources, which could hurt the combined company's business. In addition, if following the closing of the merger the combined company loses this litigation, or settles on adverse terms, Hyseq's stock price may be adversely affected.

The combined company will have anti-takeover provisions that may reduce the market price of its common stock.

Hyseq's by-laws provide that members of its board of directors serve staggered three-year terms. Hyseq's articles of incorporation provide that all stockholder action must be effected at a duly called meeting and not by a consent in writing. Hyseq's by-laws provide, however, that its stockholders may call a special meeting of stockholders only upon a request of stockholders owning at least 50% of Hyseq's capital stock. These provisions of Hyseq's articles of incorporation and by-laws, which will become the articles of incorporation and bylaws of the combined company, could discourage potential acquisition proposals and could delay or prevent a change in control. These provisions are intended to enhance the likelihood of continuity and stability in the composition of Hyseq's board of directors and in the policies formulated by its board of directors. Hyseq also intended these provisions to discourage certain types of transactions that may involve an actual or threatened change of control. Hyseq designed these provisions to reduce its vulnerability to unsolicited acquisition proposals and to discourage certain tactics that may be used in proxy fights. These provisions, however, could also have the effect of discouraging others from making tender offers for the combined company's shares. As a consequence, they also may inhibit fluctuations in the market price of the combined company's shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in the combined company's management. See Comparison of Stockholder Rights and Corporate Governance Matters.

Hyseq is permitted to issue shares of its preferred stock without stockholder approval upon such terms as its board of directors determines. Therefore, the rights of the holders of the combined company's common stock will be subject to, and may be adversely affected by, the rights of the holders of its preferred stock that may be issued in the future. In addition, the issuance of preferred stock could have a dilutive effect on the holdings of the combined company's stockholders.

On June 5, 1998, Hyseq's board of directors adopted a rights plan and declared a dividend with respect to each share of Hyseq common stock then outstanding. This dividend took the form of a right, which entitles the holders to purchase one-one thousandth of a share of Hyseq Series B junior participating preferred stock at a purchase price of \$175, subject to adjustment from time to time. These rights have also been issued in connection with each share of its common stock issued after June 15, 1998. The rights are exercisable only if

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a person or entity or affiliated group of persons or entities acquires, or has announced its intention to acquire, 15% (27.5% in the case of certain approved stockholders) or more of its outstanding common stock. The adoption of the rights plan makes it more difficult for a third party to acquire control of the combined company without the approval of its board of directors. See Comparison of Stockholder Rights and Corporate Governance Matters.

Nevada Revised Statutes Sections 78.411 through 78.444 prohibit an interested stockholder, under certain circumstances, from entering into specified combination transactions with a Nevada corporation, unless certain conditions are met. Under the statute, an interested stockholder is a person who beneficially owns, directly or indirectly, 10% or more of a corporation's voting stock or an affiliate or associate of a corporation who at any time within the prior three years beneficially owned, directly or indirectly, 10% or more of a corporation's voting stock. According to the statute, Hyseq, and ultimately the combined company, may not engage in a combination within three years after an interested stockholder acquires its shares, unless (i) its board of directors approves the combination prior to the interested stockholder becoming an interested stockholder or (ii) holders of a majority of voting power not beneficially owned by the interested stockholder approve the combination at a meeting called no earlier than three years after the date the interested stockholder became an interested stockholder.

Nevada Revised Statutes Sections 78.378 through 78.3793 further prohibit an acquirer, under certain circumstances, from voting shares of a target corporation's stock after crossing certain threshold ownership percentages, unless the acquirer obtains the approval of the target corporation's stockholders. This statute only applies to Nevada corporations that do business directly or indirectly in Nevada. The combined company does not intend to do business in Nevada within the meaning of the statute. Therefore, it is unlikely that the statute will apply to the combined company.

The provisions of Hyseq's, and ultimately the combined company's, governing documents, its existing agreements and current Nevada law may, collectively:

lengthen the time required for a person or entity to acquire control of the combined company through a proxy contest for the election of a majority of its board of directors;

discourage bids for common stock of the combined company at a premium over market price; and

generally deter efforts to obtain control of the combined company.

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CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This joint proxy statement/prospectus and the other documents incorporated by reference into this joint proxy statement/prospectus may contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 with respect to the financial condition, results of operations, business strategies, operating efficiencies or synergies, competitive positions, growth opportunities for existing products, plans and objectives of management, and markets for the Hyseq common stock and Variagenics common stock and other matters. Statements in this joint proxy statement/prospectus and the other documents incorporated by reference that are not historical facts are hereby identified as forward-looking statements for the purpose of the safe harbor provided by Section 21E of the Exchange Act and Section 27A of the Securities Act of 1933. These forward-looking statements are necessarily estimates reflecting the best judgment of the respective management of Hyseq and Variagenics and involve a number of risks and uncertainties that could cause actual results to differ materially from those suggested by the forward-looking statements. These forward-looking statements should, therefore, be considered in light of various important factors, including those set forth under Risk Factors and elsewhere in this joint proxy statement/ prospectus and other important factors incorporated by reference into this joint proxy statement/ prospectus.

Words such as estimate, project, plan, intend, expect, anticipate, believe and similar expressions are intended to identify forward-looking statements. These forward-looking statements are found at various places throughout this joint proxy statement/prospectus and the other documents incorporated by reference. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this joint proxy statement/prospectus, or in the case of documents incorporated by reference, as of the date of those documents. Neither Hyseq nor Variagenics undertakes any obligation to publicly update or release any revisions to these forward-looking statements to reflect events or circumstances after the date of this joint proxy statement/prospectus or to reflect the occurrence of unanticipated events, except as required by law.

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THE MERGER

The following is a description of the material aspects of the merger. While Hyseq and Variagenics believe that the following description covers the material terms of the merger, the description may not contain all of the information that is important to you. Hyseq and Variagenics encourage you to read carefully this entire joint proxy statement/prospectus, including the merger agreement attached to this joint proxy statement/prospectus as Annex A, for a more complete understanding of the merger.

General

Each of the Hyseq board of directors and the Variagenics board of directors has approved the Agreement and Plan of Merger, dated as of November 9, 2002, by and among Hyseq, Vertical Merger Corp. and Variagenics, or the merger agreement. At the effective time of the merger, Vertical Merger Corp. will be merged with and into Variagenics, following which Variagenics will be merged with and into Hyseq. As a result of the mergers, Variagenics will cease to exist and Variagenics stockholders will be entitled to receive 1.6451 shares of Hyseq common stock for each share of Variagenics common stock they own.

Background of the Merger

It is the practice of the Hyseq board of directors and the Variagenics board of directors to review periodically with senior management of their respective companies developments at the company and strategic alternatives available to it in order to remain competitive and to enhance stockholder value. As part of Variagenics' on-going assessment of its strategic alternatives in mid-2001, Variagenics believed that it might be beneficial to Variagenics and its stockholders to explore various strategic alternatives in light of the price at which Variagenics' common stock was trading at the time. In August 2001, Variagenics board directed management to further explore Variagenics' strategic alternatives and, in connection with such strategic alternatives, decided to retain SG Cowen as Variagenics' financial advisor to assist with a transaction involving a potential business combination.

During the months of August and September 2001, Variagenics' management, with the assistance of SG Cowen, prepared a preliminary list of approximately 60 potential business combination candidate companies, including Hyseq. These companies encompassed a diverse range of strategic alternatives and included large pharmaceutical companies, large-, mid- and small-cap biotechnology companies and contract research organizations. During the fourth quarter of 2001, Variagenics, assisted by SG Cowen, contacted approximately 25 of these companies, but not Hyseq, and Variagenics initiated business and scientific diligence with several potential candidates.

In February 2002, Variagenics selected seven of these companies to present proposals for a transaction with Variagenics to either the Variagenics board of directors or a subcommittee of the board of directors. Of the seven companies, the board of directors decided to enter into further discussions with one party. However, these discussions ended in late April 2002 without the execution of a definitive agreement.

In late February 2002, Variagenics, with the assistance of SG Cowen, reinitiated discussions with previously contacted parties and made initial contact with several other companies, including Hyseq. Separately, in late January 2002, Martin Vogelbaum, a member of the board of directors of Variagenics, met Dr. Ted W. Love, the President and Chief Executive Officer of Hyseq, and a member of its board of directors, while Dr. Love was in New York meeting with existing and potential investors in Hyseq. As a result of their discussions, Mr. Vogelbaum and Dr. Love formed an initial impression that there may be some basis for a strategic relationship between the two companies, and agreed to explore the possibility further.

On February 27, 2002, Dr. George Rathmann, Chairman of the Hyseq board of directors, Dr. Love and several members of senior management of Hyseq met with Mr. Vogelbaum and several directors and members of senior management of Variagenics in Cambridge, Massachusetts, to hold general discussions regarding a possible strategic transaction between the two companies.

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Shortly thereafter, in March 2002, Mr. Vogelbaum contacted Dr. Love to place discussions on hold. In May 2002, Mr. Vogelbaum contacted Dr. Love to reinstate discussions. On May 24, 2002, Hyseq and Variagenics entered into a mutual confidentiality agreement.

On March 7, 2002, Variagenics engaged SG Cowen as its financial advisor in connection with a potential business combination involving the company.

On May 29, 2002, at a regularly scheduled meeting of the Hyseq board of directors, Dr. Love and Mr. Peter S. Garcia, Senior Vice President and Chief Financial Officer of Hyseq, reviewed for the board of directors the initial discussions with Variagenics and the rationale for a potential strategic transaction between the two companies. The board authorized Dr. Love to continue discussions with Variagenics.

From May through June 2002, Variagenics selected ten of the companies that it had either initiated or reinstated discussions with to present proposals for a transaction with Variagenics to either the Variagenics board or a subcommittee of the board. Representatives from several companies made presentations to the Variagenics board, including a presentation by Hyseq to the Variagenics board in Cambridge, Massachusetts on June 5, 2002. At a meeting of a subcommittee of the Variagenics board on June 20, 2002, with input from other board members, the subcommittee determined that Variagenics should pursue further discussions with four companies, including Hyseq, and authorized management to engage in such discussions.

Beginning the week of June 10, 2002, representatives of Variagenics and Hyseq began exchanging additional information and discussing the proposed structure and terms of a potential business combination of the two companies. On July 9, 2002, representatives of Hyseq met with representatives of Variagenics in Cambridge, Massachusetts to exchange information concerning each company's business, financial and intellectual property affairs and to further conduct due diligence.

In July 2002, Hyseq contacted Banc of America Securities to discuss engaging them as its financial advisors. Hyseq consulted with Banc of America Securities informally throughout the remaining negotiation process, and formally engaged them in September 2002.

On August 6, 2002, at a regularly scheduled meeting of the Hyseq board of directors, Dr. Love and Mr. Garcia updated the board on the status of the ongoing discussions with Variagenics. The board authorized Dr. Love to continue discussions.

On August 9, 2002, the Variagenics board met to review and discuss Variagenics' strategic alternatives, including a possible business combination with Hyseq. Following a lengthy review and discussion, a consensus emerged among the Variagenics board members that Variagenics' standalone cancer molecular diagnostics business model, with or without pharmaceutical collaborations, was unlikely to generate near term sustainable value for shareholders and that, accordingly, Variagenics should continue to explore the potential combination with Hyseq, or with a company engaged in the development of cancer therapeutics. The Variagenics board authorized management to continue discussions with Hyseq and to explore a potential business combination with two other separate companies.

On August 13, 2002, at the direction of Variagenics, a representative of SG Cowen called Dr. Love to tell him that the Variagenics board of directors was still interested in moving forward with negotiations with Hyseq. SG Cowen and Dr. Love had several further telephone conversations over the following weeks regarding a potential transaction and in order to coordinate a further meeting between management and directors of both companies.

On August 30, 2002, representatives of Hyseq met with representatives of Variagenics in New York City to continue the exchange of information concerning each other's business, financial, legal and intellectual property affairs, to further conduct due diligence and to negotiate the terms of a possible business combination. The participants discussed various possible types of strategic transactions, but eventually settled on a potential merger as the most mutually advantageous type of transaction. After the meeting, representatives of both companies held follow-up discussions by telephone into September 2002.

On September 8, 2002, Hyseq delivered to Variagenics an outline of proposed key transaction terms, including proposals with respect to transaction structure, integration issues, strategy and focus of the

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combined company, various governance issues and valuation of both companies for purposes of determining an exchange ratio.

On September 11, 2002, the Variagenics board met via conference call and determined that Hyseq's proposal was sufficiently acceptable to proceed further with negotiations, and authorized management and SG Cowen to continue negotiations with Hyseq and to continue discussions with two other companies regarding either a strategic alliance or a business combination.

On September 17, 2002, a representative of Hyseq met with representatives of Variagenics in Cambridge, Massachusetts to conduct further due diligence regarding Variagenics.

On September 19, 2002, the senior managements and legal, accounting and financial advisors of both companies participated in a telephonic conference call during which they discussed alternative structures for the combination, target dates for announcement of the transaction, the due diligence requirements of the parties and a schedule for completion of due diligence and the process for preparing and negotiating a definitive merger agreement.

From September 19, 2002 through November 8, 2002, Variagenics and Hyseq, and their respective representatives conducted due diligence concerning, among other things, the legal, financial, business and intellectual property affairs of the other party.

Despite lack of agreement regarding significant terms of a possible transaction, on September 23, 2002, Latham & Watkins, counsel to Hyseq, distributed to Variagenics and its representatives a first draft of the merger agreement. From September 24, 2002 through November 8, 2002, Hyseq and Variagenics, together with their respective advisors and counsel, negotiated the terms of the definitive merger agreement and the ancillary agreements.

Throughout September and October 2002, Dr. Love held a number of telephone conversations with Mr. Vogelbaum and a representative of SG Cowen regarding the proposed transaction. On September 30, 2002, while at a conference in Europe, Dr. Love met with Mr. Jean-Francois Formela, another member of the Variagenics board of directors and a representative of SG Cowen, and held further discussions.

From October 1, 2002 through October 3, 2002, representatives of Variagenics met with representatives of Hyseq in Sunnyvale, California, to conduct further due diligence regarding Hyseq.

Throughout the period from August 6 through November 9, 2002, Dr. Love had periodic telephone conversations with the members of the Hyseq board of directors regarding the status of the merger discussions. On October 1, 2002, the Hyseq board of directors also received a detailed written summary of the status of negotiations, including material terms of the proposed merger agreement and material open issues.

On October 22, 2002, the Variagenics board met to, among other things, review and discuss Variagenics' strategic alternatives. The board received a presentation from a privately-held company that had expressed an interest in a business combination with Variagenics. The board also considered an orderly shut-down of the company and liquidation of its assets. The board requested that management provide the board with detailed information and financial projections for such a course of action. The board also reviewed and discussed the proposed merger with Hyseq. After review and discussion of the results of due diligence, the board concluded that several modifications to the proposed terms were desirable, and requested that its advisors seek to negotiate such modified terms. After further discussion, the board again concluded that a standalone cancer molecular diagnostics business model, with or without pharmaceutical collaborations, was unlikely to generate near-term sustainable value for stockholders and that, accordingly, Variagenics should continue to explore the potential combination with Hyseq, or with a company engaged in the development of cancer therapeutics.

On October 23, 2002, Mr. Vogelbaum with SG Cowen contacted Dr. Love to discuss the proposed modifications to the merger agreement.

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On November 1, 2002, the Variagenics board met via teleconference to receive an update concerning the proposed merger with Hyseq. After review and discussion of the update, the board determined that further modifications to the proposed terms were desirable, and requested that its advisors seek to negotiate such modified terms. The board also considered an orderly shut-down of the company and liquidation of its assets, using financial information and projections that had been prepared by the management of Variagenics. After review and discussion of the information and projections, a consensus of the board emerged that such a course of action was unlikely to generate value for stockholders comparable to the value perceived in the proposed merger with Hyseq and was, therefore, an undesirable outcome among the strategic alternatives being considered.

Later that day, representatives of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., or Mintz Levin, Variagenics' legal advisors, contacted representatives of Latham & Watkins to present the further modifications requested by the Variagenics board.

On November 3, 2002, the Hyseq board of directors held a special telephonic meeting to consider the further modifications proposed by Variagenics and agreed on counterproposals to Variagenics. Dr. Love contacted Mr. Vogelbaum, and Hyseq's financial and legal advisors contacted the financial and legal advisors of Variagenics, to communicate the counterproposals.

On November 6, 2002, Dr. Love and Mr. Vogelbaum held a telephone conversation to discuss Variagenics' response to Hyseq's counterproposal. Similar conversations occurred between the companies' legal advisors. From November 6 until November 8, the companies and their legal and financial advisors held several conversations to resolve outstanding issues and complete negotiation of the merger agreement and voting agreements.

On November 8, 2002, the Variagenics board and senior management met via teleconference to, among other things, receive an update concerning the proposed merger with Hyseq and consider the proposed terms of the merger. The board reviewed and discussed the update in detail. Representatives of Mintz Levin then described in detail the terms of the proposed agreement and the negotiations that had taken place with Hyseq and its representatives regarding the merger agreement, and the board's fiduciary duties in making a decision to approve a transaction of this type and the board asked questions regarding the merger agreement. Representatives of SG Cowen then described the procedures that it had followed in conducting its financial analysis with respect to the exchange ratio, and the board asked questions regarding that analysis. SG Cowen then orally delivered its opinion, subsequently confirmed in writing, which stated that, as of that date, the proposed exchange ratio under the merger agreement was fair, from a financial point of view, to Variagenics' stockholders. After lengthy discussion, during which the board reviewed and discussed Variagenics' strategic alternatives in detail, and asked several questions of the representatives of SG Cowen and Mintz Levin concerning the procedures that had been undertaken and the standards for review of the decision to be made by the board, the board determined that the proposed transaction was advisable, approved the merger agreement in the form in which it had been presented at the meeting, and resolved to include the board's recommendation in the proxy statement to be sent to stockholders of Variagenics in connection with the merger.

On November 9, 2002, the Hyseq board of directors held a special telephonic meeting, at which all of Hyseq's directors, other than Mr. Robert Weist, Hyseq's senior management and its financial and legal advisors were present. At the meeting, after representatives of Latham & Watkins had reviewed with the directors their fiduciary duties, Hyseq's senior management and representatives of Latham & Watkins updated the Hyseq board on developments since the November 3 board meeting. Representatives of Banc of America Securities made a financial presentation to the Hyseq board and delivered Banc of America Securities' oral opinion, subsequently confirmed in writing, that the exchange ratio pursuant to the merger agreement was fair from a financial point of view to Hyseq. Hyseq's senior management and representatives of Latham & Watkins updated the Hyseq board on the final results of Hyseq's due diligence review, and representatives of Latham & Watkins reviewed legal matters, including the terms of the proposed merger agreement and voting agreements. Following a lengthy discussion, the Hyseq board of directors unanimously approved the merger agreement and the transactions contemplated by it, including the issuance of shares in the merger, and

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unanimously resolved to recommend that the Hyseq stockholders vote to approve the issuance of shares in the merger.

The merger agreement and the voting agreements were executed by the parties later that day. On November 11, 2002, the companies issued a joint press release announcing the merger.

On November 22, 2002, Variagenics received an unsolicited business combination proposal from a third party. From November 25, 2002 through December 12, 2002, Variagenics and its representatives analyzed the proposal and conducted due diligence with respect to the party making such proposal and its business, including discussions with such party. On December 12, 2002, the Variagenics board of directors determined that such proposal was not in the best interests of Variagenics or its stockholders and determined to discontinue discussions with such party.

Reasons for the Merger-Hyseq

The Hyseq board of directors has unanimously approved the merger agreement and the transactions contemplated by the merger agreement, and recommends that the Hyseq stockholders vote FOR approval of the issuance of Hyseq common stock in connection with the merger.

In reaching its decision to approve the merger agreement, the Hyseq board of directors consulted with senior members of Hyseq's management team regarding the strategic and operational aspects of the merger and the results of the due diligence efforts undertaken by management and third party consultants. In addition, the Hyseq board of directors held discussions with representatives of Banc of America Securities regarding the past and current business operations, financial condition and future prospects of Variagenics. The Hyseq board of directors also consulted with Banc of America Securities as to the fairness, from a financial point of view to Hyseq, of the exchange ratio. The Hyseq board of directors also consulted with Hyseq's internal counsel and with representatives of Latham & Watkins regarding legal due diligence matters and the terms of the merger agreement and related agreements. Hyseq's management also retained KPMG to provide certain advisory services with respect to financial due diligence matters. In reaching its decision to approve the merger agreement, the Hyseq board of directors considered a variety of factors, a number of which are summarized below:

the potential strategic and other benefits of the merger, including the complementary nature of the businesses of Variagenics and Hyseq and the opportunity for significant cost savings, including through a reduction in force by the combined company and savings from consolidation of corporate and administrative infrastructures;

historical information concerning Variagenics' and Hyseq's respective businesses, financial performance and condition, operations, technology, management, competitive position and stock performance;

the fact that the merger would strengthen Hyseq's product focus and development pipeline, and hence its competitive position, through the following means:

- the financial resources of the combined company would expedite the development of alfineprase, a novel thrombolytic that Hyseq is currently developing in collaboration with Amgen;
- the financial resources and combined expertise of the two companies would facilitate the development of Hyseq's drug development pipeline based on its proprietary human proteins and significant intellectual property; and
- the combined company would benefit from Variagenics' proprietary cancer diagnostic program, which is focused on development of novel, high value molecular diagnostic products to guide the treatment of patients with colorectal cancer;

the combined company would benefit from the significant intellectual property assets of the two companies, including Hyseq's patents and patent applications relating to full and partial gene sequences and Variagenics' patents and patent applications relating to proprietary single nucleotide polymorphisms;

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the combined company is anticipated to have sufficient financial resources to fund operations through approximately December 2004;

the combined company would benefit from the strong partnerships of both companies, including, on the Hyseq side, partnerships with Amgen, Kirin and Deltagen, and, on the Variagenics side, a partnership with Novartis;

the combined company would benefit from the combined management expertise of the two companies, as well as the expertise of directors from both companies. The Hyseq board of directors also considered that Dr. Rathmann would be Chairman of the board of directors of the combined company and Dr. Love would be its Chief Executive Officer;

various strategic alternatives to the Merger, including remaining as an independent company and the consequent need that Hyseq would have to undertake further fundraising, as well as the difficult prevailing market conditions for public and private fundraising;

the general terms of the merger agreement, including:

- the fixed exchange ratio provides certainty as to the number of shares of Hyseq common stock to be issued to Variagenics stockholders and the percentage of the total shares of Hyseq common stock that current Variagenics stockholders will own after the merger. The Hyseq board of directors also considered the premium that the merger consideration implied;
- the provisions of the merger agreement that limit the ability of Variagenics to solicit other acquisition offers. The Hyseq board of directors also considered the provisions that require the payment of a \$1.75 million termination fee by Hyseq or Variagenics if the merger agreement is terminated due to specified reasons. The Hyseq board of directors believed that these provisions were reasonable under the circumstances; and
- the conditions to consummation of the merger, in particular the likelihood of obtaining the necessary stockholder approvals, the absence of any regulatory conditions and the likelihood that the merger would be completed;

the presentation of Banc of America Securities and the opinion of Banc of America Securities to the effect that, as of November 9, 2002, and subject to and based upon the considerations in its opinion, the exchange ratio pursuant to the merger agreement is fair, from a financial point of view, to Hyseq. See The Merger Opinion of Financial Advisor Hyseq;

the expected qualification of the merger and upstream merger, together, as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code resulting in the shares of Hyseq common stock being received by Variagenics stockholders free of federal income tax;

the terms of the stockholder voting agreements between Hyseq and certain of the officers and directors of Variagenics. The Hyseq board of directors noted that these stockholders, which as of the date of the Hyseq board meeting approving the merger beneficially owned approximately 15% of the outstanding shares of Variagenics common stock, have agreed to vote for approval of the merger agreement and against any competing proposal; and

the expected purchase accounting treatment of the merger as an acquisition of Variagenics by Hyseq.

In addition, the Hyseq board of directors also identified and considered a variety of potentially negative factors in its deliberations concerning the merger, a number of which are summarized below:

the risk that the potential benefits sought in the merger might not be fully realized;

the possibility that the merger might not be completed, or that completion might be unduly delayed;

the increased difficulty that Hyseq would have in fundraising prior to closing of the merger;

the effect of public announcement of the merger on Hyseq's stock price;

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the potential impact of the merger on the strategic partners, employees and customers of the companies, as well as any rights that might accrue under contractual arrangements if the merger and upstream merger, individually or collectively, were deemed to constitute a change in control ;

the fact that the Hyseq common stock to be issued in the merger will represent approximately 63% of the outstanding common stock of the combined company, and thus existing Hyseq stockholders would experience significant dilution in their percentage ownership of Hyseq as a result of the merger;

the risk that management's efforts to integrate the two companies will disrupt Hyseq's operations;

the substantial costs incurred in connection with the merger, including costs of integrating the businesses of the two companies, severance costs associated with reduction in personnel, and transaction expenses arising from the merger;

the risk that despite the efforts of the combined company, key management and employees might not remain employed by the combined company; and

various other risks associated with the merger and the businesses of Hyseq, Variagenics and the combined company described in the section entitled "Risks Factors" and in the documents incorporated by reference into this joint proxy statement/prospectus.

The Hyseq board of directors concluded, however, that overall, the potentially negative factors associated with the merger were outweighed by the potential benefits of the merger.

The above discussion of the factors considered by the Hyseq board of directors is not intended to be exhaustive, but is believed to set forth the principal factors considered by the Hyseq board of directors. The Hyseq board of directors collectively reached the unanimous conclusion to approve the merger agreement in light of the various factors described above and other factors that each member of the Hyseq board of directors felt were appropriate. In view of the wide variety of factors considered by the Hyseq board of directors in connection with its evaluation of the merger and the complexity of these matters, the Hyseq board of directors did not consider it practical, and did not attempt, to quantify, rank or otherwise assign relative weights to the specific factors it considered in reaching its decision. Rather, the Hyseq board of directors made its recommendation based on the totality of information presented to and the investigation conducted by it. In considering the factors discussed above, individual directors may have given different weights to different factors.

THE HYSEQ BOARD OF DIRECTORS UNANIMOUSLY RECOMMENDS THAT HYSEQ STOCKHOLDERS VOTE FOR APPROVAL OF THE ISSUANCE OF HYSEQ COMMON STOCK IN THE MERGER.

Reasons for the Merger Variagenics

Beginning in mid-2001, Variagenics' board recognized that the market for Variagenics' pharmacogenomics products and services was not developing and growing as planned. In an effort to determine a business strategy that would generate improved returns to Variagenics stockholders, Variagenics' board and management, with the assistance of Variagenics' financial advisor, implemented a process that extended over 14 months, and involved the evaluation of more than 60 opportunities, discussions with approximately 17 different companies and extensive discussions and meetings regarding business combination transactions with two different companies. Variagenics' board also gave consideration to other strategic alternatives, as well as paying stockholders a liquidating dividend. Upon completion of this process, a majority of the Variagenics board has determined that the terms of the merger with Hyseq and the merger agreement are fair to, and in the best interests of, Variagenics and its stockholders, has approved the merger agreement and the consummation of the merger and recommends that you vote your shares in favor of the merger and vote to adopt the merger agreement. The Variagenics board considered and reviewed with Variagenics management

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and Variagenics' legal and financial advisors the positive factors listed below, among various others, in reaching its decision to approve the merger and the merger agreement:

Strategic Factors

the strategic fit of combining Variagenics' molecular diagnostic program, proprietary SNP database and its significant cash reserves, people and facilities with Hyseq's novel thrombolytic alfineprase, biotherapeutic drug development pipeline, strong management team and product and clinical development expertise, which will give the combined, product-focused company the capability to capture maximum value from the potential upside in proprietary drug development and molecular diagnostics;

the forward integration of Variagenics with a biotherapeutic product-focused company such as Hyseq will allow Variagenics' stockholders the opportunity to participate in a significantly larger, more diversified company, with greater share liquidity;

the extensive search for a business combination partner for Variagenics that had been undertaken by Variagenics management, with the assistance of SG Cowen, and, following such thorough search, the fact that no other party had presented Variagenics with a business combination or acquisition proposal that would be more favorable from a financial and strategic point of view to Variagenics and its stockholders than the merger;

Hyseq's novel thrombolytic alfineprase, being developed with Amgen and which had recently entered Phase I clinical trials in eight U.S. centers, could potentially be a faster and more effective thrombolytic for a variety of indications representing a potentially significant market opportunity in the U.S.;

Hyseq's large collection of secreted protein genes represented a potentially robust drug development pipeline based on Hyseq's significant intellectual property;

the anticipated rapid integration into a combined company that is expected to employ approximately 110 to 120 employees and other steps taken to ensure operational efficiencies so that the combined company is expected to have cash sufficient to fund its operations through December 2004;

the fact that Hyseq's existing subsidiary, Callida Genomics, would remain a privately-held, separately funded, majority-owned subsidiary of the combined company;

the combined company's potential to create new and enhanced partnership opportunities;

the benefits of maintaining facilities located in Sunnyvale, California and Cambridge, Massachusetts;

the fact that three of the combined company's directors would come from Variagenics would help ensure that the benefits above would be realized; and

the ability of the Variagenics board under the terms of the merger agreement to negotiate and accept an unsolicited strategic transaction which the Variagenics board determines to be superior to the merger.

Financial Factors

the fact that the merger consideration of 1.6451 shares of Hyseq common stock for each share of Variagenics common stock represented a premium of approximately 131.3% over the average of the Variagenics common stock price for the 20 trading days preceding the announcement of the merger and a premium of approximately 200.1% over the closing price of Variagenics common stock on November 8, 2002, the business day prior to announcement of the merger;

the Variagenics board's understanding that based on negotiations between Hyseq and Variagenics, the merger consideration of 1.6451 shares of Hyseq common stock for each share of Variagenics common

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stock represented the highest exchange ratio that Hyseq would be willing to consider in acquiring Variagenics common stock;

the fact that given both the extensive search for a business combination partner for Variagenics that had been undertaken by Variagenics board and management, with the assistance of SG Cowen, as described above and the historical and current market prices for Variagenics common stock and the premium being paid by Hyseq, there could be no assurances as to whether or when another favorable opportunity for a strategic business combination would arise;

the fact that as Variagenics was exploring alternative strategic transactions as described in the section entitled "Background of the Merger," the alternative of paying Variagenics stockholders a liquidating dividend was believed to have been a less attractive and less valuable, from a financial point of view, than the merger;

the opinion, dated November 8, 2002, of SG Cowen, Variagenics financial advisor, as to the fairness, from a financial point of view, as of that date, of the exchange ratio pursuant to the merger agreement to the holders of Variagenics common stock, as described below under the section entitled "Opinion of Variagenics Financial Advisor";

the expected purchase accounting treatment of the merger as an acquisition of Variagenics by Hyseq;

the benefits to the combined company provided by Variagenics significant additional financial resources to fund the further clinical development of Hyseq's novel thrombolytic alfineprase and to accelerate Hyseq's biotherapeutic drug development pipeline, in light of Hyseq's cash position as outlined in the section entitled "Hyseq Management's Discussion and Analysis of Financial Condition and Results of Operations Liquidity and Capital Resources;" and

the fact that the merger was designed to be tax-free to Variagenics and its stockholders; and the enhanced liquidity that the Hyseq common stock would provide Variagenics stockholders since, following the merger, Hyseq common stock is anticipated to trade on the Nasdaq National Market with a higher trading volume.

In the course of its deliberations, the Variagenics board reviewed with Variagenics management and Variagenics legal and financial advisors a number of additional factors that the Variagenics board deemed relevant to the merger, including, but not limited to:

the strategic importance to Variagenics of the proposed merger;

the consideration to be received by Variagenics stockholders in the merger;

current financial market conditions and historical market prices, volatility and trading information with respect to the Variagenics common stock;

the information concerning Variagenics and Hyseq's respective businesses, prospects, strategic business plans, financial performances and conditions, results of operations, technology positions, management and competitive positions;

Variagenics management's view of the financial condition, results of operations and businesses of Variagenics before and after giving effect to the merger based on management due diligence and presentations by Variagenics management regarding operational aspects of the merger and the results of management's operational and legal due diligence review;

the views of Variagenics management and the Variagenics board as to the effect of the merger on the core business of Variagenics;

the belief by the Variagenics board that if Variagenics remained an independent public company with a standalone cancer molecular diagnostics business model, with or without pharmaceutical collaborations, there would unlikely be sufficient near-term sustainable value generated for the Variagenics stockholders given, among other factors, the difficulties in continuing such business

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model and the current state of capital markets for companies of Variagenics size and market capitalization;

the belief by the Variagenics board that Variagenics should capitalize on current market conditions while it still had a strong balance sheet, with significant cash reserves, and considerable research and technology assets;

the likelihood that the merger will be completed, including in particular the likelihood of obtaining the necessary stockholder approvals and the absence of any regulatory conditions;

the terms of the merger agreement, including the parties respective representations, warranties and covenants, and the conditions to the parties respective obligations; and

the impact of the merger on Variagenics strategic partners, employees and customers.

During the course of its deliberations concerning the merger, the Variagenics board also identified and considered a variety of potentially negative factors that could materialize as a result of the merger, including, but not limited to:

the risk that the potential benefits sought in the merger might not be fully realized;

the risk that Hyseq s novel thrombolytic alfineprase would fail in clinical trials or not achieve the expected results or market potential;

the risk that Hyseq s collection of secreted proteins and its biotherapeutic product development pipeline might not result in any commercial products;

the cost of Hyseq s leasing and having the option to own real estate facilities in excess of current and near term needs;

the risk that Variagenics molecular diagnostic program and/or proprietary SNP database would not or could not be strategically integrated with Hyseq s alfineprase and biotherapeutic drug development pipeline;

the risk that the expected operational efficiencies might not be achieved and that the combined company would not have cash sufficient to fund its operations through December 2004;

the risk that the combined company might not be able to raise financing on acceptable terms when necessary;

the possibility that the merger might not be consummated and the effect of the public announcement of the merger on Variagenics partners, customers and employees;

the challenges and significant costs, both financially and in terms of managerial efforts, to integrate the two businesses;

the possibility that the market value of the shares to be issued by Hyseq might decline;

the risk that despite the efforts of the combined company, key technical and management personnel might not remain employed by the combined company;

the transaction costs involved in connection with closing the merger; and

the other risks described under the section entitled Risk Factors.

The foregoing factors are not intended to be an exhaustive list of all factors considered. In view of the wide variety of factors considered in connection with its evaluation of the merger and the complexity of these matters, a majority of the Variagenics board found it impractical to, and did not, quantify or otherwise assign relative weights to the specific factors discussed above and considered in connection with its determination. In addition, a majority of the Variagenics board did not reach any specific conclusion with respect to each of the factors considered or any aspect of any particular factor. Instead, a majority of the Variagenics board conducted an overall analysis of the factors described above, including thorough discussion with and

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questioning of Variagenics' management and its legal and financial advisors. While a majority of the Variagenics board of directors concluded that the merger is advisable and fair to and in the best interests of Variagenics and its stockholders, one Variagenics director voted against the merger, principally because such director believed that the potentially negative factors identified above outweighed the expected benefits of the merger. A second Variagenics director abstained from voting in favor of or in opposition to the merger, because such director was unable to reach a conclusion on the advisability of the merger in light of the potentially negative factors identified above.

Taking into account all of the material facts, matters and information, including those described above, a majority of the Variagenics board of directors believes that the merger and the other transactions contemplated by the merger agreement are advisable and fair to and in the best interests of Variagenics and its stockholders.

THE VARIAGENICS BOARD OF DIRECTORS RECOMMENDS THAT VARIAGENICS STOCKHOLDERS VOTE FOR APPROVAL OF THE MERGER AND ADOPTION OF THE MERGER AGREEMENT.

Opinion of Financial Advisor – Hyseq

Hyseq retained Banc of America Securities LLC to act as its sole financial advisor in connection with the merger. Banc of America Securities is a nationally recognized investment banking firm and regularly engages in the valuation of businesses and their securities in connection with mergers and acquisitions, negotiated underwritings, secondary distributions of listed and unlisted securities, private placements and valuations for corporate and other purposes. Hyseq selected Banc of America Securities to act as its financial advisor on the basis of Banc of America Securities' experience and expertise in transactions similar to the merger, its reputation in the investment community and its historical investment banking relationship with Hyseq.

As part of this engagement as financial advisor to Hyseq, Banc of America Securities was asked to render an opinion to the Hyseq board of directors as to the fairness, from a financial point of view, to Hyseq of the exchange ratio provided for in connection with the merger. On November 9, 2002, Banc of America Securities delivered its oral opinion, which opinion was subsequently confirmed by delivery of its written opinion dated November 9, 2002, to the board of directors of Hyseq that, as of that date and subject to the various assumptions summarized below, the exchange ratio in the merger was fair, from a financial point of view, to Hyseq.

The full text of Banc of America Securities' written opinion to the board of directors of Hyseq, dated November 9, 2002, is attached as Annex C to this joint proxy statement/prospectus. This opinion sets forth the assumptions made, procedures followed, other matters considered and limits of the review undertaken. **Hyseq incorporates the Banc of America Securities opinion into this document and summary of opinion by reference and urges you to read the opinion in its entirety. This section is only a summary of the Banc of America Securities opinion and as a summary is qualified and not a substitute for the full text of such opinion.**

Banc of America Securities' analyses and opinion were prepared for and addressed to the Hyseq board of directors and are directed only to the fairness, from a financial point of view, of the exchange ratio in the merger to Hyseq. It does not constitute an opinion as to the merits of the merger or a recommendation to any stockholder as to how to vote on the proposed merger. The exchange ratio was determined through negotiations between Hyseq and Variagenics and not pursuant to recommendations of Banc of America Securities. Although Banc of America Securities provided advice to the Hyseq board of directors during such negotiations, Banc of America Securities did not recommend any specific form of consideration or any specific exchange ratio, or that any specific form of consideration or any specific exchange ratio constituted the only appropriate form or amount of consideration in connection with the merger. In furnishing its opinion, Banc of America Securities did not admit that it is an expert as that term is used in the Securities Act of 1933, nor did Banc of America Securities admit that its opinion constitutes a report or valuation within the

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meaning of the Securities Act. Statements to that effect are included in the Banc of America Securities opinion.

In arriving at its opinion, Banc of America Securities:

reviewed certain publicly available financial statements and other business and financial information of Hyseq and Variagenics, respectively;

reviewed certain internal financial statements and other financial and operating data concerning Hyseq and Variagenics, respectively;

analyzed certain financial forecasts prepared by the management teams of Hyseq and Variagenics, respectively;

discussed the past and current operations, financial condition and prospects of Hyseq with senior executives of Hyseq and discussed the past and current operations, financial condition and prospects of Variagenics with senior executives of Variagenics;

reviewed and discussed with senior executives of Hyseq information relating to certain strategic, financial and operational benefits anticipated from the merger;

reviewed the pro forma impact of the merger on Hyseq's cash flow, consolidated capitalization and financial ratios;

reviewed and discussed with senior executives of Hyseq and Variagenics certain information concerning the capital resources and liquidity requirements of Hyseq and Variagenics and the availability of alternative financing to Hyseq;

reviewed and considered in the analysis, information prepared by members of senior management of Hyseq and Variagenics relating to the relative contributions of Hyseq and Variagenics to the combined company;

reviewed the reported prices and trading activity for Variagenics common stock and Hyseq common stock;

compared the prices and trading activity of Variagenics common stock and Hyseq common stock with that of certain other publicly traded companies Banc of America Securities deemed relevant;

compared certain financial terms to financial terms, to the extent publicly available, of certain other business combination transactions Banc of America Securities deemed relevant;

participated in discussions and negotiations among representatives of Variagenics and Hyseq and their financial and legal advisors;

reviewed the November 6, 2002 draft of the merger agreement and certain related documents; and

performed such other analyses and considered such other factors as Banc of America Securities deemed appropriate.

In conducting Banc of America Securities' review and arriving at its opinion, Banc of America Securities assumed and relied upon, without independent verification, the accuracy and completeness of the information reviewed by Banc of America Securities for the purposes of its opinion. With respect to the financial forecasts, including information relating to certain strategic, financial and operational benefits anticipated from the merger, Banc of America Securities assumed that they have been reasonably prepared on bases reflecting the best currently available estimates and good faith judgments of the future financial performance of Hyseq and Variagenics. Banc of America Securities assumed that the merger would be consummated in accordance with the terms and conditions set forth in the merger agreement, including, among other things, that the merger would be treated as a tax-free reorganization, pursuant to the Internal Revenue Code of 1986. Banc of America Securities did not make any independent valuation or appraisal of the assets or liabilities of Hyseq, nor has Banc of America Securities been furnished with any such appraisals.

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As is customary in the rendering of fairness opinions, Banc of America Securities based its opinion on financial, economic, market and other conditions as in effect on, and the information made available to Banc of America Securities as of, November 9, 2002. It was understood that, although subsequent developments may affect Banc of America Securities' opinion, Banc of America Securities does not have any obligation to update, revise or reaffirm its opinion. Banc of America Securities' opinion did not address the prices at which Hyseq common stock will trade following consummation of the merger. The opinion of Banc of America Securities expressed in its opinion letter was provided for the information of the Hyseq board of directors. Banc of America Securities expressed no opinion or recommendation as to how the shareholders of Hyseq and Variagenics should vote with respect to the merger.

In accordance with customary investment banking practice, Banc of America Securities employed generally accepted valuation methods in reaching its opinion. The following is a summary of the material financial analyses that Banc of America Securities utilized in providing its opinion. Some of the summaries of financial analyses are presented in tabular format. In order to understand the financial analyses used by Banc of America Securities more fully, you should read the tables together with the related text. The tables alone do not constitute a complete description of the financial analyses utilized by Banc of America Securities.

Analysis of Implied Financing Discount. Banc of America Securities analyzed forecasts prepared by the management of Hyseq of Hyseq's cash funding requirements through 2008. As of November 9, 2002, Hyseq had sufficient cash and lines of credit to finance its projected operations through the first quarter of 2003. Banc of America Securities calculated that, based on Hyseq management estimates, the merger with Variagenics would provide Hyseq with access to \$40.0 million to \$46.0 million in cash currently held by Variagenics, which, according to projections of the combined company's financing requirements derived from combining forecasts of Hyseq's and Variagenics, cash funding requirements prepared by each company's respective management and assuming cost savings from certain headcount reductions identified by Variagenic's management, would adequately finance the combined company's operations through 2004.

Banc of America Securities analyzed various financing alternatives for Hyseq, including a private placement of Hyseq stock. Banc of America Securities concluded that, due to difficult equity market conditions, Hyseq could not raise sufficient funding in a single private placement to finance its projected operations through 2004 and would need to undertake a series of smaller financings. In addition, Banc of America Securities forecasted that any stock offered by Hyseq in a private placement would be sold at a significant discount to the market price of Hyseq's stock. Banc of America Securities estimated that any stock sold by Hyseq in a private placement would be sold at a discount to the market price of its common stock of at least 25%.

Banc of America Securities calculated that the \$40.0 to \$46.0 million in cash that Hyseq would obtain access to through successful completion of the merger implied a financing discount of 13.8% to 25.7% to Hyseq's closing stock price on November 7, 2002.

Discounted Cash Flow Analysis. Banc of America Securities performed discounted cash flow analyses by using financial cash flow projections of Hyseq and Variagenics for fiscal year 2003 through fiscal year 2008 prepared by the respective company management. In conducting this analysis, Banc of America Securities assumed that the companies would perform in accordance with these projections. Banc of America Securities first estimated the terminal values of the projected cash flows by applying perpetuity growth rates to Hyseq's and Variagenics' projected 2008 debt-free free cash flows, which rates ranged from 6% to 8%. Banc of America Securities then calculated the present values of the projected cash flows and the terminal values using discount rates ranging from 18% to 22% for Hyseq and 20% to 24% for Variagenics. Based on the results of this analysis, Banc of America Securities derived an implied exchange ratio reference range of 2.128 to 2.791.

Contribution Analysis. Banc of America Securities utilized the projections of the management of Hyseq and the projections of the management of Variagenics to compare the pro forma ownership of the combined company to the level implied by the pro forma contribution by each of Hyseq and Variagenics to the

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EBITDA and Net Income of the combined company, adjusted to reflect the companies' respective net debt balances, assuming completion of the merger. The purpose of this analysis was to assess the fairness from a financial point of view of the exchange ratio based on specific estimated future operating and financial information comparing the contribution of Hyseq and Variagenics to the combined company with the percentage of the combined company that each company's stockholders would hold upon completion of the merger.

The following table sets forth the ownership levels suggested by the selected financial performance benchmarks, as compared to the pro forma fully diluted ownership and implied exchange ratios after the merger.

	Implied Ownership Level		Implied Exchange Ratio
	Hyseq	Variagenics	
Projected 2007 EBITDA	31.8%	68.2%	1.976x
Projected 2008 EBITDA	28.4%	71.6%	2.315x
Projected 2007 Net Income	72.3%	27.7%	0.371x
Projected 2008 Net Income	49.9%	50.1%	0.950x

Premium Paid Analysis. Banc of America Securities reviewed ten acquisitions of public biotechnology companies announced since December 1999 that had aggregate values ranging from \$25 million to \$275 million (based on data provided by public filings). With respect to these transactions, Banc of America Securities analyzed the percentage premium of equity value paid above closing equity value one trading day, two weeks and four weeks prior to the announcement of the transaction. This analysis indicated the following median premiums paid in such transactions:

Period Prior to Announcement	Median Percentage Premium Paid	Implied Exchange Ratio
One Day	60.5%	0.933x
Two Weeks	53.9%	0.894x
Four Weeks	74.1%	1.012x

The premiums paid analysis compared the merger to selected transactions on the basis that the selected transactions were deemed to be the most relevant given the factors set forth above. Consequently, Banc of America Securities did not include every transaction that could be deemed to occur in the biotechnology industry.

Banc of America Securities noted that the corresponding premiums implied by the terms of this transaction one trading day and four weeks prior to the announcement of the merger are set forth in the following table:

Period Prior to Announcement	Percentage Premium Paid
One Day	128.0%
Two Weeks	138.7%
Four Weeks	164.7%

Although the selected transactions were used for comparative purposes, none of these transactions is directly comparable to the merger, and none of the companies in such transactions is directly comparable to Hyseq or Variagenics. Accordingly, an analysis of the foregoing results is not mathematical. Rather, it involves complex considerations and judgments concerning differences in historical and projected financial and operating characteristics of the companies involved and other factors that could affect the premiums paid in the transactions to which the merger is being compared.

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Historical Exchange Ratio Analysis. Banc of America Securities reviewed the ratios of the closing stock prices per share of Hyseq common stock to those of Variagenics common stock over certain periods ending November 7, 2002. This stock price analysis indicated that for the twelve months ended November 7, 2002, the average of the ratios of the closing prices of Hyseq common stock and Variagenics common stock was 1:0.512. Banc of America Securities also reviewed the following averages of the ratios of the closing prices of Hyseq's stock and Variagenics' stock over the following periods prior to November 7, 2002.

Trading Period	Average Ratio
Previous Month	0.688x
Previous Three Months	0.627x
Previous Six Months	0.581x

Banc of America Securities also noted that the ratio of the closing market prices of Hyseq common stock and Variagenics common stock on November 7, 2002 of \$1.40 and \$0.95, respectively, was approximately 1:0.679.

The summary set forth above does not purport to be a complete description of all the analyses performed by Banc of America Securities. The preparation of a fairness opinion involves various determinations as to the most appropriate and relevant methods of financial analyses and the application of these methods to the particular circumstances and, therefore, such an opinion is not readily susceptible to partial analysis or summary description. Banc of America Securities did not attribute any particular weight to any analysis or factor considered by it, but rather made qualitative judgments as to the significance and relevance of each analysis and factor. Accordingly, notwithstanding the separate factors summarized above, Banc of America Securities believes, and has advised Hyseq's board of directors, that its analyses must be considered as a whole and that selecting portions of its analyses and the factors considered by it, without considering all analyses and factors, could create an incomplete view of the process underlying its opinion. In performing its analyses, Banc of America Securities made numerous assumptions with respect to industry performance, business and economic conditions and other matters, many of which are beyond the control of Hyseq and Variagenics. These analyses performed by Banc of America Securities are not necessarily indicative of actual values or future results, which may be significantly more or less favorable than suggested by such analyses. In addition, analyses relating to the value of businesses do not purport to be appraisals or to reflect the prices at which businesses or securities may actually be sold. Accordingly, such analyses and estimates are inherently subject to uncertainty, being based upon numerous factors or events beyond the control of the parties or their respective advisors, none of Hyseq and Variagenics, Banc of America Securities or any other person assumes responsibility if future results are materially different from those projected. As mentioned above, the analyses supplied by Banc of America Securities and its opinion were among the factors taken into consideration by Hyseq's board of directors in making its decision to enter into the merger agreement and should not be considered as determinative of such decision.

Pursuant to a letter agreement, Hyseq has agreed to pay certain fees to Banc of America Securities for its financial advisory services provided in connection with the transaction. Banc of America Securities is entitled to a fee of \$100,000 upon execution of a definitive agreement and \$900,000 upon consummation of the transaction. Hyseq's board of directors was aware of this fee structure and took it into account in considering Banc of America Securities' fairness opinion and in approving the merger. Regardless of whether a transaction is proposed or completed, Hyseq has agreed to reimburse Banc of America Securities, immediately upon Banc of America Securities' request, for all reasonable out-of-pocket expenses, including reasonable fees and disbursements of Banc of America Securities' counsel, and has agreed to indemnify Banc of America Securities against certain liabilities, including liabilities under the federal securities laws. The terms of the fee arrangement with Banc of America Securities, which are customary in transactions of this nature, were negotiated at arm's length between Hyseq and Banc of America Securities.

Banc of America Securities and its affiliates have, in the past, performed various financial advisory and financing services for Hyseq, including having acted as sole placement agent in connection with Hyseq's \$15.0 million common stock private placement on April 8, 2002, and Banc of America Securities has

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received customary fees for such services. In addition, in the ordinary course of its business, Banc of America Securities and its affiliates are engaged in a broad range of securities activities and financial services, including trading or otherwise effecting transactions in debt or equity securities of Hyseq and Variagenics for their own account and for the accounts of their customers, and accordingly, may at any time hold a long or short position in such securities.

Opinion of Financial Advisor-Variagenics

Pursuant to an engagement letter dated March 7, 2002, Variagenics retained SG Cowen Securities Corporation to render an opinion to the board of directors of Variagenics as to the fairness, from a financial point of view, to the stockholders of Variagenics of the exchange ratio pursuant to the merger agreement.

On November 8, 2002, SG Cowen delivered certain of its written analyses and its oral opinion to the Variagenics board of directors, subsequently confirmed in writing as of the same date, to the effect that, and subject to the various assumptions set forth therein, as of November 8, 2002, the exchange ratio received pursuant to the merger agreement was fair, from a financial point of view, to the stockholders of Variagenics.

The full text of the written opinion of SG Cowen, dated November 8, 2002, is attached as Annex D and is incorporated into this joint proxy statement/prospectus by reference. Holders of Variagenics common stock are urged to read the opinion in its entirety for the assumptions made, procedures followed, other matters considered and limits of the review by SG Cowen. The summary of the written opinion of SG Cowen set forth herein is qualified in its entirety by reference to the full text of such opinion. SG Cowen's analyses and opinion were prepared for and addressed to the Variagenics board and are directed only to the fairness, from a financial point of view, of the exchange ratio pursuant to the merger agreement, and do not constitute an opinion as to the merits of the merger or a recommendation to any stockholder as to how to vote on the proposed merger. The exchange ratio was determined through negotiations between Variagenics and Hyseq and not pursuant to recommendations of SG Cowen.

In arriving at its opinion, SG Cowen reviewed and considered such financial and other matters as it deemed relevant, including, among other things:

a draft of the merger agreement dated November 6, 2002;

certain publicly available information for Variagenics and certain other relevant financial and operating data furnished to SG Cowen by Variagenics' management;

certain internal financial analyses, financial forecasts, reports and other information concerning Variagenics furnished to SG Cowen by Variagenics' management (referred to as the Variagenics forecasts);

certain publicly available information for Hyseq and certain other relevant financial and operating data furnished to SG Cowen by Hyseq's management;

certain internal financial analyses, financial forecasts, reports and other information concerning Hyseq furnished to SG Cowen by Variagenics' management (referred to as the Hyseq forecasts), including forecasts focused on the Alfimeprase business of Hyseq on a stand-alone basis (referred to as the Alfimeprase forecasts);

the amounts and timing of the cost savings and related expenses expected to result from the merger furnished to SG Cowen by Variagenics management (referred to as the expected synergies);

financial projections in a Wall Street analyst report for Variagenics;

discussions SG Cowen had with members of Variagenics' and Hyseq's management concerning the historical and current business operations, financial conditions and prospects of Variagenics and Hyseq, and such other matters SG Cowen deemed relevant;

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certain operating results, the reported price and trading history of the shares of Variagenics common stock as compared to operating results, the reported price and trading histories of certain publicly traded companies SG Cowen deemed relevant;

certain operating results, the reported price and trading history of the shares of Hyseq common stock as compared to the operating results, the reported price and trading histories of certain publicly traded companies SG Cowen deemed relevant;

certain financial terms of the merger as compared to the financial terms of certain selected business combinations SG Cowen deemed relevant;

based on the Variagenics forecasts, the cash flows generated by Variagenics on a stand-alone basis to determine the present value of the discounted cash flows;

based on the alfimeprase forecasts, the cash flows generated by the alfimeprase business of Hyseq on a stand-alone basis to determine the present value of the discounted cash flows;

a liquidation analysis of Variagenics furnished to SG Cowen by Variagenics; and

such other information, financial studies, analyses and investigations and such other factors that SG Cowen deemed relevant for the purposes of its opinion.

In conducting its review and arriving at its opinion, SG Cowen, with Variagenics' consent, assumed and relied, without independent investigation, upon the accuracy and completeness of all financial and other information provided to it by Variagenics and Hyseq, respectively, or which was publicly available. SG Cowen did not undertake any responsibility for the accuracy, completeness or reasonableness of, or independently to verify, this information. In addition, SG Cowen did not conduct, nor did it assume any obligation to conduct, any physical inspection of the properties or facilities of Variagenics or Hyseq. SG Cowen further relied upon the assurance of management of Variagenics that they were unaware of any facts that would make the information provided to SG Cowen incomplete or misleading in any respect. Variagenics directed SG Cowen to use for the purposes of its opinion and analyses the Hyseq forecasts and alfimeprase forecasts provided to SG Cowen by Variagenics management. SG Cowen, with Variagenics' consent, assumed that the Variagenics forecasts and the description of the expected synergies which SG Cowen examined were reasonably prepared by the management of Variagenics on bases reflecting the best currently available estimates and good faith judgments of such management as to the future performance of Variagenics and that such projections, and the Hyseq forecasts, alfimeprase forecasts and description of expected synergies, and the Wall Street projections used in SG Cowen's analyses, provide a reasonable basis for its opinion.

SG Cowen did not make or obtain any independent evaluations, valuations or appraisals of the assets or liabilities of Variagenics or Hyseq, nor was SG Cowen furnished with these materials. With respect to all legal matters relating to Variagenics and Hyseq, SG Cowen relied on the advice of legal counsel to Variagenics; however, Variagenics' counsel was not asked to, nor did it, provide any legal advice to SG Cowen. SG Cowen's services to Variagenics in connection with the merger were comprised of rendering an opinion from a financial point of view of the exchange ratio pursuant to the merger agreement. SG Cowen's opinion was necessarily based upon economic and market conditions and other circumstances as they existed and could be evaluated by SG Cowen on the date of its opinion. It should be understood that although subsequent developments may affect its opinion, SG Cowen does not have any obligation to update, revise or reaffirm its opinion and SG Cowen expressly disclaims any responsibility to do so.

In rendering its opinion, SG Cowen assumed, in all respects material to its analysis, that the representations and warranties of each party contained in the merger agreement are true and correct, that each party will perform all of the covenants and agreements required to be performed by it under the merger agreement and that all conditions to the consummation of the merger will be satisfied without waiver thereof. SG Cowen assumed that the final form of the merger agreement would be substantially similar to the last draft received by SG Cowen prior to rendering its opinion. SG Cowen also assumed that all governmental, regulatory and other consents and approvals contemplated by the merger agreement would be obtained and that, in the course of obtaining any of those consents, no restrictions will be imposed or waivers made that

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would have an adverse effect on the contemplated benefits of the merger. Variagenics informed SG Cowen, and SG Cowen assumed, that the merger will be treated as a tax-free reorganization.

SG Cowen's opinion does not constitute a recommendation to any stockholder as to how the stockholder should vote on the proposed merger. SG Cowen's opinion does not imply any conclusion as to the likely trading range for Hyseq common stock following consummation of the merger or otherwise, which may vary depending on numerous factors that generally influence the price of securities. SG Cowen's opinion is limited to the fairness, from a financial point of view, as of the date of its opinion, of the exchange ratio pursuant to the merger agreement. SG Cowen expresses no opinion as to the underlying business reasons that may support the decision of the Variagenics board to approve, or Variagenics' decision to consummate, the merger.

The following is a summary of the principal financial analyses performed by SG Cowen to arrive at its opinion. Some of the summaries of financial analyses include information presented in tabular format. In order to fully understand the financial analyses, the tables must be read together with the text of each summary. The tables alone do not constitute a complete description of the financial analyses. Considering the data set forth in the tables without considering the full narrative description of the financial analyses, including the methodologies and assumptions underlying the analyses, could create a misleading or incomplete view of the financial analyses. SG Cowen performed certain procedures, including each of the financial analyses described below, and reviewed with the management of Variagenics the assumptions on which such analyses were based and other factors, including the historical and projected financial results of Variagenics and Hyseq. No limitations were imposed by the Variagenics board with respect to the investigations made or procedures followed by SG Cowen in rendering its opinion.

Pro Forma Ownership. SG Cowen reviewed the pro forma ownership in the combined company by the holders of Variagenics common stock. SG Cowen noted that, on a diluted basis, holders of Variagenics common stock would own approximately 63% of the combined company, based on the Hyseq closing stock price on November 7, 2002.

Stock Trading History. To provide contextual data and comparative market data, SG Cowen reviewed the historical market prices of Variagenics common stock for the twelve month period ended November 7, 2002. SG Cowen noted that over the indicated period the high, mean and low closing prices of Variagenics common stock were \$3.30, \$1.89 and \$0.66, respectively.

SG Cowen also reviewed the historical market prices of Hyseq common stock for the twelve month period ended November 7, 2002. SG Cowen noted that over the indicated period the high, mean and low closing prices of Hyseq common stock were \$8.65, \$4.10 and \$1.12, respectively.

Historical Stock Trading Analysis. SG Cowen analyzed the closing prices of Variagenics common stock over various periods ending November 7, 2002. The table below lists the stock prices for those periods and the premium or discount implied by the offer price of \$2.30 in the merger, based on Hyseq's closing stock price of \$1.40 on November 7, 2002, to the historical stock price.

Period	Statistic	Premium/(Discount) Implied by Offer Price
Spot Stock Price		
November 7, 2002	\$0.95	142.4%
Latest Twelve Month High	3.30	(30.2)
Latest Twelve Month Low	0.66	249.0
Twenty Days Prior	0.74	211.2
Average Stock Price		
Latest Twenty Days	\$0.90	156.3%
Latest Two Months	0.91	153.7
Latest Three Months	0.98	134.6
Latest Six Months	1.14	101.5
Latest Twelve Months	1.89	21.9

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Historical Exchange Ratio Analysis. SG Cowen analyzed the ratios of the closing prices of Variagenics common stock to those of Hyseq common stock over various periods ending November 7, 2002. The table below lists the ratios for those periods and the premium or discount implied by the exchange ratio of 1.6451 in the merger to the historical exchange ratios.

Period	Statistic	Premium/(Discount) Implied by Exchange Ratio
Spot Exchange Ratio		
November 7, 2002	0.6786x	142.4%
Latest Twelve Month High	0.8699	89.1
Latest Twelve Month Low	0.2993	449.7
Twenty Days Prior	0.5034	226.8
Average Exchange Ratio		
Latest Twenty Days	0.6862x	139.7%
Latest Two Months	0.6274	162.2
Latest Three Months	0.6103	169.6
Latest Six Months	0.5828	182.3
Latest Twelve Months	0.5144	219.8

Analysis of Selected Publicly Traded Companies. To provide contextual data and comparative market information, SG Cowen compared selected historical and projected operating and financial data and ratios of Variagenics and Hyseq to the corresponding financial data and ratios of two groups of publicly traded companies that SG Cowen deemed relevant for the purposes of comparison to Variagenics and to the corresponding financial data and ratios of other publicly traded companies that SG Cowen deemed to be relevant for the purposes of comparison to Hyseq.

The Variagenics comparable companies consisted of:

Enabling SNP Technologies Companies

Illumina, Inc.
Orchid BioSciences, Inc.
Third Wave Technologies, Inc.

Nanogen, Inc.
Pyrosequencing AB
Transgenomic, Inc.

Discovery Using SNPs Companies

deCODE genetics, Inc.
Genome Therapeutics Corp.
Lynx Therapeutics, Inc.

Genaisance Pharmaceuticals, Inc.
Hyseq

The Hyseq comparable companies consisted of:

Celera Genomics Group
Deltagen, Inc.
Incyte Genomics, Inc.
Myriad Genetics, Inc.
Sangamo BioSciences, Inc.

CuraGen Corp.
Genome Therapeutics Corp.
Lexicon Genetics Inc.
Rigel Pharmaceuticals, Inc.
Sequenom, Inc.

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SG Cowen reviewed the value of the total outstanding equity (referred to as equity value) and the equity value plus net cash (referred to as enterprise value) of the Variagenics and Hyseq comparable companies. These analyses, which are based on closing stock prices on November 7, 2002, indicated the values as set forth in the following table:

	<u>High</u>	<u>Median</u>	<u>Mean</u>	<u>Low</u>	<u>Value Implied by Exchange Ratio</u>
	(\$ in millions)				
Variagenics comparable companies					
Equity value	\$ 144.1	\$ 38.7	\$ 57.3	\$ 14.2	\$58.1
Enterprise value	90.2	22.5	20.9	(33.8)	(0.1)
Hyseq comparable companies					
Equity value	\$715.8	\$148.2	\$231.4	\$ 38.7	NA
Enterprise value	324.0	4.5	21.9	(155.1)	NA

SG Cowen noted that, as of November 7, 2002, Variagenics' equity and enterprise values were \$23.1 million and \$(35) million, respectively, and that Hyseq's equity and enterprise values were \$32.7 million and \$38.1 million, respectively. In conducting this analysis, SG Cowen reviewed the multiples of the transaction and the Variagenics and Hyseq comparable companies and found them to be not meaningful because of the nature of the parties' revenue streams during the projection period.

Although the Variagenics and Hyseq comparable companies were used for comparison purposes, none of those companies is directly comparable to Variagenics or Hyseq. Accordingly, an analysis of the results of such a comparison is not purely mathematical, but instead involves complex considerations and judgments concerning differences in historical and projected financial and operating characteristics of the Variagenics and Hyseq comparable companies and other factors that could affect the public trading value of the Variagenics and Hyseq comparable companies and Variagenics and Hyseq.

Analysis of Selected Transactions. SG Cowen reviewed the financial terms of nine transactions involving the acquisition of public companies in the genomics industry in stock-for-stock transactions (referred to as genomics transactions), which were announced since November 7, 1999. These transactions were (listed as target/ acquiror):

Visible Genetics Inc./ Bayer Corp. (Diagnostics Division)

Genset S.A./ Serono S.A.

MediChem Life Sciences, Inc./ deCODE genetics, Inc.

Genomica Corp./ Exelixis, Inc.

Gemini Genomics plc/ Sequenom, Inc.

Rosetta Inpharmatics, Inc./ Merck & Co., Inc.

Aurora BioSciences Corp./ Vertex Pharmaceuticals Inc.

Agritope, Inc./ Exelixis, Inc.

Oxford Asymmetry International plc/ Evotec BioSystems AG

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SG Cowen reviewed the equity value and the enterprise value in the genomics transactions announced since November 7, 2001 and since November 7, 1999. These analyses indicated the values as set forth in the following table:

	<u>High</u>	<u>Median</u>	<u>Mean</u>	<u>Low</u>	<u>Value Implied by Exchange Ratio</u>
(\$ in millions)					
One Year					
Equity value	\$ 109.9	\$ 80.9	\$ 75.2	\$ 28.8	\$ 58.1
Enterprise value	103.1	51.7	51.4	(0.9)	(0.1)
Three Years					
Equity value	\$ 615.7	\$ 109.9	\$ 259.4	\$ 28.8	\$ 58.1
Enterprise value	501.1	103.1	209.7	(0.9)	(0.1)

Although the genomics transactions were used for comparison purposes, none of those transactions is directly comparable to the merger, and none of the companies in those transactions is directly comparable to Variagenics or Hyseq. Accordingly, an analysis of the results of such a comparison is not purely mathematical, but instead involves complex considerations and judgments concerning differences in historical financial and operating characteristics of the companies involved and other factors that could affect the acquisition value of such companies or Variagenics to which they are being compared.

Analysis of Premiums Paid in Selected Transactions. SG Cowen reviewed the premiums paid in four and nine genomics transactions announced since November 7, 2001 and since November 7, 1999, respectively. These analyses indicated the following premiums to the target closing stock price as set forth in the following table:

<u>Period Prior to Announcement</u>	<u>High</u>	<u>Median</u>	<u>Mean</u>	<u>Low</u>	<u>Premium Implied by Exchange Ratio</u>
One Year					
One Day	143.3%	35.3%	60.3%	27.1%	142.4%
Twenty Days	205.5	99.4	90.9	(40.7)	211.2
Three Years					
One Day	143.3%	41.4%	59.3%	26.3%	142.4%
Twenty Days	205.5	88.6	92.8	(40.7)	211.2

SG Cowen also reviewed the premiums paid in nine and 26 public, stock-for-stock transactions involving biopharmaceutical companies announced since November 7, 2001 and since November 7, 1999, respectively. These analyses indicated the following premiums to the target closing stock price as set forth in the following table:

<u>Period Prior to Announcement</u>	<u>High</u>	<u>Median</u>	<u>Mean</u>	<u>Low</u>	<u>Premium Implied by Exchange Ratio</u>
One Year					
One Day	143.3%	35.7%	54.7%	7.9%	142.4%
Twenty Days	205.5	74.9	76.3	(40.7)	211.2
Three Years					
One Day	143.3%	31.1%	38.0%	(24.2)%	142.4%
Twenty Days	205.5	47.3	60.9	(40.7)	211.2

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SG Cowen also reviewed the premiums paid in 19 and 41 public, stock-for-stock transactions involving healthcare companies announced since November 7, 2001 and since November 7, 1999, respectively. These analyses indicated the following premiums to the target's closing stock price as set forth in the following table:

Period Prior to Announcement	High	Median	Mean	Low	Premium Implied by Exchange Ratio
One Year					
One Day	121.0%	34.5%	47.5%	(34.7)%	142.4%
Twenty Days	164.7	80.0	73.5	(40.8)	211.2
Three Years					
One Day	121.0%	30.1%	37.9%	(34.7)%	142.4%
Twenty Days	216.4	59.6	62.3	(40.8)	211.2

SG Cowen also reviewed the premiums paid in 67 and 368 public, stock-for-stock transactions involving companies in all industries (including industries outside of healthcare) announced since November 7, 2001 and since November 7, 1999, respectively. These analyses indicated the following premiums to the target's closing stock price as set forth in the following table:

Period Prior to Announcement	High	Median	Mean	Low	Premium Implied by Exchange Ratio
One Year					
One Day	505.1%	18.9%	37.0%	(24.9)%	142.4%
Twenty Days	491.8	22.3	43.1	(45.2)	211.2
Three Years					
One Day	505.1%	25.0%	29.9%	(35.0)%	142.4%
Twenty Days	491.8	31.7	42.9	(55.1)	211.2

Although the premiums paid in the selected transactions were used for comparison purposes, none of those transactions is directly comparable to the merger, and none of the companies in those transactions is directly comparable to Variagenics or Hyseq. Accordingly, an analysis of the results of such a comparison is not purely mathematical, but instead involves complex considerations and judgments concerning differences in historical financial and operating characteristics of the companies involved and other factors that could affect the acquisition value of such companies or Variagenics to which they are being compared.

Review of Liquidation Analysis. SG Cowen reviewed a liquidation analysis of Variagenics' assets to calculate the potential range of net proceeds available for distribution upon liquidation of Variagenics, based on projections made by Variagenics' management relating to, among other things, the potential market value of Variagenics' assets, the amount of Variagenics' current liabilities and the potential amount of expenses associated with a liquidation. SG Cowen noted that, based on such projections, the net proceeds available upon liquidation at December 31, 2002 and March 31, 2003 were \$1.82 per share and \$1.67 per share, respectively.

Discounted Cash Flow Analysis. SG Cowen estimated a range of enterprise values for Variagenics based upon the discounted present value of the projected cash flows of Variagenics described in the Variagenics forecasts for the fiscal years ended December 31, 2003 through December 31, 2008, and of the terminal value of Variagenics at December 31, 2008, based upon multiples of revenue. In performing this analysis, SG Cowen used discount rates ranging from 14% to 18% and terminal multiples of revenue ranging from 4.0 times to 6.0 times. Using this methodology, the implied enterprise value of Variagenics ranged from \$(89.6) million to \$(45.0) million.

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SG Cowen did not perform a discounted cash flow analysis of the Hyseq forecasts because the results would not have been meaningful. Instead, SG Cowen estimated a range of enterprise values for Hyseq based upon the discounted present value of the projected cash flows of the alfimeprase business of Hyseq on a stand-alone basis as described in the alfimeprase forecasts for the fiscal years ended December 31, 2003 through December 31, 2016, and of the terminal value of the alfimeprase business at December 31, 2016, based upon multiples of revenue. In performing this analysis, SG Cowen used discount rates ranging from 20% to 30% and used terminal multiples of revenue ranging from 1.0 times to 2.0 times. Using this methodology, the implied enterprise value of the alfimeprase business of Hyseq on a stand-alone basis ranged from \$5.5 million to \$77.8 million.

The summary set forth above does not purport to be a complete description of all the analyses performed by SG Cowen. The preparation of a fairness opinion involves various determinations as to the most appropriate and relevant methods of financial analyses and the application of these methods to the particular circumstances and, therefore, such an opinion is not readily susceptible to partial analysis or summary description. SG Cowen did not attribute any particular weight to any analysis or factor considered by it, but rather made qualitative judgments as to the significance and relevance of each analysis and factor. Accordingly, notwithstanding the separate factors summarized above, SG Cowen believes, and has advised the Variagenics board, that its analyses must be considered as a whole and that selecting portions of its analyses and the factors considered by it, without considering all analyses and factors, could create an incomplete view of the process underlying its opinion. In performing its analyses, SG Cowen made numerous assumptions with respect to industry performance, business and economic conditions and other matters, many of which are beyond the control of Variagenics and Hyseq. These analyses performed by SG Cowen are not necessarily indicative of actual values or future results, which may be significantly more or less favorable than suggested by such analyses. In addition, analyses relating to the value of businesses do not purport to be appraisals or to reflect the prices at which businesses or securities may actually be sold. Accordingly, such analyses and estimates are inherently subject to uncertainty, being based upon numerous factors or events beyond the control of the parties or their respective advisors. None of Variagenics, Hyseq, SG Cowen or any other person assumes responsibility if future results are materially different from those projected. The analyses supplied by SG Cowen and its opinion were among several factors taken into consideration by the Variagenics board in making its decision to enter into the merger agreement and should not be considered as determinative of such decision.

SG Cowen was selected by the Variagenics board to render an opinion to the Variagenics board because SG Cowen is an internationally recognized investment banking firm and because, as part of its investment banking business, SG Cowen is continually engaged in the valuation of businesses and their securities in connection with mergers and acquisitions, negotiated underwritings, secondary distributions of listed and unlisted securities, private placements and valuations for corporate and other purposes. In addition, in the ordinary course of its business, SG Cowen and its affiliates trade the equity securities of Variagenics and Hyseq for their own accounts and for the accounts of their customers, and, accordingly, may at any time hold a long or short position in such securities. SG Cowen and its affiliates in the ordinary course of business have from time to time provided, and in the future may continue to provide, commercial and investment banking services to Variagenics and Hyseq, including serving as a financial advisor on potential acquisitions and as an underwriter on equity offerings, and have received and may in the future receive fees for the rendering of such services. In particular, in July 2000, SG Cowen acted as a co-manager of Variagenics' initial public offering.

Pursuant to the SG Cowen engagement letter, if the transaction is consummated, SG Cowen will be entitled to receive a customary transaction fee. Variagenics has also agreed to pay a customary fee to SG Cowen for rendering its opinion, which fee shall be credited against any transaction fee paid. Additionally, Variagenics has agreed to reimburse SG Cowen for its out-of-pocket expenses, including attorneys' fees, and has agreed to indemnify SG Cowen against certain liabilities, including liabilities under the federal securities laws. The terms of the fee arrangement with SG Cowen, which are customary in transactions of this nature, were negotiated at arm's length between Variagenics and SG Cowen, and the Variagenics board was aware of

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the arrangement, including the fact that a significant portion of the fee payable to SG Cowen is contingent upon the completion of the merger.

Regulatory Approvals Required for the Merger

Under the merger agreement, both Hyseq and Variagenics have agreed to use their reasonable best efforts to obtain all required governmental approvals and avoid any action or proceeding by a governmental entity in connection with the execution of the merger agreement and completion of the merger. Neither Hyseq nor Variagenics is aware, however, of any material federal or state regulatory requirements or approvals required for the execution of the merger agreement or completion of the merger, other than filing a certificate of merger in Delaware at or before the effective time of the merger.

Material United States Federal Income Tax Consequences of the Transaction

The following general discussion summarizes the anticipated material U.S. federal income tax consequences of the Transaction to holders of shares of Variagenics common stock. It is based upon the Internal Revenue Code and other laws, regulations, rulings and decisions in effect as of the date of this proxy statement/ prospectus, all of which are subject to change, possibly with retroactive effect. This discussion addresses only those U.S. Holders, as defined below, of shares of Variagenics common stock who hold their shares of Variagenics common stock as a capital asset, and does not address all of the U.S. federal income tax consequences that may be relevant to particular stockholders in light of their individual circumstances or to stockholders who are subject to special rules, including:

financial institutions;

insurance companies;

non-U.S. Holders;

tax-exempt entities;

dealers in securities;

persons who are subject to the alternative minimum tax provisions of the Internal Revenue Code;

persons who hold shares of Variagenics common stock as a hedge against currency risk, or as part of a constructive sale or conversion transaction;

holders whose shares of Variagenics common stock are qualified small business stock for purposes of Sections 1202 and 1045 of the Internal Revenue Code;

persons who acquired shares of Variagenics common stock pursuant to the exercise of an employee stock option or otherwise as compensation or through a tax-qualified retirement plan;

persons who hold 5% or more of the outstanding shares of Variagenics common stock; or

persons who hold shares of Variagenics common stock as part of an integrated investment (including a straddle or other risk reduction transaction) composed of shares of Variagenics common stock and one or more other positions.

This discussion does not consider tax consequences under state, local and foreign laws in this summary, nor do they discuss the tax consequences of any transactions, other than the Transaction discussed herein (whether or not a stockholder undertakes those transactions in connection with the Transaction discussed herein).

Neither Hyseq nor Variagenics has requested or intends to request a ruling from the Internal Revenue Service with respect of any of the U.S. federal income tax consequences of the Transaction. As a result there can be no assurance that the Internal Revenue Service will not disagree with or challenge any of the conclusions described below, or that the conclusions will be upheld by a court if challenged.

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For the purposes of this discussion, the term U.S. Holder means:

a citizen or resident of the U.S.;

a corporation, partnership or other business entity created or organized under the laws of the U.S. or any of its political subdivisions;

a trust that (i) is subject to the supervision of a court within the U.S. and the control of one or more U.S. persons or (ii) has a valid election in effect under applicable United States Treasury Department regulations to be treated as a U.S. person; or

an estate that is subject to U.S. federal income tax on its income regardless of its source.

Exchange of Shares of Variagenics Common Stock for Shares of Hyseq Common Stock

It is a condition to the closing of the merger that Hyseq shall have received an opinion from its legal counsel, Latham & Watkins, and Variagenics shall have received an opinion from its legal counsel, Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., in each case dated the date of the effective time of the merger, to the effect that on the basis of the facts, representations and assumptions set forth in such opinion, the Transaction will be treated as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code. Neither Hyseq nor Variagenics may waive this condition to the merger after Variagenics stockholders have approved the merger unless further stockholder approval is obtained with appropriate disclosure. These opinions will be based on representations contained in representation letters provided by Hyseq and Variagenics substantially in the forms attached to the merger agreement as exhibits, all of which must continue to be true and accurate in all respects as of the effective time of the merger. The opinions will not be binding on the Internal Revenue Service or the courts.

Assuming that all of the representations contained in the representation letters provided by Hyseq and Variagenics continue to be true and accurate in all respects as of the effective time of the merger and that the Transaction is treated as a reorganization within the meaning of Section 368(a) of the Internal Revenue Code:

neither Hyseq nor Variagenics will recognize gain or loss in the Transaction;

no gain or loss will be recognized for federal income tax purposes by Variagenics stockholders who exchange their shares of Variagenics common stock for shares of Hyseq common stock pursuant to the Transaction (except to the extent of cash received instead of a fractional share of Hyseq common stock, as discussed below);

each Variagenics stockholder's aggregate tax basis in the shares of Hyseq common stock that he or she receives upon completion of the Transaction will be the same as his or her aggregate tax basis in the shares of Variagenics common stock surrendered upon completion of the Transaction (reduced by any tax basis allocable to fractional shares exchanged for cash); and

the holding period of the shares of Hyseq common stock received will include the holding period of the shares of Variagenics common stock surrendered.

Cash Received Instead of Fractional Shares

The payment of cash to a Variagenics stockholder instead of a fractional share of Hyseq common stock generally will result in the recognition of capital gain or loss measured by the difference between the amount of cash received and the portion of the tax basis of the Variagenics common stock allocable to that fractional share interest. In the case of an individual, capital gains are generally subject to U.S. federal income tax at the reduced rates applicable to long-term capital gains if such individual has held his or her shares of Variagenics common stock for more than one year at the time of the Transaction, and at ordinary income rates (as a short-term capital gain) if the individual has held his or her Variagenics common stock for one year or less at the time of the Transaction.

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Reporting Requirements

Each Variagenics stockholder that receives shares of Hyseq common stock pursuant to the Transaction will be required to file a statement with his or her federal income tax return setting forth his or her basis in the shares of Variagenics common stock surrendered and the fair market value of the shares of Hyseq common stock and cash received pursuant to the Transaction, and to retain permanent records of these facts relating to the Transaction.

Backup Withholding

A Variagenics stockholder may be subject to backup withholding on any cash payment in lieu of fractional shares made to a Variagenics stockholder unless that stockholder:

furnishes a correct taxpayer identification number and certifies that he or she is not subject to backup withholding on the substitute Form W-9 or successor form included in the letter of transmittal that will be mailed to Variagenics stockholders shortly after completion of the Transaction; or

is otherwise exempt from backup withholding.

Any amounts withheld under the backup withholding rules will be allowed as a refund or credit against a holder's United States federal income tax liability, provided the holder furnishes the required information to the Internal Revenue Service.

THIS SUMMARY DOES NOT DISCUSS TAX CONSEQUENCES THAT MAY VARY WITH OR ARE CONTINGENT ON INDIVIDUAL CIRCUMSTANCES. MOREOVER, IT DOES NOT ADDRESS ANY NON-INCOME TAX CONSEQUENCES, NOR ANY NON-U.S. OR ANY STATE OR LOCAL TAX CONSEQUENCES OF THE TRANSACTION. THE SUMMARY DOES NOT ADDRESS THE TAX CONSEQUENCES OF ANY TRANSACTION OTHER THAN THE TRANSACTION DISCUSSED HEREIN, AND DOES NOT BIND THE INTERNAL REVENUE SERVICE. ACCORDINGLY, HOLDERS OF SHARES OF VARIAGENICS COMMON STOCK ARE URGED TO CONSULT THEIR TAX ADVISORS AS TO THE SPECIFIC TAX CONSEQUENCES TO THEM OF THE TRANSACTION, INCLUDING THE APPLICABILITY AND EFFECT OF FEDERAL, STATE, LOCAL AND FOREIGN INCOME AND OTHER TAX LAWS TO THEIR PARTICULAR CIRCUMSTANCES.

Accounting Treatment

In accordance with accounting principles generally accepted in the United States of America, Hyseq will account for the merger using the purchase method of accounting. Under this method of accounting, Hyseq will record the market value (based on an average of the closing prices of Hyseq common stock for a range of trading days from two days before and after November 11, 2002, the announcement date) of its common stock issued in the merger, the fair value of Hyseq options and warrants issued in exchange for the options and warrants to purchase shares of Variagenics common stock and the amount of direct transaction costs associated with the merger as the estimated purchase price of acquiring Variagenics. Hyseq will allocate the estimated purchase price to the net tangible and identifiable intangible assets acquired (primarily cash, marketable securities, and long-term assets, principally plant and equipment), based on their respective fair values at the date of the completion of the merger.

To the extent that the estimated fair value of the net assets acquired exceeds the estimated purchase price, the estimated fair values of long-lived assets would be proportionately reduced for purchase accounting purposes. After such a reduction in values and in accordance with Statement of Financial Accounting Standards No. 141, Business Combinations, any remaining excess would be recorded as an extraordinary gain in Hyseq's statement of operations upon consummation of the merger.

The allocation of the purchase price is preliminary, and given Variagenics' historical consumption of its working capital, the estimated negative goodwill of approximately \$4.2 million may be substantially reduced, eliminated, or become positive goodwill upon completion of the final purchase price allocation. The purchase

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price allocation will remain preliminary until Hyseq completes a third party valuation of identifiable intangible assets acquired, evaluates restructuring plans to be taken following consummation of the merger, and determines the fair values of other assets and liabilities acquired. The final determination of the purchase price allocation is expected to be completed as soon as practicable after consummation of the merger. The final amounts allocated to assets and liabilities acquired could differ from the amounts presented in the unaudited pro forma condensed combined financial statements.

The determination of accounting acquirer in a business combination in accordance with Statement of Financial Accounting Standards No. 141 requires consideration of multiple factors, including voting rights, any significant minority voting rights, governance and senior management of the combined enterprise, as well as any premium that was paid. Given the composition of the board of directors and senior management of the combined company, as well as the premium paid by Hyseq, Hyseq was determined to be the accounting acquirer.

Listing of Hyseq Common Stock

Hyseq will use reasonable best efforts to:

cause the shares of Hyseq common stock to be issued in the merger to be approved for listing on the Nasdaq National Market prior to the completion of the merger; and

cause the shares of Hyseq common stock to be reserved for issuance upon the exercise of converted Variagenics stock options to be approved for listing on the Nasdaq National Market prior to the completion of the merger.

Delisting and Deregistration of Variagenics Common Stock

If the merger is completed, Variagenics common stock will be delisted from the Nasdaq National Market and deregistered under the Securities Exchange Act of 1934, and Variagenics will no longer file periodic reports with the SEC.

Restrictions on Sales of Shares of Hyseq Common Stock Received in the Merger

The shares of Hyseq common stock to be issued in the merger will be registered under the Securities Act of 1933 and will be freely transferable, except for shares of Hyseq common stock issued to any person who is deemed to be an affiliate of Variagenics prior to the merger. Persons who may be deemed to be affiliates of Variagenics prior to the merger include individuals or entities that control, are controlled by, or are under common control with Variagenics prior to the merger, and may include officers and directors, as well as significant stockholders of Variagenics prior to the merger. Affiliates of Variagenics prior to the merger may not sell any of the shares of Hyseq common stock received by them in connection with the merger except pursuant to:

an effective registration statement under the Securities Act of 1933 covering the resale of those shares;

an exemption under paragraph (d) of Rule 145 under the Securities Act of 1933; or

any other applicable exemption under the Securities Act of 1933.

Hyseq's registration statement on Form S-4, of which this joint proxy statement/prospectus is a part, does not cover the resale of shares of Hyseq common stock to be received by affiliates of Variagenics in the merger.

Hyseq has agreed that, as soon as practicable, but in any event not more than thirty days after the completion of the merger, it will prepare and file with the SEC a registration statement on Form S-3 or other comparable form it is eligible to use, covering the resale of Hyseq common stock held by those stockholders who were affiliates (as defined in the Securities Exchange Act) of Variagenics at the time of the consummation of the merger but are not affiliates of Hyseq after the consummation of the merger.

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Interests of Directors and Executive Officers of Hyseq in the Merger

In considering the recommendation of the Hyseq board of directors that Hyseq stockholders vote in favor of approval of the merger agreement, Hyseq stockholders should be aware that some Hyseq executive officers and directors may have interests in the merger that may be different from, or in addition to, their interests as stockholders of Hyseq.

These interests relate to or arise from, among other things:

the retention of some of the officers and directors of Hyseq as officers and directors of the surviving corporation;

the execution of severance agreements between Hyseq and each of Peter Garcia, Linda Fitzpatrick, Li-Hsien Rin-Laures, William Bennett, Walter Funk, Nina Giles and Luis Pena that could result in the payment of severance payments and certain other benefits to those people;

an employment agreement with Dr. Love that could result in the payment of severance payments, acceleration of stock option vesting and certain other benefits to Dr. Love; and

an amendment to the terms of a line of credit from Dr. Rathmann to Hyseq.

The Hyseq board of directors was aware of these interests during its deliberations of the merits of the merger and in determining to recommend to Variagenics stockholders that they vote for the proposal to adopt the merger agreement.

Governance Structure and Management Positions

The merger agreement provides for the initial composition of the board of directors of the surviving entity, the nominating committee of that board of directors and selected executive officer positions for the surviving entity. See *Directors, Management and Operations Following the Merger*.

Severance Agreements and Other Arrangements

Hyseq has entered into severance agreements with Peter Garcia, Linda Fitzpatrick, Li-Hsien Rin-Laures, William Bennett, Walter Funk, Nina Giles and Luis Pena.

Each of the severance agreements provides that, in the event an executive's employment is terminated by Hyseq other than for cause and other than as a result of executive's death or disability, or by the executive for good reason, within six months following the consummation of the merger, the executive will receive six months of salary continuation payments and six months of continued benefits coverage.

For purposes of the severance agreements, termination for cause generally means the executive's termination by Hyseq as a result of the executive's gross negligence or willful misconduct in the performance of duties to Hyseq where that gross negligence or willful misconduct has resulted or is likely to result in substantial and material damage to Hyseq or its subsidiaries, repeated unexplained or unjustified absence from Hyseq, a material and willful violation of any federal or state law, executive's commission of any act of fraud with respect to Hyseq, or executive's conviction of a felony or a crime involving moral turpitude causing material harm to the standing and reputation of Hyseq.

For purposes of the severance agreements, an executive may terminate his or her employment with Hyseq for good reason following the occurrence, after the consummation of the merger of any one or more of the following events without his or her consent: any change in the executive's position with Hyseq that materially reduces his or her duties or level of responsibility as in effect immediately preceding the consummation of the merger, any reduction of executive's base compensation (other than in connection with a general decrease in base salaries for most similarly situated employees of the company or a successor corporation), or the relocation of the company's offices at which executive is principally employed immediately prior to the consummation of the merger to a location more than 30 miles from those offices.

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In January 2001, Hyseq entered into an employment agreement with Dr. Love. Pursuant to the agreement, in the event Dr. Love's employment with Hyseq terminates other than for cause or there exists good reason for Dr. Love to terminate his employment with Hyseq,

any options granted to Dr. Love over the first four years of his employment, beginning January 11, 2001, will immediately become vested and exercisable;

Dr. Love's right to exercise his options will be extended by eighteen months;

Dr. Love will immediately receive a lump sum payment equal to twelve months of his then-current base salary; and

Dr. Love's health, disability and life insurance benefits and those for his family will continue for an additional twelve months.

For purposes of the employment agreement, "good reason" includes events such as the material reduction of Dr. Love's authority, duties, title or responsibilities, the material reduction of Dr. Love's salary, and termination of Dr. Love's employment within one year after a change of control. However, Hyseq and Dr. Love have agreed that the merger will not constitute a change of control for purposes of defining good reason.

In August 2001, Hyseq received a commitment from Dr. Rathmann to provide a line of credit of up to \$20.0 million in aggregate principal amount, available for draw down through August 5, 2003. As of November 1, 2002, \$10.0 million remained available for draw-down under the line of credit. In the event of a change of control of Hyseq, the line of credit expires and Dr. Rathmann has no further obligation to make any advances to Hyseq. However, Dr. Rathmann and Hyseq have agreed that the merger shall not constitute a change of control of Hyseq and therefore the line of credit will not expire.

Stock Option Plans

All options granted under Hyseq's 1995 Stock Option Plan, as amended, and Hyseq's Non-Employee Director Stock Option Plan, as amended, only become immediately exercisable in the event of a change of control (as defined in that plan). Hyseq's board of directors adopted a resolution providing that the merger will not constitute a change of control under these plans.

In 2001, Hyseq granted options to purchase shares of common stock to certain of its officers in connection with and as an inducement to their commencement of employment with Hyseq that were not approved by its stockholders. All of those options become immediately exercisable in the event of a change of control (as defined those option agreements). Hyseq's board of directors also adopted a resolution providing that merger will not constitute a change of control under those option agreements.

Interests of Directors and Executive Officers of Variagenics in the Merger

In considering the recommendation of the Variagenics board of directors that Variagenics stockholders vote in favor of approval of the merger agreement, Variagenics stockholders should be aware that some Variagenics executive officers and directors may have interests in the merger that may be different from, or in addition to, their interests as stockholders of Variagenics.

Officers and directors of Variagenics who own Variagenics common stock will be able to exchange their shares of Variagenics common stock for shares of Hyseq common stock on the same terms as all the other stockholders of Variagenics.

As of the record date, the members of the Variagenics board of directors and current executive officers of Variagenics beneficially own 6,243,474 shares of Variagenics common stock, and accordingly are eligible to receive a maximum aggregate amount of \$10.3 million or 10,271,139 shares of Hyseq common stock in the merger. In addition, as of the record date, these board members and current executive officers hold options to acquire 1,301,713 shares of Variagenics common stock, with exercise prices ranging from \$0.54 to \$17.69 per share, which will be assumed by Hyseq and be converted into options to acquire shares of Hyseq

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common stock on the same terms as all the other holders of Variagenics stock options. For more information about these options, you should read the section of this joint proxy statement/prospectus entitled "Treatment of Securities in the Merger" beginning on page 60.

Other interests relate to or arise from, among other things:

the possible retention of some of the officers and directors of Variagenics as officers and directors of the combined company;

the severance provisions in the existing employment agreements between Variagenics and each of Joseph S. Mohr, Richard P. Shea, Mark Adams, Anne L. Bailey and Vincent P. Stanton that could result in severance payments and limited benefits coverage to those people;

approval by the board of directors of an aggregate of \$250,000 in bonus payments to the current executive officers of Variagenics payable upon the closing of the merger;

the extension of the termination period for options held by its executive officers from three months to twelve months following the termination of employment; and

the amendment of Mr. Mohr's employment agreement to provide outplacement counseling services upon the termination of Mr. Mohr's employment or the cash value of such services.

The Variagenics board of directors was aware of these interests during its deliberations of the merits of the merger and in determining to recommend to Variagenics stockholders that they vote for the proposal to adopt the merger agreement.

Governance Structure and Management Positions

The merger agreement provides for the initial composition of the board of directors of the combined company, the nominating committees of that board of directors and selected executive officer positions for the combined company. See "Directors, Management and Operations Following the Merger."

Indemnification; Directors and Officers Insurance

Under the merger agreement, Hyseq has agreed to indemnify all directors, officers and employees of Variagenics and its subsidiaries to the fullest extent permitted by law for all acts or omissions occurring at or prior to the merger by such individuals in such capacities. Hyseq has also agreed to provide, for six years after the merger, directors' and officers' liability insurance in respect of acts or omissions occurring prior to the merger covering each person currently covered by the directors' and officers' liability insurance policy of Variagenics on terms and in amounts no less favorable than those of the policies of Variagenics, provided that Hyseq will not be required to pay an annual premium for the insurance in excess of \$1,250,000. Hyseq has agreed to cause to be maintained charter and bylaw provisions with respect to indemnification and advancement of expenses that are at least as favorable to the intended beneficiaries as those contained in charter and bylaws of Variagenics as in effect on the date the merger agreement was signed.

Employment Agreements with Severance and Other Arrangements

Variagenics has entered into employment agreements with Joseph S. Mohr, Richard P. Shea, Mark Adams, Anne L. Bailey and Vincent P. Stanton.

Each of the employment agreements contains a severance provision providing that, in the event an executive's employment is terminated by Variagenics other than for cause and other than as a result of executive's death or disability, or by the executive for good reason, the executive will receive six months of salary continuation payments.

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For purposes of the severance provisions, termination for cause generally means the executive's termination by Variagenics as a result of:

the executive's gross negligence or willful misconduct in the performance of duties to Variagenics where that gross negligence or willful misconduct has resulted or is likely to result in substantial and material damage to Variagenics or its subsidiaries;

repeated unexplained or unjustified absence from Variagenics;

a material and willful violation of any federal or state law;

executive's commission of any act of fraud with respect to Variagenics; or

executive's conviction of a felony or a crime involving moral turpitude causing material harm to the standing and reputation of Variagenics.

For purposes of the severance provisions, an executive may terminate his or her employment with Variagenics for good reason following the occurrence, after the completion of the merger, of any one or more of the following events without his or her consent:

any change in the executive's position with Variagenics that materially reduces his or her duties or level of responsibility as in effect immediately preceding the consummation of the merger;

any reduction of executive's base compensation (other than in connection with a general decrease in base salaries for most similarly situated employees of the company or a successor corporation); or

the relocation of the company's offices at which executive is principally employed immediately prior to the completion of the merger to a location more than 30 miles from those offices.

In addition to the above definition of good reason, one executive may also terminate employment with Variagenics for good reason if Variagenics breaches any material terms of the employment agreement.

Directors, Management and Operations Following the Merger

Hyseq and Variagenics expect that, initially following completion of the merger, the businesses and operations of the combined company will, except as described in this joint proxy statement/prospectus, be continued substantially as the business and operations of Hyseq and Variagenics are conducted prior to the merger. Hyseq and Variagenics expect that the combined company will undertake a comprehensive review of its business, operations, capitalization and management with a view to optimizing development of the combined company.

Immediately following the completion of the merger, the board of directors of the combined company shall consist of seven members, four of whom shall be designated by Hyseq and three of whom shall be designated by Variagenics. The Hyseq directors shall include Dr. Rathmann, who shall be Chairman of the board of directors of the combined company, Dr. Love, Ms. Mary Pendergast and Mr. Richard Brewer and the Variagenics directors shall include Dr. Philippe O. Chambon, Dr. Jean-Francois Formela and Mr. Martin A. Vogelbaum. Upon completion of the merger, a majority of the members of the nominating committee shall consist of directors designated by Hyseq. Under the merger agreement, the parties have agreed that for a period of not less than three years from and after the completion of the merger, at least a majority of the members of the board of directors and of the nominating committee shall consist of directors either designated by Hyseq prior to the merger or subsequently nominated by the nominating committee. Dr. Love shall be the Chief Executive Officer of the combined company.

Hyseq expects that, shortly following completion of the merger, the combined company shall consist of approximately 110-120 employees.

Continuing Hyseq Directors

George B. Rathman, Ph.D. has served as Chairman and a member of Hyseq's Board of Directors since February 2000. Dr. Rathman served as Hyseq's Chief Executive Officer from May 2000 to March 2001, and

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also served as Hyseq's President from May 2000 to January 2001. Prior to joining Hyseq, Dr. Rathman was a founder of ICOS Corporation, a publicly-held biopharmaceutical company, in 1990 and served as its Chairman until January 2000. While at ICOS, he also served as Chief Executive Officer and President from September 1991 until June 1999. In 1980, he co-founded Amgen, Inc., a publicly-held biotechnology company. He was a director of Amgen until 1993 and at various times also served as its Chairman of the Board, President and Chief Executive Officer. Dr. Rathman was also associated with Abbott Laboratories, Inc., a healthcare products manufacturer, where from 1975 to 1977 he was Director of Research and Development and from 1977 to 1980 he was Divisional Vice President. Dr. Rathman received his Ph.D. in physical chemistry from Princeton University.

Ted W. Love, M.D. has served as Hyseq's President since January 2001, Chief Executive Officer since March 2001, and as a member of Hyseq's Board of Directors since February 2001. Dr. Love served as Hyseq's President and Chief Operating Officer from January 2001 until March 2001. Prior to joining Hyseq, Dr. Love served as Senior Vice President of Development at Advanced Medicine, Inc. Dr. Love served as a Research Physician and Vice President of Product Development at Genentech, Inc. from 1992 to 1998. Dr. Love holds a B.A. in Molecular Biology from Haverford College and an M.D. from Yale Medical School.

Richard B. Brewer has served as a member of Hyseq's Board of Directors since May 2002. Since September 1998, Mr. Brewer has served as President, Chief Executive Officer and Director for Scios, Inc., a publicly-held biopharmaceutical company. From February 1996 to June 1998, Mr. Brewer served as the Executive Vice President of Operations and then as Chief Operating Officer of Heartport, Inc., a publicly-held medical device company. From 1984 to 1995, Mr. Brewer served in various capacities for Genentech Europe Ltd., Genentech Canada, Inc. and Genentech, Inc., most recently as Senior Vice President, U.S. Sales and Marketing. Mr. Brewer received a B.S. from Virginia Polytechnic Institute and an M.B.A. from Northwestern University.

Mary K. Pendergast has served as a member of Hyseq's Board of Directors since May 2002. Ms. Pendergast has been Executive Vice President, Government Affairs of Elan Corporation since January 1998. Ms. Pendergast was Deputy Commissioner/Senior Advisor to the Food and Drug Administration, Department of Health and Human Services from November 1990 to January 1998. Ms. Pendergast received her L.L.M. from Yale Law School in 1977, her J.D. from the University of Iowa College of Law in 1976 and her B.A. from Northwestern University in 1972.

Continuing Variagenics Directors

Philippe O. Chambon, M.D., Ph.D. has served as a member of Variagenics' Board of Directors since July 1999. Since January 1997, Dr. Chambon has been a General Partner of the Sprout Group. He joined the Sprout Group in May 1995. From May 1993 to April 1995, Dr. Chambon served as Manager in the Healthcare Practice of The Boston Consulting Group, a leading management consulting firm. From September 1987 to April 1993, he was an executive with Sandoz Pharmaceutical (Novartis), where he had late-stage product development and pre-marketing responsibilities. Dr. Chambon currently serves as a member of the board of directors of Deltagen, Inc., Pharsight Corp. and several privately-funded biotechnology companies. Dr. Chambon holds an M.D. and a Ph.D. from the University of Paris and an M.B.A. from Columbia University.

Jean-Francois Formela, M.D. has served as a member of Variagenics' Board of Directors since June 1997. Dr. Formela was a partner of Atlas Venture from 1993 to 1995, and has been a General Partner of Atlas since 1995. From 1989 to 1993, Dr. Formela served at Schering-Plough, most recently as Senior Director, Medical Marketing and Scientific Affairs, where he had biotechnology licensing and marketing responsibilities. Dr. Formela serves on the board of directors of deCODE Genetics, Inc., Exelixis, Inc. and several private companies. Dr. Formela holds an M.D. from Paris University School of Medicine and an M.B.A. from Columbia University.

Martin A. Vogelbaum has served as a member of Variagenics' Board of Directors since June 1997. Since June 2000, Mr. Vogelbaum has been a General Partner of Apple Tree Partners. Previously, he was a General Partner of Oxford Bioscience Partners. Prior to joining Oxford in 1993, he held senior executive

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positions at the public and investor relations firms of Burns McClellan, Inc. and Hill & Knowlton, where he implemented marketing and investor initiatives for biotechnology and pharmaceutical companies. Previously, he was a Research Associate in the Bone Marrow Transplant Unit at Memorial Sloan-Kettering Cancer Center. Mr. Vogelbaum received his A.B. in biology and history from Columbia University.

Additional Information Regarding Variagenics Continuing Directors

Compensation of Directors

Variagenics directors are reimbursed for expenses incurred to attend meetings of the board of directors and any committees of the Board of Directors. Pursuant to the terms of Variagenics Amended 1997 Employee, Director and Consultant Stock Option Plan, the board of directors has the discretion to grant options to non-employee directors.

In June 2001, Drs. Chambon and Formela and Mr. Vogelbaum were each awarded options to purchase 5,000 shares of Variagenics common stock at a purchase price of \$3.90 per share. Each such option became fully vested upon each director's compliance with Variagenics requirements for attendance at meetings of the board of directors.

In March 2002, Mr. Vogelbaum was awarded options to purchase 100,000 shares of Variagenics common stock at a purchase price of \$2.62 per share. Such options were fully vested on the date of grant.

In June 2002, Drs. Chambon and Formela and Mr. Vogelbaum were each awarded options to purchase 5,000 shares of Variagenics common stock at a purchase price of \$1.41 per share. Each such option vests equal monthly installments over twelve months.

Compensation Committee Interlocks and Insider Participation

No member of the Compensation Committee of Variagenics board of directors was at any time during the fiscal year ended December 31, 2001, or formerly, an officer or employee of Variagenics or any subsidiary of Variagenics. No executive officer of Variagenics has served as a director or member of the Compensation Committee (or other committee serving an equivalent function) of any other entity, while an executive officer of that other entity served as a director of or member of the Compensation Committee of Variagenics.

Certain Relationships and Related Transactions

In July 2002, Variagenics entered into an exclusive license agreement with Renegade Therapeutics, Inc. Under this agreement, Variagenics will license to Renegade certain of Variagenics intellectual property in exchange for an upfront license fee in the amount of \$75,000 payable in Renegade fully-vested founders' stock and a \$20,000 reimbursement for Variagenics patent prosecution expenses and valuation report expenses. No cash or stock has been received to date in connection with this agreement. The agreement contains provisions for royalty and milestone payments based on the commercialization of related technology and the issuance of the first U.S. patent with respect to the technology among others. One of the officers and stockholders of Renegade is a director and stockholder of Variagenics and is expected to be a director of Hyseq upon the completion of the merger.

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THE MERGER AGREEMENT

The following summary describes certain material provisions of the merger agreement, which is included in this joint proxy statement/prospectus as Annex A and is incorporated by reference into this joint proxy statement/prospectus. This summary may not contain all of the information about the merger agreement that is important to you. Hyseq and Variagenics encourage you to read the merger agreement carefully in its entirety.

General Terms of the Merger Agreement

On November 9, 2002, Variagenics and Hyseq entered into the merger agreement. The merger will become effective upon the filing of a properly executed certificate of merger with the Secretary of State of the State of Delaware in accordance with the Delaware General Corporation Law.

The merger will be completed through a reverse triangular, stock-for-stock merger in which Vertical Merger Corp., a Delaware corporation and a wholly-owned subsidiary of Hyseq, will merge with and into Variagenics. As a result of the merger, the separate corporate existence of Vertical Merger Corp. will cease and Variagenics will be the surviving entity. Immediately thereafter, Variagenics will be merged upstream into Hyseq and Hyseq will be the surviving entity. Hyseq and Variagenics anticipate that shortly after the mergers, the combined company will change its name to a new name that has not yet been determined.

Treatment of Securities in the Merger

Variagenics Shares

At the effective time of the merger, each share of Variagenics common stock issued and outstanding immediately prior to the merger, other than shares held by Variagenics, Hyseq or any wholly-owned subsidiary of Hyseq or Variagenics, will be automatically converted into the right to receive 1.6451 fully paid and nonassessable shares of Hyseq common stock, sometimes referred to herein as the merger consideration. At the effective time of the merger, all shares of Variagenics common stock will no longer be outstanding and will automatically be canceled and retired and will cease to exist, and each certificate previously representing any such shares will thereafter represent only the right to receive the shares of Hyseq common stock to be issued as consideration upon the surrender of those certificates, without interest. No fractional shares of Hyseq common stock will be issued; instead, a cash payment will be made to the holders of shares of Variagenics common stock who would otherwise be entitled to receive a fractional share of Hyseq common stock. See Cash Instead of Fractional Shares.

All shares of Variagenics common stock owned by Hyseq or any of its subsidiaries will be automatically cancelled and retired and shall cease to exist and no merger consideration or other consideration will be delivered in exchange. In addition, each share of Variagenics common stock held in the company treasury and each share of Variagenics common stock, if any, owned by any wholly-owned subsidiary of Variagenics immediately prior to the effective time will be canceled and extinguished without any conversion thereof.

Each share of common stock of Vertical Merger Corp. issued and outstanding immediately prior to the effective time will be converted into and be exchanged for one newly and validly issued, fully paid and nonassessable share of common stock of the surviving corporation.

If, between the date of the merger agreement and the effective time of the merger, the outstanding shares of Variagenics common stock or Hyseq common stock are changed into a different number of shares or a different class by reason of any reclassification, recapitalization, reorganization, split-up, stock dividend, stock combination, exchange of shares, readjustment or otherwise, as the case may be, then the number of shares of Hyseq common stock issuable in the merger will be proportionately adjusted.

Variagenics Stock Options

At the effective time of the merger, each outstanding unexpired and unexercised option to purchase shares of Variagenics common stock will be automatically converted into an option to purchase shares of

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Hyseq common stock, in a number determined by multiplying the number of Variagenics shares that were issuable upon exercise of the Variagenics option immediately prior to the effective time by 1.6451, rounded down to the nearest whole number of shares of Hyseq common stock. The exercise price per share of these options will equal the per-share exercise price of the corresponding Variagenics option divided by the exchange ratio, rounded up to the nearest whole cent. The converted Hyseq options will be subject to the same terms and conditions as the corresponding Variagenics options.

Within five business days after the effective time of the merger, Hyseq will file a registration statement on Form S-3 or Form S-8, or any successor or other appropriate forms, covering the shares of Hyseq common stock underlying the assumed options and will use its best efforts to keep that registration statement current and effective for so long as the assumed options remain outstanding.

Variagenics Employee Stock Purchase Plan

At the effective time of the merger, each outstanding purchase right under the Variagenics 2000 Employee Stock Purchase Plan (ESPP) will be exercised for the purchase of shares of Variagenics common stock at the price per share determined pursuant to the ESPP on the date immediately prior to the closing of the merger. Variagenics has agreed to take all action necessary to provide that the ESPP will be terminated immediately prior to the effective time of the merger and that no person will have any further right to purchase Variagenics common stock under the ESPP.

Variagenics Warrants

At the effective time of the merger, each warrant to acquire shares of Variagenics common stock outstanding immediately prior thereto will be automatically converted into a warrant to purchase shares of Hyseq common stock. The Variagenics warrants so converted will continue to have, and be subject to, the same terms and conditions as set forth in the applicable warrant agreements as in effect immediately prior to the effective time, except that, in accordance with, and without duplication of, the provisions set forth in the applicable warrant: (a) each such Variagenics warrant will be exercisable solely for a number of shares of Hyseq common stock equal to the product of the number of shares of Variagenics common stock subject to such Variagenics warrant immediately prior to the effective time of the merger multiplied by 1.6451, rounded down to the nearest whole number of shares of Hyseq common stock, and (b) the per share exercise price will equal the per share exercise price of the corresponding Variagenics warrant divided by the exchange ratio, rounded up to the nearest whole cent.

Exchange of Variagenics Stock Certificates for Hyseq Stock Certificates

Exchange Agent

U.S. Stock Transfer Corporation will be the exchange agent responsible for the exchange of stock certificates representing Variagenics common stock for stock certificates representing Hyseq common stock. The exchange agent will accept your certificates for shares of Variagenics common stock, each a Variagenics certificate, and exchange them for certificates representing shares of Hyseq common stock and cash instead of fractional shares of Hyseq common stock.

Exchange Procedures

Prior to the effective time of the merger, Hyseq will deposit with the exchange agent, for the benefit of the holders of shares of Variagenics common stock, certificates representing the shares of Hyseq common stock issuable in the merger.

Within five business days after the effective time, the exchange agent will mail to each holder of record of a Variagenics certificate, a letter of transmittal and instructions for exchanging his or her Variagenics certificate for the merger consideration. After receipt of the transmittal forms, each holder of a Variagenics certificate will be able to surrender his or her Variagenics certificate to the exchange agent and receive in exchange a certificate representing that number of whole shares of Hyseq common stock to which the holder

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of the Variagenics certificate is entitled, together with any cash which may be payable instead of fractional shares of Hyseq common stock and any dividends or other distributions with respect to Hyseq common stock having a record date and paid after the effective time of the merger. In the event of a transfer of ownership of shares of Variagenics common stock which is not registered on the transfer records of Variagenics, a certificate representing the proper number of shares of Hyseq common stock, any cash instead of fractional shares of Hyseq common stock and applicable dividends and distributions may be issued and paid to a transferee if the Variagenics certificate representing the applicable Variagenics shares is presented to the exchange agent, accompanied by all documents required to evidence and effect such transfer and by evidence that any applicable stock transfer taxes have been paid. The consideration to be issued in the merger will be delivered by the exchange agent as promptly as practicable following surrender of a Variagenics certificate and any other required documents. No interest will be payable on the merger consideration, regardless of any delay in making payments.

Dividends and Other Distributions

Holders of shares of Variagenics common stock will not be entitled to receive any dividends or distributions payable by Hyseq in respect of Hyseq common stock until they exchange their Variagenics certificates for shares of Hyseq common stock. After they deliver their Variagenics certificates to the exchange agent, those stockholders will receive, subject to applicable law, the amount of dividends or other distributions on Hyseq common stock having a record date after the effective time previously paid and, at the appropriate payment date, the amount of dividends or other distributions on Hyseq common stock with a record date after the effective time of the merger and a payment date after the surrender of such Variagenics certificates, without interest.

Cash Instead of Fractional Shares

No fractional shares of Hyseq common stock will be issued upon the surrender of Variagenics certificates. No dividend or distribution will relate to any fractional share of Hyseq common stock that would otherwise be issuable in the merger, and any fractional shares of Hyseq common stock will not entitle the owner to any voting rights of a Hyseq stockholder.

Holders of shares of Variagenics common stock otherwise entitled to fractional shares of Hyseq common stock will receive from Hyseq an amount of cash, rounded down to the nearest whole cent, without interest, equal to the product of the fractional share number multiplied by the average closing price per share of Hyseq common stock for the twenty consecutive trading days ending on the second trading day immediately prior to the effective time of the merger. Payments will occur as soon as practicable after the determination of the amount of cash, if any, to be paid to each holder of Variagenics common stock with respect to any fractional shares and following compliance with the exchange procedures and in the letter of transmittal provided by the exchange agent. No dividend or distribution with respect to Hyseq common stock will be payable on or with respect to any fractional share and fractional share interests will not entitle the holders to any rights of a stockholder of Hyseq.

Other Exchange Provisions

Any amount held by the exchange agent on behalf of the former holders of shares of Variagenics common stock that remains undistributed to the former Variagenics stockholders for six months after the effective time of the merger will be delivered to Hyseq, upon demand. Following such delivery, former Variagenics stockholders that have not validly exchanged Variagenics certificates for the merger consideration will be required to look to Hyseq for payment of the merger consideration.

Appraisal Rights

Under applicable state law, neither Hyseq stockholders nor Variagenics stockholders will have appraisal rights in connection with the merger.

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None of the exchange agent, Hyseq, Vertical Merger Corp. or Variagenics will be liable to any holder of shares of Variagenics common stock for shares of Hyseq common stock, or dividends and distributions, or for any cash delivered to a public official pursuant to any applicable abandoned property, escheat or similar law.

If a Variagenics certificate has been lost, stolen or destroyed, the exchange agent will issue the Hyseq common stock, cash instead of fractional shares of Hyseq common stock and unpaid dividends and distributions on shares of Hyseq common stock upon receipt of an affidavit with respect to that loss, theft or destruction and a reasonable indemnity.

Representations and Warranties

In the merger agreement, Variagenics and Hyseq make customary representations and warranties to each other about their respective companies related to, among other things:

corporate organization and similar corporate matters;

capital structure;

corporate authority to enter into, and carry out the obligations under, the merger agreement and the enforceability of the merger agreement;

approval of the merger agreement by the boards of directors of Variagenics and Hyseq;

the fairness opinion of the financial advisor to each of the boards of directors of Variagenics and Hyseq;

absence of a breach of organizational documents, laws or material agreements as a result of the merger agreement and the merger;

required governmental consents and approvals;

compliance with laws;

documents filed with the SEC and the financial statements included in those documents;

employee and labor matters and employee benefit plans;

specified material contracts;

litigation matters;

environmental matters;

intellectual property matters;

filing of tax returns, payment of taxes and other tax related matters;

insurance policies maintained by Variagenics and Hyseq;

leased real property and equipment;

payment of fees to finders, brokers or investment bankers in connection with the merger; and

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interested stockholder matters.

Hyseq and Vertical Merger Corp. also made additional representations and warranties to Variagenics related to, among other things:

amending the Hyseq Rights Agreement;

the corporate organization, qualification and ownership of Vertical Merger Corp.; and

matters related to U.S. Food and Drug Administration filings, correspondence and communications.

The representations and warranties given by Variagenics, Hyseq and Vertical Merger Corp. do not survive completion of the merger.

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Covenants

The merger agreement contains customary covenants as well as specific covenants relating to the conduct of the respective parties businesses pending completion of the merger.

Conduct of Business by Variagenics and Hyseq Prior to the Merger

Variagenics and Hyseq have agreed that, prior to the completion of the merger or termination of the merger agreement, except as contemplated by the merger agreement or unless the parties shall otherwise consent in writing, Variagenics and Hyseq will and will cause each of their subsidiaries to:

maintain their existence in good standing under applicable law;

conduct operations only in the ordinary and usual course of business consistent with past practice;

use reasonable best efforts to keep available the services of current officers, key employees and consultants; and

preserve current relationships with their customers, suppliers and other persons with which they have significant business relations as is reasonably necessary to preserve substantially intact its business organization.

In addition, Variagenics and Hyseq will not and will not permit any of their subsidiaries to, between the date of the merger agreement and the effective time of the merger, do any of the following without the other's prior written consent, unless as otherwise contemplated by the merger agreement and subject to certain exceptions:

amend its certificate or articles of incorporation, by-laws or other organizational documents;

issue, sell, pledge, dispose of, grant, transfer or encumber any of its capital stock, convertible securities, or rights, warrants or options to acquire any capital stock or convertible securities, or amend the terms of any such securities;

sell, pledge, dispose of, transfer, lease, license, or encumber any material property or assets;

sell, pledge, dispose of, transfer, lease, license, abandon, fail to maintain or encumber any intellectual property;

enter into any contract or series of related contracts, or any amendment or series of related amendments of one or more contracts, involving aggregate receipts, payments or expenses in excess of \$500,000;

enter into any material commitment or transaction outside the ordinary course of business consistent with past practice;

declare or pay any dividends or make other distributions;

alter its capital stock, including, among other things, by way of stock splits, combinations, reclassifications and substitutions;

repurchase, redeem or otherwise acquire any of its capital stock;

incur any indebtedness for borrowed money or issue any debt securities or assume, guarantee or endorse, or otherwise as an accommodation become responsible for, the obligations of any person for borrowed money;

terminate, cancel or agree to any material and adverse change in, any material contract;

make or authorize any capital expenditure materially in excess of the budget as previously provided to each other prior to the date of the merger agreement;

make or authorize any material loan to any person outside the ordinary course of business;

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enter into any agreement or arrangement that limits or otherwise restricts them or any of their subsidiaries or any of their respective affiliates or any successors, including the surviving corporation, from engaging or competing in any line of business or in any geographic area;

increase the compensation or benefits payable or to become payable to its directors, officers or employees;

grant any rights to severance or termination pay to, or enter into any employment or severance agreement with, any director, officer or other employee;

establish, adopt, enter into or amend any collective bargaining, bonus, profit sharing, thrift, compensation, stock option, restricted stock, pension, retirement, deferred compensation, employment, termination, severance or other plan, agreement, trust, fund, policy or arrangement for the benefit of any director, officer, consultant or employee;

take any affirmative action to amend or waive any performance or vesting criteria or accelerate vesting, exercisability or funding under stock options or an option plan;

make any material change in accounting policies or procedures;

make any material tax election or settle or compromise any material liability for taxes, including but not limited to, change any annual tax accounting period or change any method of tax accounting;

amend or terminate, or waive, release or assign any material rights to any confidentiality or standstill agreement;

write up, write down or write off the book value of any assets;

acquire, or agree to acquire, from any person any assets (not including intellectual property), operations, business or securities except for permitted capital expenditures and assets in the ordinary course of business;

take any action that is intended or would reasonably be expected to result in any of the conditions to the merger not being satisfied;

adopt a stockholder rights agreement, or poison pill, except Hyseq may amend or change its stockholder rights agreement, as contemplated by the merger agreement;

acquire, or agree to acquire, from any person, any intellectual property, except in the ordinary course of business; and

authorize or enter into any agreement or otherwise make any commitment to do any of the foregoing.

The above mentioned covenants will not prevent Hyseq from issuing an aggregate of up to 4,607,171 shares of Hyseq common stock and/or warrants for the purchase of Hyseq common stock in one or more financings, subject to certain limitations more fully set forth in the merger agreement. However, subject to the negotiation of mutually acceptable documentation, Variagenics will have a right to first enter into an agreement with Hyseq providing for the issuance of any such shares or warrants to purchase such shares to Variagenics on substantially similar terms as the terms on which Hyseq proposed to sell to a third party.

Each of the parties agreed that neither will, nor will they permit any of their respective subsidiaries to, take any action that would disqualify the merger as a reorganization within the meaning of Section 368(a) of the U.S. tax code.

No Solicitation

The merger agreement contains detailed provisions prohibiting Variagenics and Hyseq from seeking an alternative transaction. Under these no solicitation provisions, Variagenics and Hyseq, as well as their

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officers, directors, subsidiaries and representatives, have agreed that until the merger agreement is terminated, they will not:

solicit, initiate, encourage, knowingly facilitate or induce any inquiry with respect to, or the making, submission or announcement of, an acquisition proposal, as described below;

participate in discussions or negotiations or take any other action to facilitate inquiries or the making of a proposal that constitutes an acquisition proposal or would reasonably be expected to lead to an acquisition proposal;

furnish to any person any nonpublic information in connection with or in response to any acquisition proposal;

engage in discussions with respect to any acquisition proposal;

approve, endorse or recommend any acquisition proposal; or

enter into any letter of intent or similar document or any agreement, commitment or understanding contemplating or related to any acquisition proposal.

However, the merger agreement does not prevent Variagenics or Hyseq from entering into discussions, or furnishing confidential information in connection with receiving a superior proposal, as described below, or an acquisition proposal, if in connection with receiving such acquisition proposal, the board of directors concludes in good faith that the proposed consideration is more favorable to its stockholders than the transactions contemplated by the merger agreement and which could reasonably be expected to result in a superior proposal. Within three days after receiving such superior proposal or acquisition proposal, the party in receipt of such proposal must provide notice to the other party of the identity of the party making the acquisition proposal or superior proposal and the material terms and conditions of such proposal. The party receiving the notice may request that the other party negotiate in good faith for a period of not less than five business days to revise the merger agreement so that any such acquisition proposal or superior proposal no longer constitutes a superior proposal.

In response to the receipt of a superior proposal that has not been withdrawn and continues to constitute a superior proposal after negotiation described in the preceding paragraph, the board of directors of the party receiving the superior proposal may withhold or withdraw its recommendation that the stockholders of such company approve the matters to be voted on set forth in the merger agreement and, in the case of a superior proposal that is a tender or exchange offer made directly to its stockholders, recommend acceptance of such offer if:

that party's stockholder meeting has not occurred; and

the board of directors of such party concludes in good faith that, in light of such superior proposal, the failure of the board of directors to take such action would result in a breach of its fiduciary obligations.

An acquisition proposal means, with respect to Variagenics or Hyseq, any offer or proposal concerning any:

merger, consolidation, business combination or similar transaction in which the stockholders immediately prior to the proposed transaction would own less than 90% of any class of equity securities of the surviving entity;

merger, consolidation, business combination or similar transaction in which the individuals comprising the board of directors prior to such transaction would not constitute a majority of the board of directors of the surviving or resulting entity;

sale or other disposition of assets, in a single transaction or series of related transactions, representing 10% or more of its consolidated assets;

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issuance, sale or other disposition of securities to any person (other than Dr. Rathmann) or group representing 10% or more of its voting power; or

transaction in which any person (other than Dr. Rathmann) shall acquire beneficial ownership, or the right to acquire beneficial ownership or any group shall have been formed which beneficially owns or has the right to acquire beneficial ownership of, 10% or more of its outstanding voting capital stock.

A superior proposal means, with respect to Variagenics or Hyseq, any bona fide offer or proposal that:

either

concerns any merger, consolidation, business combination or similar transaction in which the stockholders immediately prior to such transaction would own less than 50% of the voting power of the surviving entity (or the ultimate parent entity); or

concerns any sale or other disposition directly or indirectly of assets representing 67% or more of its consolidated assets; or

concerns any merger, consolidation, business combination or similar transaction in which the stockholders immediately prior to such transaction would own less than 65% of the voting power of the surviving entity, and the individuals comprising the board of directors immediately prior to such transaction do not constitute a majority of the board of directors of the surviving entity (or the ultimate parent entity);

its board of directors in good faith concludes that the terms of the proposal are more favorable to its stockholders than the merger; and

is, in its good faith judgment, reasonably likely to be consummated.

Reasonable Best Efforts

Hyseq and Variagenics have agreed to use their reasonable best efforts to:

take all appropriate action and do all things necessary or advisable under applicable law or otherwise to consummate the transactions contemplated by the merger agreement as promptly as practicable; and

obtain all required governmental consents and approvals and make all necessary filings with respect to the merger under federal or state securities laws and other applicable laws.

Hyseq and Variagenics have agreed to give notices to third parties, and use their reasonable best efforts to obtain third party consents, including those necessary to consummate the transactions under the merger agreement or to prevent the occurrence of a material adverse effect.

Hyseq has agreed to use commercially reasonable efforts to:

obtain waivers from specified holders of warrants to purchase Hyseq common stock providing that the transactions under the merger agreement do not constitute a change in control under the warrants; and

obtain a similar waiver to a promissory note held by Affymetrix.

Nasdaq Quotation

Hyseq has agreed to use its reasonable best efforts to cause the shares of Hyseq common stock issuable in the merger, including the shares of Hyseq common stock reserved for issuance with respect to Variagenics stock options and warrants, to be approved for listing on the Nasdaq National Market.

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Employee Matters

With respect to each Hyseq benefit plan employees of Variagenics participate in after the merger, Hyseq will give Variagenics employees who remain employed by Hyseq after the merger full credit for time worked at Variagenics in terms of eligibility and vesting, including for severance benefits and vacation entitlement, such that service with Variagenics will be treated as if it were service with Hyseq. However, service credit will not be given where such crediting would result in a duplication of benefits or to the extent such service was not recognized under the applicable Variagenics benefit plan. Hyseq will waive limitations for pre-existing condition exclusions and waiting periods under any Hyseq welfare benefit plans to the same extent waived under the applicable Variagenics benefit plan. Continuing Variagenics employees will also be given credit for amounts paid under a corresponding benefit plan during the same period for purposes of applying deductibles, co-payments and out-of-pocket maximums.

At the request of Hyseq, Variagenics will terminate its 401(k) plan effective on the closing date of the merger.

Indemnification; Insurance

Hyseq has agreed to cause the surviving corporation to indemnify and hold harmless, and provide advancement of expenses to, all past and present directors, officers and employees of Variagenics for acts or omissions occurring at or prior to the effective time in their capacities as such pursuant to Variagenics' certificate of incorporation, by-laws, individual indemnity agreements or otherwise, and such obligations will continue in full force and effect from the effective time until the later of:

the expiration of the applicable statute of limitations with respect to any claims against the directors or officers arising out of such acts or omissions; or

in the case of any claims made prior to the expiration of the applicable statute of limitations, the final disposition of such claims.

In addition, for six years following the effective time of the merger, Hyseq will, or will cause the surviving corporation to, maintain in effect for the benefit of Variagenics' directors and officers currently covered by the officers' and directors' liability insurance policies of Variagenics an insurance and indemnification policy that provides coverage for acts or omissions occurring prior to the effective time of the merger on terms and in amounts no less favorable than those of the Variagenics' policies in effect as of the date of the merger agreement. The surviving corporation will not be required to pay an annual premium for the directors and officers insurance in excess of \$1,250,000, but if the annual premiums of such insurance coverage would exceed \$1,250,000, Hyseq will obtain a policy with the greatest coverage available for a cost not exceeding that amount.

Conditions to the Merger

The respective obligations of Hyseq, Vertical Merger Corp. and Variagenics to effect the merger are subject to the satisfaction or waiver of a number of customary conditions before completion of the merger, including:

the registration statement on Form S-4 covering the shares of Hyseq common stock to be issued in the merger, of which this joint proxy statement/prospectus is a part, shall have been declared effective and not the subject of any stop order or proceeding by the SEC seeking a stop order;

approval of the merger shall have been obtained by the stockholders of Variagenics and Hyseq;

no governmental entity, nor any federal or state court of competent jurisdiction shall have enacted, issued, promulgated, enforced or entered any statute, rule, regulation, executive order, decree, judgment or injunction or order which prevents or prohibits consummation of the merger;

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all consents, approvals and authorizations of any governmental entity required to consummate the merger, the failure of which to be obtained or taken, would have a material adverse effect, shall have been obtained; and

the shares of Hyseq common stock issuable to Variagenics stockholders in the merger and such other shares of Hyseq common stock to be reserved for issuance in connection with the merger shall have been approved for listing on the Nasdaq National Market.

Additional Conditions to Obligations of Hyseq

The obligation of each of Hyseq and Vertical Merger Corp. to complete the merger and the transactions contemplated thereby is subject to the satisfaction or waiver of each of the following additional conditions:

Variagenics representations and warranties will be true and correct (without giving effect to any materiality provision) at and as of the effective time of the merger as if made at and as of such time, except where the failure of such representations and warranties to be true and correct would not result in a material adverse effect;

Variagenics representation and warranty with respect to its balance of cash, cash equivalent, short-term and long-term investments as of October 31, 2002 shall be true and correct in all respects as of October 31, 2002;

Variagenics will have performed or complied in all material respects with all agreements and covenants required by the merger agreement prior to the effective time of the merger; and

Hyseq will have received the opinion of Latham & Watkins, dated as of the effective time of the merger, to the effect that on the basis of the facts, representations and assumptions set forth in such opinion, the Transaction will be treated for federal income tax purposes as a reorganization within the meaning of Section 368(a) of the U.S. tax code.

Additional Conditions to Obligations of Variagenics

The obligation of Variagenics to complete the merger and the transactions contemplated thereby is subject to the satisfaction or waiver of each of the following additional conditions:

Hyseq's representations and warranties will be true and correct (without giving effect to any materiality provision) at and as of the effective time of the merger as if made at and as of such time except where the failure of such representations and warranties to be true and correct would not result in a material adverse effect;

Hyseq will have performed or complied in all material respects with all agreements and covenants required by the merger agreement prior to the effective time of the merger;

Variagenics will have received the opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., dated as of the effective time of the merger, to the effect that on the basis of the facts, representations and assumptions set forth in such opinion, the Transaction will be treated for federal income tax purposes as a reorganization within the meaning of Section 368(a) of the U.S. tax code;

Hyseq will have caused its stockholder rights agreement to be amended so that neither Variagenics nor any of its affiliates or stockholders executing a voting agreement shall become an acquiring person, and no share acquisition date or distribution date (as such terms are defined in the stockholder rights agreement) will occur;

Hyseq will have caused its articles of incorporation to be amended to reflect a new name to be mutually agreed upon by Hyseq and Variagenics;

Hyseq will not have received an order from the FDA placing the Phase I studies of alfimeprase on clinical hold based on an alfimeprase-caused death(s); and

Hyseq's board of directors will have been determined by mutual consent of Hyseq and Variagenics.

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Termination of the Merger Agreement

The merger agreement may be terminated, at any time prior to the effective time, whether or not the Hyseq or Variagenics stockholders have approved the merger, by:

mutual written consent of Variagenics and Hyseq, which consent shall have been approved by action of their respective boards of directors;

by either Hyseq or Variagenics if the merger has not been completed by May 31, 2003, provided that such party's actions or failure to act has not caused or resulted in the failure of the merger to occur by May 31, 2003;

by either Hyseq or Variagenics if any governmental entity shall have issued an order, decree or ruling or taken any other action permanently restraining, enjoining or otherwise prohibiting the merger;

by either Hyseq or Variagenics upon twenty days prior notice of its intent to terminate the merger agreement so long as the terminating party is not in material breach of its representations, warranties, covenants or agreements under the merger agreement and the non-terminating party has breached any of its representations, warranties, covenants or agreements contained in the merger agreement and the breach would result in the failure to satisfy the closing conditions to the merger agreement, and cannot be cured prior to May 31, 2003;

by either Hyseq or Variagenics, if the board of directors of the other party shall have withdrawn or adversely modified or resolved to withdraw or adversely modify, its recommendation for the approval of the merger;

by either Hyseq or Variagenics, if the board of directors of the other party shall have approved or recommended, or resolved to approve or recommend, to its stockholders an acquisition proposal other than the merger;

by either Hyseq or Variagenics, at any time prior to the approval of its stockholders, upon five business days prior notice to the other party, if its board of directors shall have determined that an acquisition proposal received by it is a superior proposal; or

by either Hyseq or Variagenics, if either party shall not have obtained stockholder approval of the merger.

Termination Fees

Variagenics and Hyseq have each agreed that in the event a party terminates for breach of any representations, warranties, covenants or agreements contained in the merger agreement, the breaching party will pay the terminating party's merger expenses, up to a maximum of \$750,000.

Variagenics has agreed to pay Hyseq \$1,750,000, if:

Variagenics' board of directors terminates the merger agreement because it has determined that an acquisition proposal is a superior proposal;

Hyseq terminates the merger agreement because Variagenics has withdrawn or adversely modified or resolved to withdraw or adversely modify its recommendation to its stockholders to approve the merger, or has approved or recommended or resolved to approve or recommend another acquisition proposal;

Hyseq terminates the merger agreement because Variagenics breaches its covenants with respect to holding its stockholders meeting;

Hyseq or Variagenics terminates the merger agreement because Variagenics stockholders have failed to adopt the merger agreement and, at that time, an acquisition proposal between Variagenics and a third party has been announced and not withdrawn and a competing transaction, as described below,

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between Variagenics and a third party has been closed within twelve months after the termination of the merger agreement; or

Hyseq or Variagenics terminates the merger agreement because the merger has not closed by May 31, 2003 and, at that time:

an acquisition proposal between Variagenics and a third party has been announced and not withdrawn;

following the existence of such acquisition proposal and prior to such termination, Variagenics intentionally breached its covenants or agreements in any material respect, which breach materially contributed to the failure to close the merger by May 31, 2003; and

a competing transaction between Variagenics and a third party has been closed within twelve months after the termination of the merger agreement.

Hyseq has agreed to pay Variagenics \$1,750,000, if:

Hyseq's board of directors terminates the merger agreement because it has determined that an acquisition proposal is a superior proposal;

Variagenics terminates the merger agreement because Hyseq has withdrawn or adversely modified or resolved to withdraw or adversely modify its recommendation to its stockholders to approve the merger, or has approved or recommended or resolved to approve or recommend another acquisition proposal;

Variagenics terminates the merger agreement because Hyseq breaches its covenants with respect to holding its stockholders meeting;

Hyseq or Variagenics terminates the merger agreement because Hyseq stockholders have failed to adopt the merger agreement and, at that time, an acquisition proposal between Hyseq and a third party has been announced and not withdrawn and a competing transaction between Hyseq and a third party has been closed within twelve months after the termination of the merger agreement; or

Hyseq or Variagenics terminates the merger agreement because the merger has not closed by May 31, 2003 and, at that time:

an acquisition proposal between Variagenics and a third party has been announced and not withdrawn;

following the existence of such acquisition proposal and prior to such termination, Hyseq intentionally breached its covenants or agreements in any material respect, which breach materially contributed to the failure to close the merger by May 31, 2003; and

a competing transaction between Hyseq and a third party has been closed within twelve months after the termination of the merger agreement.

A competing transaction means, with respect to Variagenics and Hyseq:

any merger consolidation business combination or similar transaction in which its stockholders immediately prior to the transaction would own less than 70% of any class of equity securities of the surviving or resulting entity (or the ultimate parent entity);

any merger consolidation business combination or similar transaction in which the individuals comprising the board of directors prior to such transaction would not constitute a majority of the board of directors of the surviving or resulting entity (or the ultimate parent entity);

the sale or other disposition of assets, in a single transaction or series of related transactions, representing 50% or more of its consolidated assets;

the issuance, sale or other disposition of securities to any person (other than Dr. Rathmann) or group representing 30% or more of its voting power; or

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any transaction in which any person (other than Dr. Rathmann) acquires beneficial ownership or the right to acquire beneficial ownership or any group shall have been formed which beneficially owns or has the right to acquire beneficial ownership of 30% or more of its outstanding voting capital stock.

Expenses

All fees and expenses incurred in connection with the merger agreement will be paid by the party incurring those fees and expenses, whether or not the merger is completed. However, the parties will each pay one-half of the expenses related to printing, filing and mailing this joint proxy statement/prospectus and all SEC and other regulatory filing fees incurred in connection with this joint proxy statement/prospectus.

Amendment; Waiver

Amendment

The merger agreement may be amended by the mutual written agreement of Variagenics and Hyseq at any time prior to the effective time of the merger.

Waiver

At any time prior to the effective time of the merger, Hyseq or Variagenics may, in writing:

extend the time for the performance of any of the obligations or other acts of the other party;

waive any inaccuracies in the representations and warranties contained in the merger agreement or in any document delivered pursuant to the merger agreement as to the other party; and

waive compliance with any of the agreements or conditions contained in the merger agreement as to the other party.

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STOCKHOLDER VOTING AGREEMENTS

The following summary describes certain material provisions of the stockholder voting agreements, the forms of which are attached to this joint proxy statement/prospectus as Annex B and are incorporated by reference into this joint proxy statement/prospectus. This summary may not contain all of the information about the stockholder voting agreements that is important to you. Hyseq and Variagenics encourage you to read the stockholder voting agreements carefully in their entirety.

As an inducement to each party to enter into the merger agreement and in connection with the execution and delivery of the merger agreement, (i) directors and officers of Variagenics and selected affiliates of those directors and current executive officers who beneficially own and are entitled to vote an aggregate of 3,515,143 shares of Variagenics common stock or approximately 14.6% of the outstanding Variagenics common stock as of the record date and (ii) all of Hyseq's directors and officers who hold and are entitled to vote an aggregate of 3,621,573 shares of Hyseq common stock or approximately 15.7% of the outstanding Hyseq common stock as of the record date each entered into a stockholder agreement.

Pursuant to the terms of the stockholder agreements, each stockholder who signed a stockholder agreement has agreed to vote (i) in the case of the Variagenics stockholders, in favor of the adoption and approval of the merger agreement, and in the case of the Hyseq stockholders, in favor of approval of the issuance of Hyseq common stock in connection with the merger, (ii) against any action or agreement that could compete with, prevent, impede, interfere with, attempt to discourage or adversely affect the merger or inhibit the timely consummation of the merger, (iii) against any action or agreement that would result in any material breach of any covenant, representation or warranty or any other obligation under the merger agreement of the company in which the stockholder holds common stock and (iv) except for the merger agreement, against any merger, consolidation, business combination, reorganization, recapitalization, liquidation or sale or transfer of any material assets of the company in which the stockholder holds common stock.

The stockholder agreements terminate upon the earliest to occur of (i) the effective time of the merger, (ii) the date of termination of the merger agreement if the merger agreement is terminated (A) by mutual agreement, (B) by either party if a governmental entity issues a final and nonappealable order prohibiting the merger or (C) by either party if either party fails to obtain the stockholder approvals required by the merger agreement and (iii) the later of May 9, 2003 and all other events triggering a termination right set forth in the merger agreement. See The Merger Agreement Termination of the Merger Agreement.

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UNAUDITED PRO FORMA CONDENSED COMBINING FINANCIAL STATEMENTS

The following unaudited pro forma condensed combining financial statements have been prepared to give effect to the proposed merger of Hyseq and Variagenics using the purchase method of accounting and the assumptions and adjustments described in the accompanying notes to unaudited pro forma condensed combining financial statements.

The determination of accounting acquirer in a business combination in accordance with Statement of Financial Accounting Standards No. 141 requires consideration of multiple factors, including voting rights, any significant minority voting rights, governance and senior management of the combined enterprise, as well as any premium that was paid. Given the composition of the board of directors and senior management of the combined company, as well as the premium paid by Hyseq, Hyseq was determined to be the accounting acquirer.

The unaudited pro forma condensed combining balance sheet gives effect to the merger of Hyseq and Variagenics as if it had occurred on September 30, 2002. The unaudited pro forma condensed combining statements of operations give effect to the proposed merger of Hyseq and Variagenics as if it had occurred on January 1, 2001 and January 1, 2002, respectively. The pro forma information is based upon the historical consolidated financial statements of Hyseq and the historical consolidated financial statements of Variagenics and the assumptions, estimates and adjustments described in the notes to the unaudited pro forma condensed combining financial statements. The assumptions, estimates and adjustments are preliminary and have been made solely for purposes of developing such pro forma information.

Under the purchase method of accounting, the aggregate consideration paid is allocated to the tangible and identifiable intangible assets acquired and liabilities assumed on the basis of their fair values on the transaction date. As of September 30, 2002, the fair value of the net assets acquired exceeds the estimated purchase price. As a result, the estimated fair values of certain long-lived assets were reduced to zero for purchase accounting purposes. After this reduction in values, and in accordance with Statement of Financial Accounting Standards No. 141 (or SFAS No. 141), Business Combinations, estimated remaining negative goodwill of approximately \$4.2 million would be recorded as an extraordinary gain in Hyseq's statement of operations upon consummation of the merger. However, given Variagenics' historical consumption of its working capital, the estimated negative goodwill of approximately \$4.2 million may be substantially reduced, eliminated or become positive goodwill upon completion of the final purchase price allocation. The extraordinary gain has been excluded from the pro forma condensed combining statements of operations due to its non-recurring nature.

The unaudited pro forma condensed combining financial statements are presented for illustrative purposes only and are not necessarily indicative of the consolidated financial position or consolidated results of operations that would have been reported had the merger occurred on the date indicated, nor do they represent a forecast of the consolidated financial position at any future date or the consolidated results of operations for any future period. Furthermore, no effect has been given in the unaudited pro forma condensed combining statements of operations for synergistic benefits that may be realized through the combination of the two companies or costs that may be incurred in integrating their operations. The unaudited pro forma condensed combining financial statements should be read in conjunction with the historical consolidated financial statements, including the notes thereto, and management's discussion and analysis of financial condition and results of operations of Hyseq and Variagenics covering those periods incorporated by reference into this joint proxy statement/prospectus.

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September 30, 2002**

(In thousands, except per share data)

(unaudited)

Nine Months Ended September 30, 2002

	Historical		Pro Forma	
	Hyseq	Variagenics	Adjustments	Combined
Revenues:				
Product sales	\$	\$ 450	\$	\$ 450
Contract revenues and other	22,915	592		23,507
Total revenues	22,915	1,042		23,957
Operating expenses:				
Cost of product sales		236		236
Research and development	40,885	16,792	(1,376)(E)	56,301
General and administrative	9,102	9,187	(136)(E)	18,153
Restructuring and related charges	610	1,974		2,584
Total operating expenses	50,597	28,189	(1,512)	77,274
Loss from operations	(27,682)	(27,147)	1,512	(53,317)
Interest income	70	1,206		1,276
Interest expense	(934)	(259)		(1,193)
Gain (loss) on sale of fixed assets	(34)			(34)